Critical Decisions in Urology

Third Edition
Notice: The authors and publisher have made every effort to ensure that the patient care recommended herein, including choice of drugs and drug dosages, is in accord with the accepted standard and practice at the time of publication. However, since research and regulation constantly change clinical standards, the reader is urged to check the product information sheet included in the package of each drug, which includes recommended doses, warnings, and contraindications. This is particularly important with new or infrequently used drugs. Any treatment regimen, particularly one involving medication, involves inherent risk that must be weighed on a case-by-case basis against the benefits anticipated. The reader is cautioned that the purpose of this book is to inform and enlighten; the information contained herein is not intended as, and should not be employed as, a substitute for individual diagnosis and treatment.
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Preface

Physicians make decisions on a daily basis. Some are relatively simple and respond to a common problem, but others are complex and are based on multiple inputs, including a patient’s symptoms, laboratory studies, and, often-times imaging data. The conclusion of the decision-making process often leads to an avenue of therapy, whether it be observational, pharmacologic, or surgical. Frequently, multiple options are available, and factors such as patient age and expectation often influence this process.

Algorithms, or decision trees, are a technique by which specific clinical problems can be approached in a logical and organized manner. The algorithms presented in Critical Decisions in Urology are up-to-date approaches by experts in the field. Authors have presented their personal approach but have attempted to be encompassing of others’ thoughts as well. The purpose of the algorithm is to present the reader with a practical guide that will assist in evaluating and managing clinical urologic problems. The decision-making process that is presented is not meant to be dogmatic, but rather a usable method that has been successful in the author’s experience.

Importantly, remember that the most significant aspect of the algorithm lies not in the detail but rather in the process. One reader may follow the algorithm as stated, which in itself requires a decision, whereas another may disagree with the specific approach and decide to follow another course; this, too, requires a decision. The importance of the algorithm lies in its interpretation and its influence on clinical decisions. If by reading and by reviewing an algorithm, a clinician is better able to develop a specific plan of action, then we have achieved our goal.

Many have contributed to this text. All authors are experts in their field, and their efforts and thoughts are greatly appreciated by the editors. We also appreciate the effort of the staff at BC Decker Inc, particularly Ms. Paula Presutti and Montgomery Kersell. Without her input and his perseverance, this book would not have become a reality.

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October 2003
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Introduction

Algorithms, or decision trees, are commonly employed tools in business, and we all recognize that they have applications in medicine. This text is an effort to portray diagrammatically a decision-making process in urology. Each chapter is presented as an algorithm with appropriate text, and the topics vary based on a patient’s symptoms, signs, or specific disease. Important information includes patient history, physical findings, and laboratory evaluations. Therapeutic approaches are based on the authors’ experience and the interpretation of the available data.

Each algorithm can be used independently, but there are crossovers and references to others. We hope that this text will serve as a handy reference to individuals presented with both specific and broad problems that relate to the practice of urology.
The evaluation of the urologic patient requires a thorough history that relates to both the general health of the patient and the specific urologic complaints. A complete physical examination is also required. Based on these initial steps, appropriate laboratory tests should be conducted and correlated with appropriate diagnostic imaging. In most instances, assessing these data permits the physician to arrive at a proper diagnosis and to institute appropriate therapy.

The History
To obtain the history, the physician must be an interested listener who asks specific questions to further elucidate the problem. Many patients present with complaints related to pain, and it is important to characterize the pain so that its site of origin can be established. For example, renal pain characteristically results in aching in the flank or in the region of the costovertebral angle, or both, and is usually caused by distention of the renal capsule, as in acute polynephritis and acute renal ureteral obstruction. On the other hand, ureteral pain is commonly associated with the passage of stones or blood clots and tends to be localized to the flank, is colicky in nature, and, if the lower ureter is involved, tends to be localized to the lower quadrant. Children usually do not develop localizing symptoms and often present with generalized abdominal pain, nausea, and vomiting in association with acute renal or ureteral obstruction. Bladder and prostate pain are often associated with increased bladder irritability, manifested by urinary frequency, dysuria, and urinary urgency. Penile or scrotal pain is usually continuous and localized to the penis or scrotum; however, patients with acute torsion or acute testicular pain may have associated nausea and vomiting.

Another complaint of urologic patients relates to abnormalities of voiding. The act of micturition is complex; often, acute problems are readily apparent to the patient, and prompt evaluation is required. It is also important to remember that severe abnormalities can yield subtle changes that develop over a prolonged period of time. Whether the underlying disorders are inflammatory, neoplastic, neurogenic, or obstructive in nature, the symptoms of voiding dysfunction are often similar. Patients complain of urinary frequency or urgency, dysuria, hesitancy, nocturia, and enuresis. Polyuria, pneumaturia, and hematuria require careful documentation and further evaluation. When evaluating patients with hematuria, establish whether the pain and the irritative symptoms coexist and whether the hematuria is total, initial, or terminal in character.

Rarely, a patient discovers, or is discovered to have, an abdominal mass. This mode of presentation is more common in infants and young children and is usually symptomatic of a hydronephrotic or dysplastic kidney or tumor of the kidney or the adrenal gland. Patients with renal tumors may palpate the mass in the upper quadrant or may describe a sense of fullness on that side. The patient should be carefully questioned about concomitant hematuria, weight loss, and, in males, the presence of acute varicocele. Patients in chronic urinary retention may palpate a midline or a nontender mass in the suprapubic region.

Nonspecific genitourinary complaints may be related to sexual dysfunction. The patient should specifically describe the nature of the problem; the onset and frequency of the problem, as well as the patient’s partners, are key points in the evaluation. Most frequently, men complain of absent or diminished erectile potency, premature ejaculation, decreased libido, or retrograde ejaculation. The clinician should assess carefully for diabetes mellitus, vascular disease, and the use of antihypertensive medications, all of which may alter sexual function.

Physical Examination
When evaluating a specific urology problem, clinicians usually limit their evaluation to the genitourinary tract; however, patients with systemic localized disease may require general anesthesia and surgery and therefore should always have a complete evaluation.

Palpate the abdomen to detect enlargement of the kidneys and the presence of renal or other abdominal masses. Further, the bladder should be palpated and percussed to detect any distention. Inspecting and palpating the external genitalia usually reveal any pathologic processes that affect these structures. In males, the examination should be performed in both the supine and upright positions; in females, the dorsal lithotomy position is the most suitable. Carefully examine the skin and hair for inflammatory lesions, parasites, and dermatitis secondary to long-standing urinary incontinence. Note the pattern of hair distribution. In the uncircumcised male, the foreskin should be completely retracted to detect the presence of phimosis, inflammation, or tumor. Thoroughly inspect the glans, and note the position of the urethral meatus. This is particularly important when evaluating children with hypospadias and/or chordee.

The scrotum comprises several layers, including the skin, the dartos muscle, and the cremasteric muscle. Few
pathologic processes affect the scrotum. In cases of true cryptorchidism, the ipsilateral scrotum is usually underdeveloped. If the scrotum is enlarged, one should first differentiate an inguinal hernia from those structures normally present in the scrotum. All intrascrotal masses should be transilluminated to differentiate fluid-filled from solid structures. If no testicle is present in the scrotum, the clinician should carefully palpate the inguinal canal, the external ring, and the base of the penis for the missing organ. In small children with active cremasteric muscles, it is often difficult to differentiate a retractile testicle from true cryptorchidism. By having the child squat, usually the retractile testicle will be forced into the scrotum where it can be readily palpated.

In females, a complete gynecologic examination should be performed because of the intimate association between the female reproductive organs and the urinary tract. Examine the labia majora for evidence of Bartholin cysts. The patient should perform a Valsalva maneuver to determine the extent of a cystocele or the presence of a rectocele. If the patient has complained of stress urinary incontinence, the bladder should be filled and the patient asked to cough or strain to reproduce the incontinence.

A carefully performed rectal examination is mandatory. The examination can be performed with the patient in bed in the lateral or knee–chest position but most often is performed in the office examining room with the patient bending over the table. The clinician should inspect the anus and assess the tone of the rectal sphincter. This is particularly important in patients with suspected neurogenic bladder dysfunction. Prior to examining the prostate, palpate the rectal wall to detect the presence of intrinsic tumors. Examine the prostate, noting its size and consistency, and palpate the median furrow and lateral margins. Induration or firmness suggests early prostatic carcinoma, whereas a hard gland strongly suggests advanced disease. The gland may feel soft owing to secondary-to-acute inflammation or infection. Pulpation or prostatic calculi may produce crepitation; the presence of prostatic calculi should be confirmed with plain radiographs. There is a distinct interface between a nodule and the surrounding prostatic tissue in nodular hyperplasia; the carcinomatous nodule tends to blend into the surrounding tissue.

**Laboratory Evaluation**

Many laboratory studies are available for evaluation of the urologic patient, and these are evolving as methodology improves. Physicians are increasingly aware of the need to use laboratory studies in a cost-effective manner, selecting only those studies that they believe are pertinent. On admission to the hospital, most patients routinely receive a complete blood count, serum chemistry survey, and urinalysis. This broad screening approach provides the physician with a superficial metabolic and chemical survey of each patient. Many urologic patients are elderly and tend to have multiple medical problems, some of which have not been recognized. The admission laboratory screening data facilitate such recognition.

Determination of renal function plays an important role in the clinical management of many urologic patients, and several laboratory studies, including serum creatinine and blood urea and nitrogen, are available. Urinalysis is essential in evaluating all urologic patients, along with a thorough qualitative chemical analysis of proteinuria and glycosuria and a specific examination of the sediment to assess for the presence of casts, blood cells, and bacteria. More specific functional studies can be performed if required. Urine culture and sensitivity tests are important when urinary tract infection is suspected. More specific studies such as three-glass urinalysis may be helpful in diagnosis. Other specific laboratory tests such as tumor markers (prostate-specific antigen, α-fetoprotein, and β-human chorionic gonadotropin) and specific urine and serum chemistries can be obtained, depending on the specific problems of the patient.

**Diagnostic and Imaging Studies**

Cystoscopy and ureteroscopy are endoscopic procedures that are essential to evaluating the urologic patient. Direct imaging of the urinary tract is not only essential diagnostically but also often serves a therapeutic role. Cystoscopy is also key when assessing patients with voiding dysfunctions; in fact, treatment is often based on the data obtained. Studies employed to evaluate erectile dysfunction are as follows: Doppler studies to measure penile blood flow, cavernosometry to measure corporal function, and imaging studies (pelvic angiography, cavernosography) to assess both arterial supply and venous drainage.

The development of new imaging studies has greatly enhanced the diagnostic capabilities of the urologist. Plain radiographs and intravenous urography have been used for many years and continue to serve well in assessing a wide range of problems. The knowledge gained not only provides anatomic information related to the urinary tract but also often provides information related to the functional capabilities of these structures. Ultrasonography provides valuable anatomic information. This technique is often used to assess kidney size and to exclude the presence of hydronephrosis in patients for whom contrast agents are avoided because of allergy or impairment of renal function. In addition, ultrasonography is also used to assess patients with chronic renal disease or congenital abnormalities of the urinary tract and those who require ongoing careful monitoring. Repeated use of ultrasonography reduces the exposure of these patients to unnecessary irradiation. Other useful applications include bladder ultrasonography to determine residual urine, and scrotal ultrasonography is being used with increasing frequency and has various applications, specifically, to assess prostate size and assist in biopsy. Computed tomographic studies
provide finely detailed anatomic information, which has proved invaluable in assessing the urologic patient. Retrograde studies, cystography, and urethrography are used for the evaluation of specific disorders. Using cystography to detect the presence of vesicoureteral reflux is almost routine in children with recurrent urinary tract infections; urethrography is essential when stricture disease is suspected. Physicians order these more specific studies to confirm or establish a specific diagnosis. Other techniques such as positron emission tomography (PET) scanning and magnetic resonance imaging (MRI) also provide useful anatomic information.

Radionuclide studies are helpful in assessing the functional capabilities of the urinary tract, in particular, the ability of the kidneys to concentrate urine and to drain. Computer programs, which are both reliable and reproducible, allow for assessing differential renal function. Bone scans help to assess the presence of metastatic disease, namely, in patients with carcinoma of the prostate. Finally, testicular imaging is particularly useful in the pediatric patient who presents with an “acute scrotum.” Testicular imaging differentiates the torsed testicle from the acute epididymis and likely should be performed when the diagnosis is in doubt.

In summary, to evaluate the urologic patient, the clinician should begin with a careful history and a physical examination, followed by appropriate laboratory, diagnostic, and imaging studies. This process will establish the proper diagnosis so that appropriate therapy can be instituted.
SECTION 1

EVALUATION BY COMPLAINT OR LABORATORY FINDING
Hematuria can be associated with multiple medical and surgical problems, ranging from minor incidental findings to urologic neoplasm. The finding of blood in the urine prompts the need for a more thorough evaluation. Blood in the urine can originate from any site along the urinary tract. Gross blood or clots in the urine generally prompt a patient to seek medical attention, and painless gross hematuria requires a complete urologic work-up: urinalysis, culture, cytology, upper tract imaging, and cystoscopy. Patients with gross hematuria have about five times the number of life-threatening conditions when compared with patients with microscopic hematuria. Evaluating microscopic hematuria is more controversial. Evaluations of microscopic hematuria have resulted in the discovery of significant disease in 3.4 to 56% of individuals and in the discovery of malignancy in 0 to 26% of individuals. These wide ranges reflect differences in age and sex of patient populations. Hematuria is a sign of potentially life-threatening disease and deserves evaluation.

**A** Evaluation begins with a complete urologic history and physical examination. In addition, a serum creatinine should be drawn on those referred for hematuria. Frequency, urgency, dysuria, urethral discharge, and suprapubic or perineal pain suggests an inflammatory or infectious process. The clinician should look for a family history of stones, renal disease, or sickle cell anemia. Patients may give a history of recent trauma, vigorous exercise, sexual activity, or menstruation, suggesting a benign etiology. Glomerulonephritis is generally preceded by a recent upper respiratory tract infection associated with acute onset of hypertension and edema. Several medications may induce a chemical cystitis, papillary necrosis, or allergic nephritis and hematuria. A description of accompanying pain may help to localize the bleeding site. Consider total painless gross hematuria to be of neoplastic origin until proven otherwise. Blood that appears at the onset of micturition and then clears frequently originates from the prostate, seminal vesicles, or urethra. Blood originating from the bladder trigone, vesicle neck, or posterior urethra appears at the end of urination. Hematuria throughout urination suggests vesical, ureteral, or renal pathology. Patients with risk factors for significant disease should be identified and treated as high risk. These risk factors include a smoking history, an occupational exposure to chemicals or dyes (benzenes or aromatic amines), a history of gross hematuria, age ≥ 40 years, a previous urologic history, a history of irritative voiding symptoms, a history of urinary tract infection, a history of analgesic abuse, and a history of pelvic irradiation or cyclophosphamide usage.

**B** When hematuria is suspected, one must perform a urinalysis on a clean-catch, midstream, fresh urine specimen. Patients should avoid strenuous exercise or instrumentation for at least 48 hours prior to giving a sample. In addition, trauma, sexual activity, menstruation, and viral illness may result in positive results. Repeat urinalysis should be performed, and, if normal, additional evaluation is not necessary. In females, the labia should be separated and, in uncircumcised males, the foreskin retracted to avoid contamination. If there is evidence of contamination, a new specimen should be obtained and consideration given to a catheterized specimen. When dipstick is positive for blood, a microscopic evaluation for blood cells must be performed. Various studies have reported that between 13 and 21% of healthy individuals have some degree of hematuria. In 1926, Addis reported microscopic examination of overnight urine specimens from presumably healthy medical students and found red blood cells in 40 of 60 specimens. The 95 to 98% confidence limits for hematuria in a healthy population are reported as under 3 red blood cells per high-power field (RBC/HPF). The recommended definition of microscopic hematuria is ≥ 3 RBC/HPF on microscopic evaluation of the urinary sediment from two of three properly collected urinalysis specimens. Risk factors for significant urologic disease must be considered when deciding whether or not to evaluate those with < 3 RBC/HPF.
Patient with SUSPECTED HEMATURIA

A
History
Physical examination

B
Urinalysis

< 3 RBC/HPF
Evaluate if clinically suspicious

C
Urinary tract infection
Treat with Antibiotics

D
Proteinuria
Red cell casts
Dysmorphic red blood cells
Renal insufficiency
Renal consult

E
High risk
Cytology, cystoscopy, and upper tract evaluation

F
Low risk
Cytology, or cystoscopy, and upper tract evaluation

G
Abnormal cytology
Abnormality
Indicated surgical procedure

Normal
Cystoscopy

Negative
Blood

Positive
Urinalysis
Treat with Antibiotics

Normal
C In a prospective study by Khadra and colleagues, 13% of 1,930 patients evaluated for microscopic and macroscopic hematuria with a mean age of 58.3 years were found to have urinary tract infections. Those found to have urinary tract infections should undergo treatment with appropriate antibiotics and then undergo repeat urinalysis. Further evaluation is required for all men and some women to rule out anatomic abnormality that may have led to infection. If repeat urinalysis after treatment continues to have \( \geq 3 \text{ RBC/HPF} \) without evidence of infection, then work-up should continue.

D Hematuria in the presence of proteinuria or red cell casts suggests glomerular disease and warrants renal consultation. A total protein excretion of \( > 1 \text{ g/24 h} \) would be unlikely without parenchymal disease or gross hematuria. Further, the presence of a high proportion of dysmorphic red blood cells or renal insufficiency should prompt further medical evaluation.

E All patients who have been previously defined as “high risk” need to undergo cystoscopy and cytologic evaluation. Cytology can be obtained from a voided specimen or from a bladder wash at the time of cystoscopy. For low-risk patients—those who are asymptomatic and without risk factors for transitional cell carcinoma—urine cytology or cystoscopy may be performed. Cystoscopy is required for all those with positive or atypical or suspicious cytology. Cystoscopy in low-risk patients has very low yield \((< 1\%)\). Currently, there are insufficient data to recommend the routine use of voided urinary markers.

F Upper urinary tract imaging is essential for full evaluation of the renal parenchyma and pelvicaliceal system. Evaluation may consist of an intravenous urography (IVU), ultrasonography (US), computed tomography (CT) scan, or magnetic resonance imaging (MRI). In patients with normal renal function and without contraindication to contrast dye, IVU or CT urography should be considered as the initial imaging modality. If IVU is performed, physicians should be aware of its limited sensitivity in detecting small renal masses. If CT is performed, a noncontrast scan should be performed, first, followed by contrast films and a KUB or CT scout topogram in those who are high risk or without evidence of stones. US can be performed with or without retrograde studies in those with contrast allergies or poor renal function.

G Patients who have a complete urologic evaluation without pathologic findings should be closely monitored over the next 3 years. Consider repeating urinalysis, cytology, and blood pressure at 6, 12, 24, and 36 months. Further, clinical judgment must be used to determine if a complete evaluation should be repeated.
References
The etiology of abdominal masses in children varies with age. The majority of abdominal masses in the newborn are genitourinary in origin. In older children, however, a greater percentage of nonurologic causes (eg, hepatosplenomegaly owing to leukemia, lymphoma) becomes apparent.

**A** An abdominal sonogram is the initial examination of choice in evaluating abdominal masses. Ultrasonography demonstrates both the location and the density of the mass. Usually the mass can be localized into one of four areas: retroperitoneum, anterior abdomen, liver, or pelvis. Ultrasonography will identify the mass as predominantly cystic, solid, or of a mixed pattern.

**B** Most retroperitoneal masses are renal in origin, followed by adrenal and then miscellaneous causes. Those lesions identified as cystic by ultrasonography should be evaluated by computed tomography (CT) scan or magnetic resonance imaging (MRI) and, when indicated, by voiding cystourethrogram (VCUG). Benign renal masses constitute over 75% of retroperitoneal masses in infants under 1 month of age. Solid masses are usually mesoblastic nephroma or neuroblastoma. However, these are much less common than cystic masses. In children greater than 1 year of age, solid retroperitoneal masses are much more common.

**C** “Cystic” lesions of the urinary tract include hydronephrosis (ureteropelvic junction [UPJ] obstruction, posterior urethral valves, multicystic kidney), polycystic kidney, duplication anomalies, and vesicoureteral reflux. Obstruction should be evaluated further with a diuretic renogram.

**D** Anterior abdominal masses are primarily gastrointestinal in origin. An upper gastrointestinal (UGI) series and/or barium enema may be used as an initial evaluation following ultrasonography. In older children, splenomegaly may be the etiology secondary to leukemia, mononucleosis, or lymphoma.

**E** Most pelvic masses in the infant are of genital tract or bladder origin. Extrarectal pelvic masses may cause secondary hydronephrosis as well. A careful rectal examination with the bladder decompressed is essential to diagnosis.

**Additional Readings**

Abdominal Masses in Children

Child with ABDOMINAL MASS

History
Physical examination

A Ultrasonography

B Retroperitoneum

CT, MRI

Adrenal

Cystic

Solid

Mixed pattern

Adrenal hemorrhage (calcification)

Cystic

Neuroblastoma

Functional

Nonfunctional

Nuclear scan

Ureteropelvic junction obstruction

Multicystic kidney

Renal

Solid

Other

Neuroblastoma

Nephroma

Wilms’ tumor

Infantile polycystic kidney (recessive form)

Lymphoma

Abscess

Sarcoma

Pancreas

Teratoma

D Anterior abdomen

GI tract

Spleen

UGI series
Barium enema

Duplication
Mesenteric cysts
Intestinal atresia

Liver

CT scan or MRI

Solid

Cystic

Hepatoblastoma
Hemangioma
Hepatomegaly

Pregnancy

Solid

CT scan or MRI

Bladder

Hydrometrocolpos
Ovarian cyst

E Pelvis

Cystic

Lymphoma

Neuroblastoma
Rhabdomyosarcoma
Anterior meningomyelocele
Sacral teratoma
Ovarian lesion
Today, in most instances, renal masses are detected either by ultrasonography (US) or by computed tomography (CT), performed for an unrelated reason. Although many patients present with either pain or hematuria, in approximately one-half of individuals, the imaging study is carried out for evaluation of pain or nonspecific symptoms that the patient may be experiencing. The renal masses found in this setting are termed “incidental” and tend to be smaller and of lower grade than those found in the symptomatic patient. Most renal masses prove to be simple renal cysts, but renal tumors must be excluded. Treatment is often clearly indicated by imaging and laboratory studies.

A First, the clinician should perform a thorough physical examination. If a large mass is present, it is typically readily palpable. Laboratory studies are beneficial, and microscopic hematuria may be detected.

B Ultrasonography: If a renal mass is detected by intravenous urography (IVU), US also helps in differentiating a cystic lesion from a solid one. This study could also benefit patients who have had a mass detected by CT. True cysts do not require further study, but solid or indeterminate masses require CT imaging, if not previously performed. Angiomyolipoma are highly echogenic, owing to their high fat content, and, again, magnetic resonance imaging (MRI) and CT are excellent imaging studies to confirm this diagnosis. Renal malignancies are solid and heterogenous and often have indistinct borders, compared with a simple benign renal cyst.

C CT is being used with increasing frequency. Usually, the mass is initially detected with this study. The study may also be carried out following IVU or US. As with US, truly cystic masses that are seen on CT require no further evaluation; solid masses are most commonly malignant tumors and should be considered surgical lesions. Further evaluation of the indeterminate mass is required, but, generally, surgical exploration is required to establish a true diagnosis.

D The role of biopsy in assessing an indeterminate mass remains controversial. Although core or aspiration biopsies are relatively safe, the study benefits only if a positive diagnosis is established. If blood or fibrous tissue is identified, one cannot necessarily rule out the presence of a renal malignancy. This is the problem with a biopsy; in other words, it is helpful only if it is positive. Biopsies of renal masses have not been shown to be associated with tumor seeding along the punctured tract, have not shown an increase in the rate of metastases, or have not been shown to influence a patient’s survival. Aspirated cells can by studied cytologically. Helpful biochemical studies of aspirated fluid include cholesterol and lactate dehydrogenase (LDH); however, generally, these have not been definitive. Because of the reliability of US and CT, routine puncture is not required for patients with simple cystic disease or in patients with a defined solid renal mass that suggests malignancy.

E MRI or venacavography are valued in assessing tumor thrombus involving the renal vein or vena cava. CT scan and US often raise suspicion of the presence of this involvement; MRI and inferior venacavography are more definitive. These studies provide information about the extent of the thrombus and the degree of involvement, particularly within the vena cava.

F Angiography can reveal abnormal vascular patterns associated with small renal malignancies that are not detectable by other diagnostic modalities. About 10% of renal malignancies are avascular; therefore, continued observation is required for patients whose studies do not establish a diagnosis of malignancy. In the past, angiography was performed in association with partial nephrectomy and radical nephrectomy, whereas today it is unnecessary and has only limited application in those patients with exceedingly large tumors. Prior to partial or radical nephrectomy for renal cell carcinoma, evaluate the patient for metastatic disease. Similarly, ensure adequate function of the contralateral kidney. Although many urologists desire the anatomic information obtained by renal arteriography, today most exclude arteriography completely and reserve the procedure for patients with exceedingly large tumors. Angioinfarction can be performed at the time of an angiographic study, but typically this is reserved for those with large masses with potential difficulty intraoperatively of gaining control of the renal hilum and associated pedicle.

G The size and extent of the tumor thrombus, either in the renal vein or vena cava, can often dictate the type of surgical procedure. The surgeon uses a simple cavotomy to remove small thrombi below the hepatic veins. If the thrombus is above the diaphragm or extends to the right atrium, cardiopulmonary bypass is usually required. Experience with exsanguination and hypothermia has also been shown to be effective.

Additional Readings


Acute Scrotal Swelling in Children
Jack S. Elder, MD, FACS, FAAP

A Scrotal swelling may be acute or chronic, painful or painless. Abrupt onset of painful scrotal swelling necessitates prompt evaluation as some conditions, such as testicular torsion and incarcerated inguinal hernia, require emergency surgical management. The differential diagnosis is shown in Tables 5-1 and 5-2.

A detailed history is helpful in determining the cause of the swelling and includes (1) onset of pain—with testicular torsion the pain often is sudden in onset and may be associated with exercise or minor genital trauma; (2) duration of pain; (3) radiation of pain—inguinal discomfort is common with an inguinal hernia or epididymitis, and associated flank pain may occur with passage of a ureteral calculus; (4) previous episodes of similar pain, which are common in boys with intermittent testicular torsion or inguinal hernia; (5) nausea and vomiting, which are associated with testicular torsion and inguinal hernia; and (6) irritative urinary symptoms (dysuria, urgency, and frequency) indicative of a urinary tract infection, which can cause epididymitis. Boys with lower urinary tract pathology may be prone to epididymitis.

Physical examination in boys with a painful scrotum may be difficult. Some clinicians have advocated performing a spermatic cord block or administering intravenous analgesia to facilitate the examination, but such measures are usually unnecessary. Scrotal wall erythema is common in testicular torsion, epididymitis, torsion of the appendix testis, and an incarcerated hernia. In boys with a normal cremasteric reflex, testicular torsion is unlikely. Absence of a cremasteric reflex, however, is nondiagnostic.

Pertinent laboratory studies include a urinalysis and culture. A positive urinalysis is suggestive of epididymitis. Serum studies generally are not helpful in establishing a diagnosis unless a testis tumor is suspected. Following initial evaluation, imaging studies may be helpful in establishing the diagnosis. These studies include a color Doppler ultrasonography and radionuclide testicular flow scan. Imaging studies are used to assess whether testicular blood flow is normal, reduced, or increased. In addition, if a hydrocele is present and the testis is nonpalpable, or if an abnormality of the testis is found, ultrasonography may be helpful. Imaging studies are not 100% accurate; they should not be used to decide whether a boy with testicular pain should be referred for urologic care.

B If there is painless scrotal swelling and a normal testis, the most common causes are hydrocele, hernia, idiopathic scrotal edema (ISE), Henoch-Schönlein purpura (HSP), and varicocele. A hydrocele may develop with painful disorders such as torsion of the testis, epididymitis, trauma, or tumor. In such cases the testis often is not palpable.

A hydrocele is an accumulation of fluid in the tunica vaginalis. Approximately 1 to 2% of male neonates have a hydrocele. In most cases, the hydrocele is noncommunicating (the processus vaginalis was obliterated during development). In such cases, the hydrocele fluid disappears by 1 year of age. If there is a persistently patent processus, the hydrocele persists and becomes progressively larger during the day and is small in the morning. A rare variant of a hydrocele is the abdominoscrotal hydrocele, in which there is a large, tense hydrocele that extends into the lower abdominal cavity. In some older boys, a noncommunicating hydrocele may result from an inflammatory condition within the scrotum, such as testicular torsion, torsion of the appendix testis, epididymitis, or testicular tumor. The risk of a communicating hydrocele is the development of an inguinal hernia.

On examination, hydroceles are smooth and nontender. Transillumination of the scrotum confirms the fluid-filled nature of the mass. If compression of the fluid-filled mass completely reduces the size of the hydrocele, an inguinal hernia is the likely diagnosis.

Most hydroceles resolve by 12 months of age, following reabsorption of the hydrocele fluid. If the

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**Table 5-1** Differential Diagnosis of Scrotal Masses in Boys and Adolescents

<table>
<thead>
<tr>
<th>Painful</th>
<th>Painless</th>
</tr>
</thead>
<tbody>
<tr>
<td>Testicular torsion</td>
<td>Hydrocele</td>
</tr>
<tr>
<td>Torsion of appendix testis</td>
<td>Inguinal hernia*</td>
</tr>
<tr>
<td>Epididymitis</td>
<td>Varicocele*</td>
</tr>
<tr>
<td>Trauma: ruptured testis/hematoma</td>
<td>Spermatocele*</td>
</tr>
<tr>
<td>Inguinal hernia (incarcerated)</td>
<td>Testicular tumor*</td>
</tr>
<tr>
<td>Mumps orchitis</td>
<td>Henoch-Schönlein purpura*</td>
</tr>
<tr>
<td></td>
<td>Idiopathic scrotal edema</td>
</tr>
</tbody>
</table>

*Occasionally associated with discomfort.

<table>
<thead>
<tr>
<th>Table 5-2 Differential Diagnosis of Scrotal Swelling in Newborns</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrocele</td>
</tr>
<tr>
<td>Inguinal hernia (incarcerated)</td>
</tr>
<tr>
<td>Testicular tumor</td>
</tr>
<tr>
<td>Meconium peritonitis</td>
</tr>
</tbody>
</table>

*Occasionally associated with discomfort.
SECTION 1 Evaluation by Complaint or Laboratory Finding

Figure 5-1 Congenital abnormalities associated with intravaginal torsion.

hydrocele is large and tense, however, early surgical correction is recommended because it is difficult to verify that the child does not have a hernia, and large hydroceles rarely disappear spontaneously. Hydroceles persisting beyond 12 to 18 months of age are usually communicating and should be repaired. Surgical correction is similar to a herniorrhaphy. Through an inguinal incision, the spermatic cord is identified, the hydrocele fluid is drained, and a high ligation of the processus vaginalis is performed.

Inguinal hernias are similar to hydroceles and are discussed in Chapter 94, “Pediatric Hydrocele and Hernia.”

A varicocele is an abnormal dilatation of the pampiniform plexus in the scrotum. Dilatation of the pampiniform venous plexus results from valvular incompetence of the spermatic vein. Approximately 15% of adult men have a varicocele; 15% of these men are subfertile. Varicocele is the most common surgically correctable cause of subfertility in men. A varicocele is found in 5% of adolescent boys but is rare in boys aged less than 10 years. Varicoceles occur predominantly on the left side, are bilateral in 10% of cases, and rarely involve the right side only. A varicocele in a boy less than 10 years, or one on the right side, may be indicative of an abdominal or retroperitoneal mass; an ultrasonographic scan should be performed.

A varicocele usually is a painless paratesticular mass, often described as a “bag of worms.” Occasionally patients describe a dull ache in the affected testis. Usually the varicocele is decompressed when the patient is supine and prominent when standing. Testicular size should be documented because, if the affected testis is small, spermatogenesis probably has been adversely affected.

The goal of varicocelectomy is to maximize chances for fertility. Surgical treatment of varicoceles in children and adolescents is indicated in boys with a significant disparity in testicular size, pain in the affected testis, or if the contralateral testis is diseased or absent. Typically the involved testis enlarges and catches up with the normal testis over the following 1 to 2 years.

Varicocelectomy should also be considered in boys with a large varicocele, even without a disparity in testicular size. Surgical repair is performed by ligation of the veins of the pampiniform plexus through an inguinal incision or by ligating the internal spermatic vein in the retroperitoneum. The operation is carried out on an ambulatory basis.

A spermatocele is a cystic lesion containing sperm that is attached to the upper pole of the sexually mature testis. Spermatoceles are usually painless and are incidental findings on physical examination. Enlargement of the spermatocele or pain is an indication for removal.

Testicular and paratesticular tumors can occur at any age, including the newborn. Approximately 65% are malignant. Most present as a painless, hard testicular mass that does not transilluminate. Scrotal ultrasonography should be performed to confirm the finding of a testicular mass and may help to delineate the type of testis tumor. The serum tumor markers α-fetoprotein and β-human chorionic gonadotropin should be determined. Definitive therapy includes surgical exploration through an inguinal incision. In most cases a radical orchietomy, consisting of removal of the entire testis and spermatic cord, is performed, but if the ultrasonographic study or surgical exploration suggests that the tumor is benign, such as a teratoma or epidermoid cyst, removal of the mass only may be performed.

C Torsion of the appendix testis is the most common cause of testicular pain in boys between 2 and 11 years but is rare in adolescents. The appendix testis is a stalk-like structure that is a vestigial embryonic remnant of the müllerian (paramesonephric) ductal system that is attached to the upper pole of the testis. When it undergoes torsion, progressive inflammation and swelling of the testis and epididymis occur, resulting in testicular pain and scrotal erythema. The onset of pain is usually gradual. Palpation of the testis usually reveals a 3 to 5 mm, tender, indurated mass on the upper pole. In some cases, the appendage that has undergone torsion may be visible through the scrotal skin, termed the “blue dot” sign. In some boys, distinguishing torsion of the appendix from testicular torsion is difficult. In such cases, a testicular flow scan or color Doppler ultrasonography may be helpful.

The natural history of torsion of the appendix testis is for the inflammation to resolve in 3 to 10 days. Nonoperative treatment is recommended, including bed rest and analgesia with nonsteroidal anti-inflammatory medication for 5 days. If the diagnosis is uncertain, scrotal exploration is recommended.

D Testicular torsion requires prompt diagnosis and treatment to save the testis. Torsion is the most common cause of testicular pain in boys 12 years and older and is uncommon in those less than 10 years. It is caused by inadequate fixation of the testis within the scrotum resulting from a redundant tunica vaginalis, allowing excessive mobility of the testis (Figure 5-1). The abnor-
mal attachment has been termed a “bell clapper” deformity and is often bilateral. Shortly after torsion occurs, venous congestion begins; subsequently, arterial flow is interrupted. The likelihood of testis survival depends on the duration and severity of torsion. Within 4 to 6 hours of absent blood flow to the testis, spermatogenesis may be lost.

Testicular torsion produces acute pain and swelling of the scrotum. On examination, the scrotum is swollen, tender, and often difficult to examine. The cremasteric reflex is nearly always absent. The condition can be differentiated from an incarcerated hernia because swelling in the inguinal area is often absent. If the pain has lasted less than 4 to 6 hours, manual detorsion may be attempted. This maneuver is performed by rotating the testis outward (the left testis is rotated clockwise). Successful manual detorsion results in dramatic pain relief.

Treatment is prompt surgical exploration and detorsion. In 90% of cases, the gonad will survive if explored within 6 hours of torsion. Survival decreases rapidly with a delay of more than 6 hours. If the degree of torsion is 360 degrees or less, the testis may have sufficient arterial flow to allow the gonad to survive, even after 24 to 48 hours. The testis is then fixed in the scrotum with nonabsorbable sutures, termed scrotal orchiopexy, to prevent torsion in the future. The contralateral testis should be fixed in the scrotum because the condition may be bilateral. If the testis appears nonviable, orchiectomy is performed.

Testicular torsion can also occur in the fetus or neonate and results from incomplete attachment of the tunica vaginalis to the scrotal wall and is “extravaginal.” When torsion occurs in utero, the baby is usually born with a large, firm, nontender testis. Usually the ipsilateral hemiscrotum is ecchymotic. In these cases, the testis is rarely viable because torsion was a remote event. However, the contralateral testis is at increased risk for torsion until 1 month beyond term. Many pediatric urologists recommend exploration to establish the diagnosis, remove the necrotic testis, and anchor the contralateral testis. In other cases, the initial examination is normal, and acute scrotal swelling is recognized subsequently. In such cases, the testis occasionally may be saved.

Acute inflammation of the epididymis is an ascending retrograde infection from the urethra, through the vas into the epididymis. This condition causes acute scrotal pain and swelling. It is rare before puberty and should raise the question of a congenital abnormality of the wolffian duct, such as an ectopic ureter entering the vas. After puberty, epididymitis becomes progressively more common and is the principal cause of acute painful scrotal swelling in young, sexually active adult men. Urinalysis usually reveals pyuria. Epididymitis can be infectious (usually gonococcus, Chlamydia), but often the organism remains undetermined. Treatment consists of bed rest and antibiotics. Differentiation from torsion can be difficult, and in children surgical exploration is usually required.

In some children the history and/or clinical findings may be equivocal. Color Doppler ultrasonography or radionuclide testicular flow scan can be used to confirm the presence or absence of testicular blood flow. These studies should not be used for confirmation of torsion. If torsion is suspected, prompt surgical exploration is necessary.

Color Doppler ultrasonography allows assessment of testicular blood flow and testicular morphologic features. Testicular torsion is diagnosed if the blood flow is absent or reduced. Accuracy is 95% if the ultrasonographer is experienced. A false-negative study (ie, demonstrates excellent testicular blood flow) may occur in a boy with testicular torsion if the degree of torsion is less than 360 degrees and the duration of torsion is short because there may be continued testicular perfusion. In addition, in prepubertal boys, blood flow may be difficult to demonstrate in as many as 30% of normal testes.

The 99mTc-pertechnetate testicular flow scan can demonstrate whether there is blood flow to the testis. Following intravenous injection of the radionuclide, flow and static images are obtained. Testicular torsion usually appears as a “cold spot” of absent flow to the affected testis. Inflammatory conditions usually cause hyperemia. Accuracy in demonstrating blood flow is approximately 95%. A false-negative scan may occur in a boy with testicular torsion if the degree of torsion is less than 360 degrees. The test can often be obtained on an emergent basis during the day, but at night it may take 2 to 3 hours to perform and interpret the study.

Additional Readings


A Anuria, the absence of urine formation, requires prompt and thorough urologic evaluation. Most patients are asymptomatic; however, if acute obstruction secondary to stone disease is evident, the evaluation is directed toward the specific problem. The presence of associated disease, particularly malignancies, should be reviewed because ureteral metastases with associated anuria are common. If prerenal causes exist, stabilize the patient’s cardiovascular status with the use of appropriate medication and intravenous fluids, and monitor central venous pressure. Obtain serum and urine studies prior to using diuretics; such drugs alter urine formation and prevent correct interpretation of results.

B Urethral catheterization is mandatory because it is essential to differentiate between true anuria and urinary retention. If urine is present in the bladder, assess the patient for continued urine production. In the presence of urinary retention, evaluate patients for bladder outlet obstruction. Obstruction is most often caused by benign prostatic hyperplasia, prostatic carcinoma, or urethral stricture disease.

C In patients with an empty urinary bladder or lack of urine production, ultrasonography of the kidneys helps to differentiate an obstructive phenomenon, such as hydronephrosis, from chronic renal disease. It will also differentiate bilateral small kidneys and chronic renal disease from acute renal failure. In the latter situation, the kidneys are often enlarged, with altered parenchymal echogenicity. Anuria and acute failure can also result from acute arterial occlusion, either bilaterally or in a solitary functioning kidney. Arteriography is required if this process is suspected.

D When hydronephrosis is detected, radiographic studies are essential to locate the site of obstruction and assist in relieving the obstruction. After the obstruction has been relieved or bypassed and the patient has been stabilized, further evaluation and therapeutic measures can be instituted. Percutaneous nephrostomy is being used with increasing frequency; the procedure can be performed under local anesthesia, and complications are minimal. Once the patient is stabilized, further studies can be performed to localize the site of obstruction and assess its cause, and further therapy can be planned.

Additional Readings
Anuria or Oliguria

Patient with ANURIA OR OLIGURIA

History Physical examination

Catheterization

Urinary retention

Assess for bladder outlet obstruction

Bladder empty or no urine production

Ultrasonography of kidneys

Hydronephrosis

Bilateral small kidneys

Normal-size kidneys No hydronephrosis

Retrograde or antegrade pyelography

Relief of obstruction Appropriate management of underlying disorder

Hydronephrosis Bilateral small kidneys Chronic renal failure

Normal-size kidneys No hydronephrosis Acute renal failure
Antenatal Hydronephrosis

Maternal ultrasonography is used to determine fetal gestational age and well-being of the fetus in high-risk pregnancies and as a screening tool in those with a family history of congenital abnormalities, as well as normal mothers. In 1% of pregnancies, a structural fetal anomaly is detected, and often the urinary tract is involved. The probability of detecting a structural anomaly by prenatal ultrasonography depends on the experience and skill of the sonographer and usually is better late in gestation when the fetus is larger and an abnormality is easier to image.

An anomaly involving the genitourinary tract is present in as many as 1 in 50 to 1 in 100 pregnancies, depending on the sonogram criteria. Anomalies of the urinary tract detectable by prenatal ultrasonography include obstructive lesions, conditions that mimic obstruction (such as vesicoureteral reflux), cystic disease, and renal agenesis (Table 7-1). Most obstructive anomalies occur more commonly in males, and unilateral disorders are more common on the left side. The timing and type of evaluation necessary in the newborn period depend on the nature of the abnormality visualized on ultrasonography.

The human kidney is derived from the ureteral bud and the metanephric blastema. During the fifth week of gestation, the ureteral bud arises from the mesonephric (wolfian) duct and penetrates the metanephric blastema, which is an area of undifferentiated mesenchyme on the nephrogenic ridge. The ureteral bud undergoes a series of approximately 15 generations of divisions and by 20 weeks gestation forms the entire collecting system, that is, the ureter, renal pelvis, calyces, papillary ducts, and collecting tubules. Under the inductive influence of the ureteral bud, nephron differentiation begins during the seventh week. By 20 weeks, when the collecting system is completely developed, approximately one-third of the nephrons are present. Nephrogenesis continues at a nearly exponential rate and is complete by 36 weeks.

Throughout normal gestation, the placenta functions as the fetal hemodialyzer, and the fetal kidneys play a minor role in the maintenance of fetal salt and water homeostasis. Formation of urine begins between the fifth and ninth weeks of gestation. The rate of urine production increases throughout gestation and, at term, urine output is 28 to 50 mL/h. Normally, fetal urine is hypotonic. The glomerular filtration rate (GFR) has been measured at 6 mL/min per 1.73 m² at 28 weeks gestation, increasing to 25 mL/min per 1.73 m² at term, and thereafter triples by 3 months of age. The main factors responsible for this rise in GFR include an increase in the capillary surface area available for filtration, changes in intrarenal vascular resistance, and redistribution of renal blood flow to the cortical nephrons, in which the majority of nephrons are located. A congenital obstructive lesion of the urinary tract may have a deleterious effect on renal function.

In a normal fetus, the bladder is visualized as early as 14 weeks gestation. Although the kidneys also may be seen at 14 weeks, they should always be visualized by 18 weeks. Identification of a filled bladder provides evidence of renal function. Conversely, nonvisualization of the urinary bladder, particularly in association with oligohydramnios, suggests that renal function is poor. There are standards for normal fetal renal size, and kidney circumference remains constant at approximately one-fourth of the abdominal circumference throughout gestation. Normally, the fetal ureter is not seen. Fetal sex may be determined early in gestation and requires the unequivocal visualization of the penis, or scrotum, or both, or the labia majora. In one study, 40% of fetuses under 24 weeks gestation were definitely identified as to sex, with misdiagnosis occurring in only 3%.

Assessment of the amniotic fluid is important as well. During the first trimester, amniotic fluid represents a transudate of maternal plasma. Beyond 18 weeks, nearly all of the amniotic fluid is the result of voided urine. Thus, with high-grade bladder outlet obstruction or bilateral renal agenesis, the volume of amniotic fluid is severely diminished (oligohydramnios or anhydramnios). Prolonged oligohydramnios results in impairment of fetal lung development and pulmonary hypoplasia, which is fatal. Consequently, the identification of obstructive uropathy in association with oligohydramnios often is predictive of a poor outcome. Because visualization of the fetal kidneys may be marginal until 18 to 20 weeks gestation, and because fetal urine output does not contribute significantly to amniotic fluid during the first trimester, it is not uncommon for a newborn with obstructive uropathy to have a normal fetal sonogram during the first trimester. In order to be certain that renal development is normal, ultrasonography at or beyond 20 weeks gestation is necessary.
<table>
<thead>
<tr>
<th>Condition</th>
<th>Sex (Ratio)</th>
<th>Frequency</th>
<th>Kidney(s)</th>
<th>Ureter(s)</th>
<th>Bladder</th>
<th>Amniotic Fluid</th>
<th>Prognosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ureteropelvic junction obstruction (unilateral)</td>
<td>M/F (3–4:1)</td>
<td>1:2,000</td>
<td>Hydronephrosis</td>
<td>Not seen</td>
<td>Normal</td>
<td>Normal</td>
<td>Good after surgical correction</td>
</tr>
<tr>
<td>Multicystic kidney (unilateral)</td>
<td>M/F (1:1)</td>
<td>1:3,000</td>
<td>Large with cysts of variable sizes</td>
<td>Not seen</td>
<td>Normal</td>
<td>Normal</td>
<td>Good</td>
</tr>
<tr>
<td>Primary obstructive megaureter</td>
<td>M/F (3:1)</td>
<td>1:10,000</td>
<td>Hydronephrosis</td>
<td>Dilated</td>
<td>Normal</td>
<td>Normal</td>
<td>Good after surgical correction</td>
</tr>
<tr>
<td>Ectopic ureterocele or ureter</td>
<td>M/F (1:6)</td>
<td>1:10,000</td>
<td>Large cyst; possible duplex kidney</td>
<td>Dilated</td>
<td>Normal or enlarged</td>
<td>Normal</td>
<td>Good after surgical correction</td>
</tr>
<tr>
<td>Posterior urethral valves</td>
<td>Male</td>
<td>1:8,000</td>
<td>Bilateral hydronephrosis; possible cortical cysts</td>
<td>Dilated</td>
<td>Enlarged</td>
<td>Variable; diminished or absent in severe obstruction</td>
<td>Usually good after surgical correction or drainage; poor if oligohydramnios is present</td>
</tr>
<tr>
<td>Prune-belly syndrome</td>
<td>Nearly always male</td>
<td>1:40,000</td>
<td>Bilateral hydronephrosis; possible cortical cysts</td>
<td>Dilated</td>
<td>Enlarged</td>
<td>Variable; diminished or absent in severe obstruction</td>
<td>Usually fair to good; may need surgical drainage; poor if oligohydramnios is present</td>
</tr>
<tr>
<td>Vesicoureteral reflux</td>
<td>M/F (1:5)</td>
<td>1:100</td>
<td>Hydronephrosis if reflux high grade</td>
<td>Variable</td>
<td>Normal; dilated if reflux high grade</td>
<td>Normal</td>
<td>Good; may need surgical correction</td>
</tr>
<tr>
<td>Infantile polycystic kidney disease</td>
<td>M/F</td>
<td>1:6,000–1:14,000</td>
<td>Large, echogenic</td>
<td>Not seen</td>
<td>Small or not seen</td>
<td>Usually absent or severely diminished</td>
<td>Poor</td>
</tr>
<tr>
<td>Renal agenesis</td>
<td>M/F (2.0–2.5:1)</td>
<td>1:4,000 (bilateral)</td>
<td>Not seen</td>
<td>Not seen</td>
<td>Not seen</td>
<td>Severely diminished or absent</td>
<td>Stillbirth</td>
</tr>
<tr>
<td>Hydrocolpos</td>
<td>Female</td>
<td>1:1,500 (unilateral)</td>
<td>Not seen</td>
<td>Not seen</td>
<td>Normal</td>
<td>Normal</td>
<td>Good</td>
</tr>
<tr>
<td>Ovarian cyst</td>
<td>Female</td>
<td></td>
<td>Normal (cyst may be confused with kidney or bladder)</td>
<td>Not seen</td>
<td>Normal</td>
<td>Normal</td>
<td>Good after surgical correction</td>
</tr>
</tbody>
</table>
SECTION 1 Evaluation by Complaint or Laboratory Finding

A Antenatal Hydronephrosis

D Unilateral
- Postnatal evaluation

B Bilateral (or involvement of solitary kidney)
- Amniotic fluid normal
  - Follow-up ultrasonography
    - Amniotic fluid normal
      - Postnatal evaluation
    - Amniotic fluid reduced
      - Fetal karyotype
        - Consider fetal vesicoamniotic shunt
          - Na⁺ < 100 mEq/L
            - Consider fetal bladder tap (serial)
              - Na⁺ > 100 mEq/L
                - Poor prognosis
        - Postnatal evaluation
          - Favorable prognosis
            - Restores amniotic fluid
              - Postnatal evaluation
          - Poor prognosis
            - Amniotic fluid still reduced
              - Postnatal evaluation

Neonate with HYDRONEPHROSIS

A History
- Physical examination
- Antibiotic prophylaxis
- Circumcision

B Urinalysis
A potentially obstructive anomaly is recognized by demonstrating a dilated renal pelvis or calyces, ureter, and/or bladder. The later the sonogram is performed, the more likely an existing anomaly will be detected because the renal pelvis enlarges throughout gestation. Obstructive lesions are almost always characterized by a fetal renal pelvic diameter more than 10 mm after 24 to 26 weeks gestation.

B In the fetus with bilateral hydronephrosis and a distended bladder, the most important prognostic feature is the volume of amniotic fluid. If the amniotic fluid volume is normal, then renal function should be sufficient to allow normal pulmonary development. Usually the renal cortex is visualized and may be demonstrated to be normal, whereas in other cases macroscopic renal cysts may be seen, which are strongly suggestive of dysplasia. The fetus should be monitored every 2 weeks to ascertain that the volume of amniotic fluid remains normal. If oligohydramnios develops, the cause should be determined. Early delivery is not advised, except for the rare cases in which the amniotic fluid volume diminishes significantly, which may have an adverse effect on pulmonary development.

C The primary life-threatening congenital urologic anomalies include posterior urethral valves, urethral atresia, and prune-belly syndrome, which usually are characterized by bilateral hydronephrosis and a distended bladder that does not empty. Because of the adverse consequences of oligohydramnios on the developing airway, survival might be improved if amniotic fluid can be restored by bypassing the obstructive lesion with a vesicostomy or placement of a shunt between the bladder and amniotic space. The main considerations in determining fetal management include overall fetal well-being, gestational age, whether the hydronephrosis is unilateral or bilateral, amniotic fluid volume, and absence of other structural and chromosomal abnormalities.

Treatment of the obstructed fetal urinary tract by diverting the urine into the empty amniotic space may allow normal renal development to occur and restore amniotic fluid dynamics, stimulating lung development. Unfortunately, the complication rate with vesicoummi-otic shunt placement has been significant in some centers, including shunt migration, urinary ascites, stimulation of preterm labor, and chorioamnionitis. In addition, if there is significant renal dysplasia, the baby will have severe renal insufficiency or end-stage renal disease. Nevertheless, some fetuses may benefit from aggressive intervention. In recent years selection has been based on the assessment of serial fetal urinary electrolytes. The concept is that, normally, fetal urine is hypotonic. In an obstructed system with dysplasia, the fetal urinary electrolytes often include a sodium > 100 mEq/L, chloride > 90 mEq/L, and osmolarity > 210 mOsm/L. If the fetal urine shows levels in these ranges, then a repeat fetal urinary drainage procedure should be performed in 48 to 72 hours and again 48 to 72 hours after that. A downward trend to a more normal range suggests that fetal renal function may be normal and suggests that the fetus should be considered for antenatal intervention. Another important urinary parameter is β₂-microglobulin.

D In the fetus with unilateral hydronephrosis or bilateral hydronephrosis with normal amniotic fluid volume, the infant should be evaluated following delivery; early delivery of the baby is not necessary. If hydronephrosis is unilateral, usually no fetal interventional therapy is necessary unless there is dystocia from the mass, which is rare. In addition, if there is suspected bilateral ureteropelvic junction (UPJ) obstruction or urerovesi- cal junction (UVJ) obstruction and if the amniotic fluid volume is normal, then pulmonary function should be normal as well. Because the neonatal kidney has a tremendous capacity for recovery following drainage, percutaneous drainage of the fetal kidney to improve function or early delivery to allow immediate urologic surgery is unwarranted.

Hydronephrosis in the Neonate

At birth, the abdomen is inspected to detect the presence of a mass, which often is secondary to a multicystic kidney or UPJ obstruction. In addition, the newborn should be evaluated for anomalies involving other organ systems. Renal function should be monitored with periodic serum creatinines, particularly if the baby has bilateral hydronephrosis. At birth, the serum creatinine reflects maternal renal function. However, by 1 week of age, the creatinine should decrease to 0.4 mg/dL.

Neonates with hydronephrosis may be at risk for urinary tract infections (UTIs) and should be placed on antibiotic prophylaxis with either amoxicillin 50 mg daily or cephalaxin 50 mg daily. At 2 months, the prophylaxis usually is changed to trimethoprim-sulfamethoxazole. In addition, circumcision should be considered in male neonates to minimize the likelihood of UTI.

A renal and bladder sonogram should be obtained first. If the fetus has bilateral hydronephrosis, the sonogram should be obtained shortly after birth, whereas with unilateral hydronephrosis, the evaluation may be delayed for several days because neonates may have transient oliguria, and a dilated or obstructed collecting system may appear normal for the first 24 to 48 hours of life. Renal length, degree of caliectasis and parenchymal thickness, and presence or absence of ureteral dilatation should be assessed. Ideally, the severity of the hydronephrosis should be graded from 1 to 4 using the Society for Fetal Urology (SFU) scale (Table 7-2).
Table 7-2 Renal Sonogram

<table>
<thead>
<tr>
<th>Grade of Hydronephrosis</th>
<th>Central Renal Complex</th>
<th>Renal Parenchymal Thickness</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Intact</td>
<td>Normal</td>
</tr>
<tr>
<td>1</td>
<td>Slight splitting</td>
<td>Normal</td>
</tr>
<tr>
<td>2</td>
<td>Evident splitting, complex confined within renal border</td>
<td>Normal</td>
</tr>
<tr>
<td>3</td>
<td>Wide splitting pelvis dilated outside renal border, calyces uniformly dilated</td>
<td>Normal</td>
</tr>
<tr>
<td>4</td>
<td>Further dilatation of pelvis and calyces (calyces may appear convex)</td>
<td>Thin</td>
</tr>
</tbody>
</table>


Next, a voiding cystourethrogram (VCUG) should be performed. This study may demonstrate posterior urethral valves, a bladder diverticulum, or vesicoureteral reflux. Even if the neonatal sonogram is normal, a VCUG should be performed because reflux may be the cause of fetal hydronephrosis.

If the postnatal sonogram shows grade 1 or 2 hydronephrosis and the VCUG is normal, then it may be presumed that the pelvocaliectasis is physiologic or secondary to mild narrowing of the UPJ. The likelihood of obstruction is quite low, and no further immediate evaluation is necessary, but a follow-up renal sonogram in 3 to 6 months is necessary.

If the postnatal sonogram shows grade 3 or 4 hydronephrosis and there is no reflux, the upper urinary tracts must be evaluated further, ideally with a diuretic renogram using technetium 99m MAG-3, which is filtered and secreted by the renal tubules. Generally the diuretic renogram is postponed until 4 to 6 weeks of age to allow normal maturation of renal function.

Differential renal function is computed by measuring the uptake over each kidney during the first 2 to 3 minutes, before the radionuclide enters the collecting system. In addition, the efficiency of upper urinary tract drainage may be measured. On the diuretic renal scan, upper urinary tract obstruction is assessed by injecting furosemide when the renal pelvis is full, which stimulates washout of the radionuclide from the renal pelvis. If no obstruction is present, then normally half of the radionuclide is cleared from the renal pelvis within 15 minutes, termed the “half-time.” In the presence of significant upper tract obstruction at the level of the UPJ or UVJ, the half-time is longer than 20 minutes, and typically the drainage curve is flat. In some cases, the half-time is an indeterminate 15- to 20-minute range.

Numerous factors affect the interpretation of the diuretic renogram, including renal maturity, renal function, hydration status, dose of radiopharmaceutical, dose of diuretic, timing of diuretic administration, presence of vesicoureteral reflux, volume of urine in the bladder, outlined regions of interest, patient position, patient movement, capacity of the upper urinary tract, severity and site of obstruction, and method of data interpretation.

Additional Readings


A A careful review of the plain abdominal films or KUB is essential in assessing radiolucent filling defects of the renal pelvis and ureter detected on intravenous urography. Many, but not all, filling defects require confirmation and further delineation with retrograde pyelography. With appropriate radiologic techniques, cystine stones and faintly calcified matrix stones can often be detected. Renal pelvic and ureteral defects that are truly radiolucent warrant further evaluation.

B Many patients with radiolucent renal pelvic or ureteral filling defects have detectable hematuria. This finding, however, does not differentiate a benign from a malignant process. Routine urinalysis also assists in detecting the presence of infection, in assessing urinary pH, and in screening for glycosuria. Further, a positive urine cytology helps in assessing for transitional cell malignancies; therefore, this study should be obtained as part of assessing these patients. Unfortunately, a negative cytology does not exclude the presence of a malignancy.

C Computed tomography (CT) without injection of contrast material is useful in establishing the diagnosis of a nonopaque calculus. Because CT provides greater density discrimination than does conventional radiography, uric acid stones are visualized. The technique is also helpful in evaluating the poorly prepared patient. Further evaluation is required when the lucent defect is found to have the consistency of soft tissue. In these instances, intravenous contrast agents are most helpful in establishing the diagnosis. A carefully performed renal ultrasound study will provide comparable information. All stones produce sonic shadowing, which is an important diagnostic finding.

D Ureteroscopy and pyeloscopy are safe techniques that help to confirm a ureteral or renal pelvic tumor diagnosis. Similarly, the observation of blood clots or a sloughed renal papilla is confirmatory. Using these instruments, biopsies can be obtained for histologic confirmation of a suspected diagnosis.

E If ureteroscopy or pyeloscopy is unsuccessful or the appropriate instruments are unavailable, renal pelvic and ureteral brushings with cytology are useful to differentiate a malignant from a benign process. If a renal or ureteral tumor is found, appropriate management is indicated. A negative brushing warrants continued observation with repeat intravenous urography.

Additional Readings
Patient with RADIOLUCENT FILLING DEFECT

A. Review KUB
   Consider retrograde pyelography

B. Urinalysis
   Urine cytology

C. CT scan with and without intravenous contrast
   Ultrasonography

   - Truly lucent defect or
     no sonic shadowing
   - Opaque or
     sonic shadowing

   D. Ureteroscopy
      Pyeloscopy

      - Transitional cell tumor
      - Diagnosis uncertain

E. Renal pelvic brushing, biopsy, ureteroscopy

      - Appropriate therapy
      - Malignant cells
      - Negative finding
      - Observe

      Intravenous urography

Renal stone disease

Patient with RADIOLUCENT FILLING DEFECT

Truly lucent defect or
no sonic shadowing

Opaque or sonic shadowing

Renal stone disease

Blood clot Renal papilla

Observe

Observe

Appropriate therapy

Malignant cells

Negative finding

Transitional cell tumor

Diagnosis uncertain

Renal pelvic brushing, biopsy, ureteroscopy
Flank Pain

J. Patrick Spirnak, MD, FACS, and Ronald A. Rubenstein, MD

Several urologic and nonurologic disease processes can cause flank pain. Pain originating from the urinary tract is usually felt in the ipsilateral costovertebral angle, just lateral to the sacrospinalis muscle beneath the twelfth rib posteriorly. It may also radiate anteriorly toward the epigastric area. Acute distention of the renal capsule, usually from inflammation or obstruction, causes flank pain of urologic origin. The severity of the pain is associated with the acuteness of the distention.

A The differential diagnosis of flank pain includes urologic diseases of the kidneys, ureters, and bladder, as well as nonurologic diseases involving abdominal, retroperitoneal, gynecologic, and musculoskeletal structures. Evaluation begins with a complete urologic history and physical examination. Urologic history focuses on determining whether the kidneys, ureter, or bladder is involved. Dysuria, frequency, urgency, hematuria, and fevers suggest an infectious or inflammatory process. Acute pyelonephritis or cystitis may present in this manner. History may suggest renal vascular disease secondary to renal artery embolus, renal vein thrombosis, dissection of the renal artery, rupture of a renal artery aneurysm, aortic dissection, or abdominal aortic aneurysm. Renal artery embolus may present with a history of atrial fibrillation, subacute bacterial endocarditis, or cardiac mural thrombus. Renal vein thrombosis may present with a history of nephrotic syndrome, malignancies, or pregnancy. Aneurysmal disease generally presents with a history of aneurysms and vascular disease. Renal carcinoma may present as flank pain from hemorrhage within the tumor. Renal calculus, blood clot, or necrosed papilla may cause severe pain from an acute obstruction. Cases of flank pain require a urinalysis and radiologic evaluation. If the history is negative for urologic risk factors, questioning should then probe for nonurologic etiologies of pain. Physical examination for flank pain will generally demonstrate flank tenderness.

B Multiple imaging modalities have been used individually or in combination to evaluate acute flank pain. The most commonly obtained studies include plain film, ultrasonography, intravenous urography (IVU), and unenhanced helical computed tomography (CT). Plain film of the abdomen for stone detection has a reported sensitivity, ranging from 44 to 77%, and specificity between 87 and 90%. Ultrasonography for stone detection has a reported sensitivity, ranging from 10 to 28%, with a very high specificity. Combining these two modalities had a reported sensitivity of 81%. In many institutions, IVU has been the primary imaging modality for evaluating acute flank pain. IVU can provide both anatomic and functional information, as well as the site and degree of obstruction. IVU for stones and hydronephrosis associated with stones has a reported sensitivity of 64% and 90% and a specificity of 100% and 94%. IVU, however, has several drawbacks that can be avoided with CT. CT scan has a reported sensitivity of between 91 and 100% and a specificity between 94 and 98% for detection of stones. Examination takes only several minutes, avoids the use of contrast dye, and can be used in cases of renal insufficiency. In addition, CT scan can detect abnormalities unrelated to stone disease. In a study from the Departments of Urology and Radiology at Albert Einstein Medical Center in Philadelphia, 32% of patients with flank pain evaluated by CT scan were found to have noncalcious causes.

References

Primary nocturnal enuresis (PNE) is defined as bedwetting after an age at which bladder control would normally be expected. The American Psychiatric Association defines nocturnal enuresis as nighttime wetting that occurs at least twice a month in a child 5 years of age or older. Our discussions here deal with monosymptomatic bedwetting, implying no daytime voiding symptoms (see Chapter 11, “Diurnal Incontinence in Children”).

PNE has been recognized as a disturbance of childhood necessitating medical treatment since the time of the Papyrus Ebers, which is dated 1550 BC. Currently, an estimated 5 million to 7 million children in the United States have PNE. After allergic disorders, bedwetting is the most common chronic condition of childhood. Negative psychosocial consequences are common, secondary to the impact of enuresis on the patient, family members, and peers. Feelings of helplessness and isolation by the family are reinforced by lack of help by healthcare professionals.

The enuretic child is at increased risk for emotional or even physical abuse from family members and may experience stress from fear of discovery by peers. These factors contribute to the loss of self-esteem that the enuretic child often experiences. These psychosocial issues mandate an aggressive educational and management program as it is well known that patients who are successfully treated show improvement in self-perception and behavior. An additional negative impact of PNE is the economic burden for the families. A recent analysis of cost suggests that when a child wets the bed more than 3 nights per week, no treatment is associated with the highest costs for the family.

A review of the natural history, genetics, and proposed etiologic mechanisms of PNE sets the stage for a coherent management program. Initial evaluation and treatment options ranging from reassurance and family education to combined behavior modification and pharmacologic programs are reviewed. Factors predicting response to treatment are addressed. The patient’s smile and return to a more normal life pay testimony to a successful treatment program for the patient.

A The epidemiology and natural history of PNE are well known and influence treatment decisions. The attainment of control of elimination is developmentally determined, and control of urination at night is usually the last event conquered by the young child. In our society 15 to 20% of 5 year olds and 5% of 10 year olds wet the bed, with 1 to 2% continuing to wet the bed into adulthood. Fergusson and colleagues, in their classic birth cohort study of New Zealand children, demonstrated a 15% resolution of PNE each year as the child developed without active treatment. They noted that factors predictive of age of attainment of nocturnal bladder control were a family history of enuresis, the child’s developmental level at 1 and 3 years of age, and the child’s early sleep patterns. Psychosocial factors such as birth order, socioeconomic status, and family life events were not predictive. The study confirmed a belief that the etiology of PNE was “biological” and that psychosocial factors played little role in attainment of nocturnal urinary control. Consequently, for the vast majority of children who wet the bed, the “biological processes” responsible for the “symptom” abate, and social normalcy is established. This is an important detail to consider in the discussions of treatment and permanency of etiologic mechanisms.

B There is clearly a genetic component to PNE, but somatic and environmental factors have a major modulating effect. PNE in most families is inherited in an autosomal dominant mode of transmission with a high degree of penetrance (90%). Bakwin’s classic family study showed that if one parent wet the bed, 44% of their children will wet the bed, and if both parents were affected, 77% of their children will wet the bed. Twin studies comparing concordance rates have documented a significant difference in dizygotic versus monozygotic twins. The higher concordance in monozygotic twins underlines the strong genetic etiology. Eliciting the family history is clinically important as it informs the patient, who may be unaware of it, and it provides the strongest predictor for the age of attaining dryness. In children with two first-degree relatives with PNE the development of nocturnal bladder control was delayed by 1.5 years. Molecular genetic studies have identified a number of candidate chromosomes responsible for PNE. Linkage analysis has defined different loci or chromosomal intervals associated with nocturnal enuresis on four chromosomes. Locus heterogeneity allows for genes on different chromosomes to lead to the same disorder. All loci were found in large family pedigrees, including chromosomes 8, 12, 13, and 22. At present there is no specific association of genotype with gene product, protein expression, or somatic phenotype. Consequently, one cannot direct treatment based on the present level of molecular discovery, but the future looks promising as we will be able to pro-
Patient with PRIMARY NOCTURNAL ENURESIS

Presentation with PNE

Evaluation: history, physical examination, urinalysis

Abnormal

Normal

Decision to treat

No

Counseling and education

Follow-up as needed

Continued wetting?

Yes

Counseling, education, motivational and fluid management

Pharmacotherapy

Behavior modification: conditioning therapy

Combination therapy

Imipramine

DDAVP

Anticholinergics

Alarm: auditory, vibratory Sonogram bladder volume
provide more specific treatment for this heterogeneous condition.

C The symptom of bedwetting has many etiologies that are not mutually exclusive, contributing to the confusion in attempting to assign a single pathophysiologic mechanism to all children with PNE. Conceptually, the major etiologic categories are (1) nocturnal polyuria, (2) bladder capacity and function, and (3) sleep/arousal mechanisms (Figure 10-1).18 Simplistically, the bladder fills beyond capacity, and the child voids without awakening. Maturation and development of each factor is genetically determined, and clinical assessment in each child will help in treatment. Therapeutic measures should address the factor most dominant for the individual patient. The arousal failure is operational in all patients with PNE. If initial treatment is not successful, then combination therapy treating more than one factor will be necessary.

Nocturnal polyuria as a factor in PNE has many potential causes ranging from a decrease in nocturnal excretion of antidiuretic hormone (ADH) to abnormal aquaporin expression (Table 10-1). PNE can be provoked in night-dry children with increased water consumption prior to bedtime.19 The observation of decreased nocturnal ADH secretion in some children with PNE fostered a new era of investigation into potential causes and specific treatment of PNE.20,21 Although failure of ADH to increase during the night and nocturnal polyuria may occur in some children with enuresis, the frequency, mechanism, and significance of altered ADH excretion in enuresis require further clarification. Documentation of nocturnal polyuria with increased nocturnal urine output from any cause would be expected to respond to treatment with desmopressin acetate (DDAVP) combined with fluid restriction.22–24 Desmopressin responders produced larger amounts of less concentrated urine than the other children, whereas desmopressin nonresponders had smaller bladder capacity than the other groups. These results support the idea that enuretic children who respond favorably to desmopressin treatment have polyuria, whereas children with therapy-resistant enuresis have detrusor hyperactivity.25 A 2-week, home-based study was conducted on 75 children with nocturnal enuresis to monitor the frequency of enuretic episodes and the volume of nocturnal urine production. During treatment with desmopressin, nocturnal urine production in desmopressin responders decreased to levels similar to those of nonresponders. The results confirmed the previous circadian studies of urine output and emphasized the importance of nocturnal polyuria in patients with monosymptomatic enuresis. The response to desmopressin was found to correlate with the occurrence of nocturnal polyuria.23,26

The significant role of the bladder in the etiology of PNE is well recognized. The single most important urodynamic observation in PNE is a reduced bladder capacity.27 This reduction in capacity was shown to be functional, not anatomic, by measurements of bladder capacity under anesthesia.28 Many studies have demonstrated a decreased bladder capacity in children with PNE.29,30

The role of bladder instability is more controversial. Urodynamic assessment of children with PNE generally demonstrates normal compliance, end-filling instability, and coordinated sphincteric relaxation during voiding.31,32 Bladder instability does not occur in children with PNE at a higher rate than in normal subjects, and in most enuretics unstable contractions are not the cause of bedwetting. The neurologic response to the uninhibited contraction determines whether sleep wetting or awakening to void will occur, and this can be assessed by electromyographic monitoring of the pelvic floor muscles. If muscle activity occurs, it signals an arousal response and leads to awakening, whereas a silent pelvic floor during bladder contraction is associated with sleep wetting.32 In summary, bladder instability does not occur in children with PNE at a higher rate than in normal subjects, and in most enuretics unstable contractions are not the cause of sleep wetting.

![Figure 10-1](image_url) The interaction of the major factors in PNE suggests the heterogeneity in etiology and response to treatment recognized in children with PNE. Areas of overlap represent the multiple factors contributing to PNE in any one patient. PNE = primary nocturnal enuresis.

<table>
<thead>
<tr>
<th>Proposed Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decreased nocturnal ADH</td>
</tr>
<tr>
<td>Decreased aquaporin expression</td>
</tr>
<tr>
<td>Increased fractional sodium excretion</td>
</tr>
<tr>
<td>Suppressed levels of aldosterone/angiotensin II</td>
</tr>
</tbody>
</table>

Table 10-1  Etiology: Nocturnal Polyuria
A group of patients with detrusor-dependent PNE are recognized as having a resistance to DDAVP. These patients can be assessed by measurement of functional daytime bladder capacity. When this is less than 70% of that predicted for age (bladder capacity (cc) = 30 × (age + 2)) a poor response to DDAVP can be anticipated. Treatment with an anticholinergic or combination therapy is indicated.43,45

The inability of the child to awaken at night in response to bladder filling at capacity and subsequent voiding is the predominant event in PNE. Many parents as well as epidemiologic studies comment on the difficulty in awakening the enuretic child.49,50 Enuretic children, when exposed to the same auditory stimulus as nonenuretic cohorts during sleep, are more difficult to arouse.43 This serves as a protective mechanism early in infancy where awakening in response to frequent voids would not allow sustained sleep. Because sleep arousal thresholds decrease with age, the elevated arousal threshold may reflect a developmental delay.44 Nocturnal enuresis may represent a functional immaturity of the central nervous system in arousal. The arousal defect is characterized as a dual afferent and efferent problem. The sleeping child does not sense the full bladder (the afferent arousal defect), nor does the central nervous system suppress the micturition reflex during sleep (the efferent defect).41

Sleep studies monitored by electroencephalography (EEG) and cystometrics show that the bladder empties at a capacity independent of stage of sleep.31,32 Watanabe and Azuma proposed a classification of PNE based on the type of EEG sleep pattern, arousal, and simultaneous cystometry. The findings attest to the developmental acquisition of an arousal response in relation to bladder filling that is deficient in patients with PNE and may in some cases be associated with bladder instability.44

All children presenting with PNE require a thorough history, physical examination, and urinalysis. Only children with bedwetting without diurnal enuresis are discussed as evaluation and treatment differ for those with PNE alone. Most parents have poor knowledge of the specifics of their child’s bowel and voiding habits. An accurate voiding diary provides needed information on the frequency of wet nights, the number of enuretic episodes per night, and daytime toilet habits. It also provides insight into the family’s level of participation in and commitment to future treatment programs. The specific concerns of the parent(s) in regard to bedwetting and its treatment need attention as some parents need only assurance as to the developmental nature of the problem. The family living situation, number of siblings, and location of the patient’s bedroom in relation to that of the parents are important to know if conditioning treatment with an alarm system is chosen.

A detailed history to exclude diurnal enuresis, voiding dysfunction, and elimination disorders is essential. It is important to rule out constipation, because it is associated with enuresis, vesicoureteral reflux, and urinary infection.45 A prior history of urinary tract infection, urologic abnormalities, neurologic diseases, and renal disorders will influence evaluation and management. A family history of PNE and age of resolution are helpful for the patient who may be unaware of that history, and parental age of resolution is predictive of age of resolution in the patient.8 A query into the level of development and maturation in motor and speech milestones is sought because general neuromuscular and even brainstem development is delayed in patients with PNE.46 A prenatal history with a normal fetal sonogram, obtained routinely in most pregnancies, provides a free early look at the urinary tract.

Special situations associated with PNE include attention-deficit/hyperactivity disorder (ADHD), sleep apnea, and food allergy–provoked enuresis. A history of these problems is sought because treatment of PNE can change. Twenty-five to 40% of children with ADHD wet the bed and 10% of children with PNE have ADHD.47 Obstructive sleep apnea owing to enlarged tonsils and adenoids can result in increased nocturnal secretion of atrial natriuretic factor with nocturnal polyuria. In patients with sleep apnea and PNE, surgical removal of the tonsils and adenoids has been associated with resolution of PNE in 75% of cases.48,49 Food allergy is uncommon in PNE. It was recognized in children treated for migraine headache or ADHD who resolved their PNE while on a food-restricted diet.50,51

Physical examination should include abdominal, genital, and neurologic evaluation. A distended bladder and palpable stool suggest an elimination disorder that needs attention. Careful inspection of the genitalia is important to determine hymenal anatomy, labial adhesions, and anal location and to rule out meatal anomalies. If an abnormal stream is suspected, then observation of the child voiding is helpful. Careful examination of the spine for signs of occult spinal dysraphism includes inspecting for cutaneous lesions, dimples, lipomas, hairy tufts, and asymmetry of the gluteal cleft. Anal sphincter tone and anal wink are assessed. The gait is observed. A high-arched foot or slight leg-length discrepancy are significant signs of a tethered cord. Lower extremity knee and ankle reflexes are tested and strength and sensation are assessed.

In the presence of a normal history and physical examination no further testing is needed. A urinalysis, although not always necessary, provides the clinician
and parent with reassurance. The knowledge of the
ability to concentrate the urine and the absence of pro-
tein, glucose, and cellular elements in the urinalysis
exclude many diagnostic possibilities.

**E** Initial management is based on the age of the child and
the patient and parental motivation. Most patients
referred to the urologist have already failed some form
of treatment, or the patient and family are seeking infor-
mation, reassurance, and effective treatment. Patients
who have not kept a voiding log prior to the initial
assessment are given one to keep for 1 week prior to
treatment and during treatment to evaluate efficacy.
Parents of children less than 5 to 6 years of age gener-
ally want to know that their child is “okay,” and educa-
tion and reassurance are all that is necessary. We do
follow up with them over the telephone 6 to 12 months
later to continue assessment and provide further treat-
ment, if desired.

All patients are counseled regarding voiding at bed-
time and fluid restriction prior to bedtime (Table 10-2).
All treatment options incorporate motivational therapy,
which by itself is effective in the treatment of PNE
(Table 10-3).53 The therapeutic options available
include pharmacologic treatment, conditioning ther-
apy, and combination treatment. All are discussed with
the patient and family, outlining anticipated results,
potential adverse effects, and the possibility of relapse
on discontinuation of treatment. Treatment is individu-
alized and directed toward the assessed most probable
cause of PNE. Combination therapy, when needed, is
added sequentially to assess the effects of each treat-
ment.

**F** Conditioning therapy, relying primarily on the use of
alarm systems, is the most effective means of treating
PNE.54 These alarms may be auditory, vibratory, or
both.55,56 A new development is an alarm based on
bladder volume assessed by ultrasonography, which
awakens the patient prior to voiding.57,58 Patients with
the highest frequency of PNE will obtain the best
results when treated with an alarm.59 The alarm success
rate of approximately 75% is independent of the type
of alarm, and there is a low relapse rate of 20 to
30%.54,60 Reuse after relapse is associated with rapid
reconditioning.61 Factors associated with a negative
response to conditioning therapy include an unstable
family situation, family stress, lack of parental con-
cern, and more than one wet episode per night.62 There
are no singular factors predicting a favorable response
to treatment.

Alarm treatment requires a cooperative and motivat-
ed patient and family. When the child voids in bed, a
moisture-sensing device triggers the alarm, and on
awakening, urination is inhibited. The parents must
awaken their child initially or the conditioning will not
occur.64 This may necessitate a cold washcloth on the
face, standing their child at bedside, or any maneuver
known by the family to awaken their child. On awaken-
ing, the child is instructed to empty his or her bladder
in the toilet. Consequently, the parents’ bedroom needs
to be nearby, and the patient ideally should have his or
her own room. These constraints need to be addressed with
the family. The alarm must be used every night and can-
not be stopped until 25 to 30 consecutive dry nights are
achieved. This may require 3 to 6 months of use. Over-
learning, by forcing fluids at bedtime after initial suc-
cess with the alarm, has been associated with decreased
relapse.64 The most common reasons for treatment fail-
ure are inadequate duration of treatment and a lack of
both immediate, positive reinforcement and significant
commitment, leading to inconsistent use or stopping
treatment prior to completion of the conditioning
process.

**G** At present only two drugs are available with an indica-
tion to treat PNE. These are imipramine and desmo-
pressin (Table 10-4). Anticholinergics do not have a
specific indication for the treatment of PNE but are pre-
scribed alone or in combination, especially in children
with decreased bladder capacity or “detrusor-depend-
ent” PNE. These patients may have daytime frequency
and decreased daytime bladder capacity.66 The use of
drugs to treat the symptom rarely cures PNE as relapse
following short-term treatment is high. In addition, the
“placebo effect” and a spontaneous resolution rate of
15% per year need to be considered when evaluating
drug efficacy.

**H** Imipramine hydrochloride (Tofranil) is a tricyclic anti-
depressant used in the treatment of PNE since 1960.
The mechanism of action is not exactly known but
appears multifactorial. It has anticholinergic and anti-
spasmodic effects on the bladder, increasing its capaci-
ty. It has α-adrenergic action on the bladder neck,
improving bladder storage function.67 The drug has

### Table 10-2 Fluid Restriction Guidelines

<table>
<thead>
<tr>
<th>Weight (lb)</th>
<th>Fluids (oz)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 75</td>
<td>2</td>
</tr>
<tr>
<td>76–100</td>
<td>4</td>
</tr>
<tr>
<td>&gt; 100</td>
<td>6</td>
</tr>
</tbody>
</table>

### Table 10-3 Essentials of Motivational Treatment

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Active patient participation in treatment</td>
<td>Patient charting of results</td>
</tr>
<tr>
<td>Reassurance, guilt removal, positive reinforcement</td>
<td></td>
</tr>
</tbody>
</table>
TABLE 10-4 Pharmacologic Therapy for Primary Nocturnal Enuresis

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Dose</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Imipramine (Tofranil)</td>
<td>25–75 mg @ 1 h prior to bedtime based on age. Max 1.5 mg/kg/d</td>
<td>$5</td>
</tr>
<tr>
<td>Desmopressin acetate (DDAVP)</td>
<td>Nasal spray: 10–40 µg qhs</td>
<td>$$$</td>
</tr>
<tr>
<td>Oxybutynin (Ditropan)</td>
<td>5–10 mg PO @ 1 h prior to bedtime</td>
<td>$</td>
</tr>
<tr>
<td>Ditropan XL</td>
<td>5–10 mg PO @ 1 h prior to bedtime</td>
<td>$</td>
</tr>
<tr>
<td>Tolterodine (Detrol LA)</td>
<td>2–4 mg PO @ 1 h prior to bedtime</td>
<td>$</td>
</tr>
<tr>
<td>Hyoscyamine (Levsinex TC)</td>
<td>0.375 mg @ 1 h prior to bedtime</td>
<td>$</td>
</tr>
</tbody>
</table>

DDAVP is a synthetic analog of ADH. It lacks the vasoconstrictive and smooth muscle effects of ADH and has a longer duration of action. It has primarily V2 receptor-agonistic activity, resulting in increased permeability of the collecting duct via aquaporin channel-forming protein.67,77 The net result is reabsorption of water from the collecting duct in the hyperosmolar environment of the renal medulla and the urine becoming more concentrated. The decreased urine output at night is below the voiding threshold, allowing the child to sleep without urinating at night. The therapeutic use of DDAVP is based on a study of a group of patients with PNE who lacked the normal nocturnal increase in ADH and responded to replacement therapy at night.76,78 It can be given intranasally or orally, and its effects last 7 to 12 hours.

Adverse effects are uncommon; rhinitis, headache, and cough were the most frequently reported.79 Concern has been expressed regarding the rare occurrence of water intoxication and hyponatremic seizures. At least 40 cases have been reported.80–83 In most instances these patients failed to restrict their nighttime water intake. It is imperative that children and parents be aware of the need to restrict fluids at night (see Table 10-2). To minimize this risk, it has been recommended that children limit fluids to no more than 8 ounces (240 mL) on any night that DDAVP is administered.81,84 Compared with tricyclic drugs there are fewer adverse effects with DDAVP.18,74

DDAVP given nasally is started with one spray in each nostril (10 µg/spray) 1 hour prior to bedtime. This dose is given from 3 to 7 days to determine a response. The patient keeps a log for at least a week prior to treatment to measure the number of wet nights per week. If the patient is not dry on all nights, the dose is increased sequentially to a maximum of two sprays in each nostril (40 µg). If the patient has no dry nights the drug is stopped. The patient has > 50% reduction in wet nights the drug is continued for 3 to 6 months and then stopped to see if wetting recurs. If it recurs, treatment is reinstituted and the treatment cycle repeated. Treatment can be safely continued for up to 1 year.85 The dose for the DDAVP tablet is 200 µg 1 hour prior to bedtime.

Adverse effects are usually related to its anticholinergic effects and include dry mouth, blurred vision, constipation, confusion, and disorientation. Overdosage with imipramine is associated with convulsions, respiratory distress, and fatal cardiac arrhythmias.80 Parents must be warned about these side effects and the importance of keeping the medicine in a secure location away from children. When reported, tricyclic antidepressants were associated with more adverse effects than desmopressin (17.3% versus 7.1%).71 Because of these adverse effects and safety issues, the use of this drug for PNE has decreased dramatically.18

The dosage of imipramine is based on body weight at 0.9 to 1.5 mg/kg/d. It is given 30 to 60 minutes prior to bedtime. This produces a therapeutic plasma concentration in only 30% of patients. Care must be exercised when prescribing higher doses because of potential toxicity. Response to treatment is rapid when it works. Treatment duration is 3 to 6 months prior to a medication holiday. Serum levels are not correlated with response, and monitoring is of questionable value at the time of treatment.72 The drug should be weaned by reducing the dose and then the frequency of administration. In structured withdrawal programs a significantly reduced relapse rate (25%) is obtained and offers an alternative and rapid means of successfully withdrawing medication.73

Randomized controlled trials have demonstrated a statistically significant improvement in the number of wet nights while patients are taking imipramine. A response rate, defined as a 50% decrease from baseline in wet nights, can be anticipated in up to 70% of patients. Children taking imipramine have 1.3 (0.7 to 1.8) fewer wet nights per week and are 4.2 (1.2 to 15) times as likely to become dry as those receiving placebo. A long-term cure rate is reported in only 25% of patients when the drug is discontinued. The relapse rate following drug discontinuation is 60% or greater.74,75
Anticholinergic medication does not have a specific indication for the treatment of PNE. In a prior randomized controlled trial it was not efficacious. However, recent investigations have suggested the presence of a subgroup of patients with “detrusor-dependent” PNE and decreased functional bladder capacity. These patients have daytime urinary frequency and may have previously had diurnal enuresis. These patients historically responded poorly to DDAVP. In this patient population, anticholinergic medication has a role either as a secondary medication or in combination with an alarm or DDAVP. Response rates in uncontrolled, open trials vary from 40 to 70%. Adverse side effects are present in up to 17% of patients, with dry mouth being the most common.66,74

**K** Combination therapy is indicated for older patients with refractory PNE. These patients have failed monotherapy with DDAVP or an alarm trial. If not already performed, it is valuable to assess bladder capacity, polyuria, and compliance with fluid restriction as previously described. These data will help in selecting the best combination treatment. A review of published series using combination therapy reveals conflicting data based on patient selection and study design.

A recent placebo-controlled trial comparing alarm plus placebo versus alarm and DDAVP failed to show any long-term advantage of the combination therapy. However, in other selected populations, a success rate of 60 to 75% is reported. This improvement with alarm plus DDAVP was particularly pronounced in children with severe wetting, family problems, or behavioral problems. DDAVP dosage varied from 20 to 40 µg intranasally. The alarm has also been combined with imipramine (25 mg), but it was no more effective either.

The combination of DDAVP and anticholinergic drugs has an initial success rate of 60 to 80%. In a multicenter trial in adults and children with nocturnal enuresis and diurnal voiding disturbances, those treated with oxybutynin (0.2 mg/kg bid) alone had a 54% success rate. The patients treated with both oxybutynin (0.2 mg/kg bid) and DDAVP (30 µg qhs) showed a better response, with a 71% rate of success.100 In a study of patients who failed monotherapy for PNE, the combination of DDAVP (20 to 60 µg) and hyoscyamine (0.375 to 0.75 mg at bedtime) resulted in complete dryness for 57% of patients and 80% dryness in another 21% of patients with 6 months of treatment. However, a high rate of relapse off medication was noted.37

**Imipramine and Anticholinergic**

Oxybutynin and imipramine combination treatment was recently assessed. Efficacy was determined relative to the number of wet nights per week compared with the control period; a > 50% decrease in wet nights per week indicated efficacy. The mean wet nights per week decreased from 6.1 to 1.7, and efficacy was established in 20 patients (90.9%). Relapses occurred in 60% of
patients during the follow-up period. No adverse effects were reported. Other studies have not confirmed a statistically significant advantage of this combination compared with monotherapy.101

References

45. von Gontard A, Schmelzer D, Seifen S, Pukrop R. Central nervous system involvement in nocturnal enuresis: evidence of general neu-


Childhood urinary incontinence is a common condition that results in the child experiencing social embarrassment and treatment as an outcast. Incontinence is classified into two major groups: nocturnal and diurnal. Nocturnal incontinence, also known as bedwetting and enuresis, is discussed in Chapter 10, “Nocturnal Enuresis.” Diurnal incontinence, wetting during the daytime, may be functional, neuropathic, structural, or obstructive in etiology. Voiding in infancy is a reflexive act, resulting in diurnal incontinence. However, the most important factor in bladder control is the voluntary inhibition of this voiding reflex. The ability to control this reflex is usually obtained by age 5 years, and for this reason, avoid evaluating a child without an organic cause before this age.

Evaluation of children with diurnal incontinence includes several components: (1) history, (2) physical examination, (3) urine analysis, (4) urine culture if indicated, and (5) voiding diary. The diary is an important component to assess these children because it provides information on the functional bladder capacity, frequency or infrequency of voiding, and timing of the incontinence in relation to their voiding pattern. The results of this evaluation allow one to classify these children into two broad categories: primary and secondary incontinence.

Primary incontinence is the inability to be toilet trained for an extended period of time. Conversely, secondary incontinence is when the child has been toilet trained for an extended period of time and then develops daytime incontinence. Patients with primary and secondary incontinence can be divided into nine groups: (1) phimosis, (2) interlabial mass, (3) sacral dimple or tuft of hair, (4) urinary tract infection (UTI), (5) urinary frequency, (6) urinary infrequency, (7) constipation, (8) continuous wetting with a normal examination, and (9) normal evaluation. More than one of these problems can coexist.

Phimosis can be a cause of urinary soilage, resulting from urinary pooling under the phimotic skin, which can lead to balanitis, posthitis, and UTI. This condition, however, can be easily treated by circumcision or by nonsurgical means. Recently, the use of low-dose steroid creams has gained popularity in its ability to treat phimosis, eliminating the need for circumcision in many children.

All girls who present with urinary incontinence should have an introital examination to evaluate for an interlabial mass. The differential diagnosis of an interlabial mass includes rhabdomyosarcoma (sarcoma botryoides), prolapsed ureterocele, paraurethral cyst, imperforate hymen, uterovaginal prolapse, and urethral prolapse. After these children are treated accordingly, re-evaluate if the incontinence persists.

Rhabdomyosarcoma appears as a grape-like cluster with presenting symptoms of vaginal bleeding and sloughed tissue fragments passed from the vagina. After a biopsy confirms the diagnosis, then refer the patient to an oncologist.

Children with a prolapsed ureterocele typically present at age 1 month to 3 years and are irritable. It appears as a smooth, round-wall erythematous mass, which, if ischemic, can be a blue-purple-brown color. Obtain a renal-bladder sonogram, a voiding cystourethrogram (VCUG), and a renal scan. To treat, decompress the ureterocele by either an angiocatheter with aspiration of the fluid at the bedside or an endoscopic incision. It may be necessary to organize an open surgical unroofing or marsupialization of the ureterocele.

A paraurethral cyst typically appears in neonates with a cyst eccentrically displacing the meatus. Most children do not require therapy, owing to the high rate of regression during the first 4 to 8 weeks. A small percentage of cysts will require an incision. An imperforate hymen also presents in the newborn girl, with a bulging mass noted from the vagina. A hymenotomy is the treatment of choice, with a preoperative sonogram to evaluate for upper urinary tract obstruction and to determine the extent of vaginal distention.

Uterovaginal prolapse presents in the newborn girl with meningomyelocele. Although spontaneous resolution may occur, a pessary or rubber nipple may be necessary for temporary mechanical support. Urethral prolapse almost always occurs in black girls, age 1 to 9 years, presenting with bloody spotting and the urethral meatus surrounded by an erythematous protruding mucosa. Most of these children may be treated medically with estrogen cream and sitz baths.

A sacral dimple or tuft of hair may be the only physical findings that may suggest a neurologic cause (ie, spina bifida) for the incontinence. Spina bifida or myelodysplasia is a group of complex developmental anomalies caused by neural tube closure defects. This condition, which affects 1 in 1,000 births in the United States, is associated with following lesions: (1) spina bifida...
Diurnal Incontinence in Children

Patient with DIURNAL INCONTINENCE

A

History

Physical examination
Urine analysis
Urine culture
Voiding diary

B

Determine pattern of incontinence

Primary

C

Phimosis

D

Interlabial mass

E

Sacral dimple

F

UTI

G

Urinary frequency

H

Urinary infrequency

I

Constipation

J

Continuous wetting with normal examination

Secondary

Same treatment as primary incontinence

K

Ultrasonography

VCUG

Normal

Abnormal

L

Fiber, mineral oil, enemas

M

Polyethylene glycol 3350 (Miralax®)

N

Ureteral ectopia

O

Surgical correction

ACh

P

Surgical correction

Q

Urodynamics

R

Dysfunctional voiding

S

Neurogenic bladder

T

Incompetent bladder neck or urethra

U

Dysfunctional voiding

V

Urodynamic

W

ACh

X

Urodynamic

Y

Biofeedback

Z

Antibiotic plus surveillance vs surgical correction

diagram
SECTION 1 Evaluation by Complaint or Laboratory Finding

Many children with diurnal incontinence will present their parents for treatment. A careful history, physical examination, and voiding diary will allow the clinician to delineate the etiology and to prescribe proper treatment for these children. An introutal examination may demonstrate labial adhesions, resulting in urinary pooling behind the adhesions. Treat these adhesions with estrogen cream or with lysis of adhesions, which can be performed in the office. Boys may have meatal stenosis, which is treated easily with a meatotomy. If the examination is normal, the voiding diary is essential to determine the quantity of urine and the timing of each void. Most often, children who have incontinence within an hour of voiding and are dry until the next void several hours later are not completely emptying the bladder. These children are treated with double voiding, that is, having the child return to the bathroom 5 minutes after voiding to empty the residual volume. This will result in resolving the incontinence, thus emptying completely with a single void, eliminating the need to double void. The voiding diary will also identify those children with an unstable bladder, as demonstrated by frequent urination with small volumes per void. Start these children on AChs; they usually do not require urodynamic testing.

A common reason for incontinence is urinary infrequency, especially secondary incontinence. To help determine the etiology, obtain a careful history from the parents and speak directly with the child. In many children, urinary infrequency and incontinence occur only while they are in school, or the condition started while in school and has now extended to days at home. In fact, the etiology may have been social reasons or simply because the bathrooms are unclean. Similarly, the voiding diary will assist in clarifying how infrequently the child voids and will determine the quantity of urine per void. Timed voiding every 3 to 4 hours is a simple method of resolving this problem. In addition, having the parent request that the child use the nurses or teachers’ bathroom, which are typically cleaner than are the public bathrooms, may help solve the urinary infrequency. Urodynanmic testing is usually not necessary.

Constipation is a common cause of urinary incontinence with associated urinary frequency or infrequency. A child must have his back evaluated for a sacral dimple and tuft of hair; a neurologic cause may be associated with the constipation and urinary incontinence. Refer to the section on sacral dimple or tuft of hair for further discussion. Many children with a normal examination have complete resolution of all urinary problems with resolution of the constipation. To treat constipation, a simple method with over-the-counter therapy includes the use of fiber and mineral oil, with the addition of suppositories or enemas as needed. The use of polyethylene glycol 3350 (Miralax) is a second-line therapy if the more conservative methods do not resolve the constipation. Refer the child to a gastroenterologist if these therapies fail.

Children with UTIs and diurnal urinary incontinence warrant an evaluation for an anatomic cause of these problems, especially those with febrile or multiple UTIs. Evaluate for dysfunctional voiding, vesicoureteral reflux, and posterior urethral valves (in boys) with renal and bladder ultrasonography and VCUG. A nuclear cystogram is inadequate for the initial test; it will not evaluate the anatomy of the urethra properly (ie, posterior urethral valves or spinning-top urethra), bladder (ie, diverticuli or ureterocele), or ureter (ie, vesicoureteral reflux into both moieties of a duplicated collecting system). A thick-walled bladder on bladder ultrasonography and a spinning-top urethra or bladder diverticuli on VCUG are typical findings of dysfunctional voiders. Start these children on anticholinergics (ACh). If the incontinence does not resolve, then begin urodynamic testing and consider biofeedback, depending on the results of the study.

A VCUG will identify vesicoureteral reflux in children. To treat vesicoureteral reflux, prescribe antibiotic prophylaxis until the radiograph confirms that the reflux has resolved. Children may require surgical intervention, ureteral reimplantation, or endoscopic correction. Likewise, a VCUG will identify posterior urethral valves in children. These children will require resection of valves.

Many children with diurnal incontinence will present with what their parents describe as urinary frequency. A history, physical examination, and voiding diary will allow the clinician to delineate the etiology and to prescribe proper treatment for these children. An introutal examination may demonstrate labial adhesions, resulting in urinary pooling behind the adhesions. Treat these adhesions with estrogen cream or with lysis of adhesions, which can be performed in the office. Boys may have meatal stenosis, which is treated easily with a meatotomy. If the examination is normal, the voiding diary is essential to determine the quantity of urine and the timing of each void. Most often, children who have incontinence within an hour of voiding and are dry until the next void several hours later are not completely emptying the bladder. These children are treated with double voiding, that is, having the child return to the bathroom 5 minutes after voiding to empty the residual volume. This will result in resolving the incontinence, thus emptying completely with a single void, eliminating the need to double void. The voiding diary will also identify those children with an unstable bladder, as demonstrated by frequent urination with small volumes per void. Start these children on AChs; they usually do not require urodynamic testing.

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J  Girls with a normal examination require evaluation for ureteral ectopia. Ureteral ectopia occurs more commonly in females than in males, with clinical presentation being gender dependent. Females may present with urinary incontinence, whereas males never present with incontinence because the ectopia never occurs beyond the external urinary sphincter. In females, an ectopic ureteral orifice may be located proximal to the urethral sphincter (ie, within the bladder neck or proximal urethra), distal to the urethral sphincter, or outside the urinary tract (ie, vestibule, vagina, cervix, uterus, or Gartner’s duct). Those in the latter two groups may present with continuous wetting. Therefore, girls with continuous wetting require a radiographic evaluation (renal and bladder ultrasonography and VCUG) to evaluate for ureteral ectopia. Surgical options include heminephrectomy, ureteroneocystostomy, uretero-ureterostomy, and ureteropyelostomy.
Children who have a normal evaluation with the presumptive diagnosis of an unstable bladder should begin on AChs and proceed with urodynamic testing if incontinence has not resolved. Urodynamic testing may demonstrate a dysfunctional voider, a neurogenic bladder, or an incompetent bladder neck or urethra.

Children with primary incontinence with a normal evaluation or with secondary enuresis without a clear etiology should have renal and bladder ultrasonography to evaluate for an anatomic cause. Children with abnormal ultrasonography require a VCUG. Refer to the section on UTIs for further discussion.

**Additional Readings**


Urinary incontinence is defined as the involuntary loss of urine. This problem is a significant health issue, which costs in excess of 20 billion dollars per year to treat. It affects men uncommonly and is usually a manifestation of an underlying illness or the consequence of prior injury or surgery. Incontinence is much more common in women and usually reflects a less serious etiology. The diagnostic evaluation includes a thorough history and physical examination to classify the incontinence into one of several types. Key elements include previous pelvic surgeries and the presence of systemic neurologic disorders such as diabetes. A thorough medication history is equally important as many medications may have autonomic side effects. The physical examination should focus on the abdomen, pelvis, external genitalia, and a basic neurologic examination including the presence or absence of perineal sensation and evaluation of the bulbocavernosus reflex. Urodynamic studies may also help to determine and aid in formulating a treatment plan. Urinary incontinence can be broken down into several categories: stress, urge, neurogenic (reflex), overflow, congenital, and traumatic. There can also be combinations of the above.

A Stress urinary incontinence (SUI) is defined as the involuntary loss of urine associated with physical activity that increases intra-abdominal pressure. It is commonly seen in multiparous women with a weakened pelvic floor. There are three types of stress incontinence, and types IIA, IIB, and III are associated with specific anatomic defects. Type II is associated with urethral hypermobility and type III is seen with intrinsic sphincter deficiency. The Q-tip examination can assess the degree of hypermobility.1 Treatment for type II is aimed at restoring the anatomic relationship of the bladder neck and proximal urethra. This can be accomplished by any of the multiple urethropexy operations—the Burch procedure, various needle suspension procedures, the Marshall-Marchetti-Krantz procedure—or a midurethral sling.2 Type III SUI requires recreation of the sphincter mechanism and is therefore treated by a more proximal pubovaginal sling, periurethral bulking agents, or a sphincter prosthesis.3-5 One of the newer treatments for both types of incontinence is a tension-free vaginal tape (TVT). Overall, the long-term success rates are 75 to 95%.6,7

B Urge incontinence is defined as the involuntary loss of urine associated with a strong desire to void. It can occur in both males and females in the presence of a urinary tract infection, bladder outlet obstruction, or bladder cancer. De novo urge incontinence can also be the result of various suspension procedures, with an incidence from < 1% to 27%.8,9 The basic features of true urge incontinence are detrusor instability with otherwise normal anatomy, no neuropathy, and a usually normal sphincter.10 Urodynamics show a sudden rise in pressure accompanied by an urge to void or incontinence. Treatment is aimed at correcting the underlying etiology, if known. For example, in men this symptom may be due to benign prostatic hyper trophy (BPH), and it is usually relieved with transurethral resection of the prostate (TURP).11 In women, obstruction is rare and is usually due to previous pelvic surgery. If the etiology is not found, then conservative treatment is geared to eliminating the involuntary detrusor contractions via medications,12 behavior modification, electrical stimulation, or biofeedback, all with variable success rates.

C Neurogenic incontinence is a broad category that encompasses many disorders. It is defined as incontinence occurring secondary to a usually identifiable nerve lesion. The incontinence can be active (detrusor hyperreflexia)13; usually this is associated with upper motor neuron lesions. It can also be passive (sphincteric atony), which is associated more with distal lesions. A combination of the two types is possible. Often, other types of incontinence, such as urge and stress, are found simultaneously in patients with nerve injury. The micturition reflex is normally under voluntary control and is organized in the brainstem. Depending on where the lesion is, there is a wide range of presentations. If the lesion is supraspinal, micturition is physiologically normal, but awareness is altered. This occurs in cases of a cerebrovascular accident. Spinal lesions can lead to detrusor–external sphincter dyssynergia (DESD) or other manifestations of poor coordination of micturition. These lesions occur in traumatic spinal cord injury, multiple sclerosis, or other examples of transverse myelitis.14 Sacral lesions can have a variable effect, depending on the relative contribution of the parasympathetic or sympathetic system. These effects vary from bladder areflexia to sphincteric dysfunction. These types of lesions are caused by herniated disks, diabetic neuropathy, spinal cord tumors, or extensive pelvic surgery.15 The guiding principles of treatment are improvement of the neurologic condition and alleviation of the potential for upper tract deterioration. Conservative management includes anticholinergic medication or intermittent catheterization. Surgical management includes external sphincterotomy, bladder augmentation, artificial urinary sphincter, or neurostimulation.
Urinary Incontinence in Adults

Patient with URINARY INCONTINENCE

History
Physical examination
Urodynamic studies

Urinalysis
Urine culture

Determine type of incontinence

A Stress incontinence
B Urge incontinence
C Neurogenic (reflex) incontinence
D Overflow incontinence

E Congenital incontinence
F Traumatic incontinence

Goal
Obstructive
Neuropathic

Correct obstruction (TURP)
Intermittent catheterization

Conservative:
anticholinergic medication or intermittent catheterization
Surgical:
external sphincterotomy, bladder augmentation, artificial urinary sphincter, or neurostimulation

Pubovaginal sling, periurethral bulking agents, sphincter prosthesis

Improve the neurologic condition and alleviation of the potential for upper tract deterioration

Treat underlying cause if known
Identify level of neurologic lesion
Elevated postvoid residual

If not known, treat conservatively (medications, biofeedback)

Conservative:
anticholinergic medication or intermittent catheterization
Surgical:
external sphincterotomy, bladder augmentation, artificial urinary sphincter, or neurostimulation

Patients with URINARY INCONTINENCE

Males:
post-prostatectomy
Females:
fistulous communication

Correct obstruction
Intervention:
Evaluate and treat patient

Congenital incontinence
Traumatic incontinence

Postpelic fracture

Postpelic fracture

Males:
post-prostatectomy
Females:
fistulous communication

Periurethral bulking agents, AUS
Repair fistulae
Evaluate and treat

Patient with URINARY INCONTINENCE

History
Physical examination
Urodynamic studies

Urinalysis
Urine culture

Determine type of incontinence

A Stress incontinence
B Urge incontinence
C Neurogenic (reflex) incontinence
D Overflow incontinence

E Congenital incontinence
F Traumatic incontinence

Goal
Obstructive
Neuropathic

Correct obstruction (TURP)
Intermittent catheterization

Conservative:
anticholinergic medication or intermittent catheterization
Surgical:
external sphincterotomy, bladder augmentation, artificial urinary sphincter, or neurostimulation

Pubovaginal sling, periurethral bulking agents, sphincter prosthesis

Improve the neurologic condition and alleviation of the potential for upper tract deterioration

Treat underlying cause if known
Identify level of neurologic lesion
Elevated postvoid residual

If not known, treat conservatively (medications, biofeedback)

Conservative:
anticholinergic medication or intermittent catheterization
Surgical:
external sphincterotomy, bladder augmentation, artificial urinary sphincter, or neurostimulation

Patients with URINARY INCONTINENCE

Males:
post-prostatectomy
Females:
fistulous communication

Correct obstruction
Intervention:
Evaluate and treat patient

Congenital incontinence
Traumatic incontinence

Postpelic fracture

Males:
post-prostatectomy
Females:
fistulous communication

Periurethral bulking agents, AUS
Repair fistulae
Evaluate and treat
Overflow incontinence is described as the observation of incontinence accompanied by urinary retention. It is usually the result of an obstructive or neuropathic lesion producing a hypotonic bladder. This type of incontinence is usually found in men with long-standing bladder outlet obstruction owing to BPH. Common symptoms are hesitancy, decreased urinary stream, and postvoid dribbling. The key finding on physical examination is an elevated postvoid residual urine. Treatment aims to correct the obstruction. Patients with impaired detrusor contractility may benefit from intermittent catheterization. Use caution in treating incontinent patients with anticholinergics before ruling out overflow incontinence; this action may result in worsening of the urinary retention that accompanies this condition.

Congenital incontinence is usually evaluated prior to adulthood. It can be due to a number of anatomic defects. In females, an ectopic ureter can cause continuous urinary leakage. Other causes are ureteroceles or bladder extrophy. Nocturnal enuresis and/or diurnal incontinence are causes of intermittent incontinence. These causes are usually correctable in childhood with either surgery or medication.

Traumatic incontinence has a variety of causes. In males, this usually occurs after a radical prostatectomy but may also occur with an overly aggressive TURP. In many cases, postprostatectomy incontinence is transient, but it remains a persistent problem in 5 to 10% of patients. It can be caused from damage to the external urinary sphincter or from detrusor instability secondary to anastomotic stricture or bladder neck contracture. In females, the cause is usually from a fistulous communication between the urinary tract and the vagina after pelvic surgery. The fistula can involve the ureter, bladder, or urethra. This type of incontinence also refers to sphincteric damage from a pelvic fracture where the urethra was injured. Treatment for postprostatectomy incontinence is usually conservative; if it persists longer than 1 year after surgery, then periurethral injection of bulking agents or implantation of an artificial urinary sphincter (AUS) is performed. Bulking agents are of limited use in this setting; therefore, other treatment options are recommended. The long-term continence rates for AUS vary between 64 and 76%, continence being defined as using 0 to 1 pad/day. Treatment of incontinence resulting from female pelvic surgery is aimed at correction of the fistulous communication.

References
SECTION 2
THE KIDNEY
Congenital renal cystic disease consists of a spectrum of inherited or sporadically occurring conditions that may involve one kidney, both kidneys, or only a portion of the kidney. An orderly approach to an evaluation aimed at narrowing the differential diagnosis using pediatric radiographic techniques will usually allow precise identification and classification of this diverse collection of conditions.

A Congenital renal cystic disease (CRCD) may be identified on routine prenatal evaluation or as an incidental finding during postnatal radiographic evaluation. It may also be suspected from a family history of inherited disease, from physical findings such as an abdominal mass or evidence of syndromic features, or from an abnormal urinalysis or the presence of azotemia.

B The differential diagnosis and classification of CRCD are based on ultrasonographic appearance. This test will identify fluid-filled cysts or enlarged calyces, will exclude a solid tumor, and will determine whether the abnormality is unilateral or bilateral or whether it affects other organ systems. If the process is unilateral, determine whether it is focal and isolated or it appears to occupy a renal segment (upper or lower pole) or involves the entire kidney.

Further evaluation of isolated cystic disease depends on appearance, and additional studies may be necessary. Complex cysts containing septations or calcareous elements require computed tomography (CT) or magnetic resonance imaging (MRI) discrimination to exclude a proliferative process. Single or multiple simple cysts can usually be followed with serial ultrasonograms, provided that they fulfill strict criteria for benign cysts and do not include evidence of a solid component. Calyceal diverticulum and parapelvic cyst may require additional evaluation to exclude obstruction by cyst compressing infundibula or ureteropelvic junction (UPJ).

C If the lesion is unilateral, the major differential diagnosis is between hydronephrosis and multicystic kidney (MCK) (Figure 13-1). Although specific ultrasound criteria exist to distinguish one from the other, overlap often occurs. Generally, further evaluation using nuclear isotope renal scanning is required to determine whether or not the suspected cystic lesion functions (visualizes on scan) and whether the whole kidney or only a segment of the kidney is involved (Figure 13-2). MCK is characterized by complete nonfunction; however, occasionally faint amounts of isotope may be seen within the mass of cysts. When good functioning (visualizing) parenchyma is observed, it usually indicates that the suspected cystic mass is actually a hydronephrotic kidney, and additional diagnostic testing is required to determine the cause of the hydronephrosis and whether or not the kidney is obstructed.

D A cystic lesion that involves only a segment of the kidney requires further evaluation using CT, MRI, or even an intravenous pyelogram (IVP) to exclude a honeycombed septated cystic lesion (termed cystic nephroma or cystic partially differentiated nephroblastoma, if the septa contain nephroblastoma). These lesions, previously termed multilocular cysts, based on appearance, require nephrectomy, which is usually curative because of the proliferative nature of the process. Most commonly, however, the lesion will prove to be a duplication anomaly, with the poor or nonfunctioning segment representing a localized hydronephrosis or dysplasia, which often affects the upper pole.

E Bilateral cystic disease occurs in various inheritable and sporadic congenital conditions. Rare conditions, such as Jeune’s asphyxiating thoracic dysplasia and the nephronophthisis medullary cystic disease complex, may be suspected because of specific associated syn-
Congenital Renal Cystic Disease

- Risk factors
- Physical examination
- Urinalysis
- Renal function studies
- Ultrasonography
- Ultrasoundography
- Unilateral
  - Isolated
  - Segmental
  - Complete
- Bilateral
  - Sporadic
  - Inherited
- Simple/complex cyst
- Parapelvic cyst
- Calyceal diverticulum
- Renal scan
- Medullary sponge kidney
- Hydronephrosis
- CT/MRI/IVP
- MCK
- Cystic nephroma
  - Cystic partially differentiated nephroblastoma
- Occult duplication
- Autosomal dominant PCKD
- Autosomal recessive PCKD
- Medullary cystic disease
- Juvenile nephronophthisis
- Syndromic cystic disease
- Glomerulocystic disease
- Tuberous sclerosis
- Von Hippel-Lindau disease

Figure 13-2 Renal scan demonstrates nonfunctioning left kidney with absence of radioisotope uptake. Tracer is seen in right kidney and bladder.

dromic abnormalities or a strong family history. Dilated collecting ducts in medullary sponge kidney, rarely seen in young children, generally require an IVP and a family history for diagnosis. Polycystic kidney disease (PCKD) is always a concern in patients with bilateral cystic disease. The infantile variety, which has an autosomal recessive transmission, may be recognized early in the neonatal period if the kidneys are large and finely honeycombed or at a later age in less severe cases. Although adult type or autosomal dominant PCKD can be diagnosed antenatally or in infancy, generally, it does not assume its classic appearance of large bilateral cyst-distorted kidneys until early adulthood because it usually progresses inexorably toward end-stage renal disease by the fifth decade. Imaging studies supported by a positive family history and signs and symptoms of hematuria, hypertension, and palpable masses permit accurate diagnosis.

Additional Reading
Adult Polycystic Kidney Disease

Elizabeth J. Anoia, MD, and Michael G. Oefelein, MD

A Adult polycystic kidney disease (ADPKD) is a systemic, hereditary disorder with an approximate incidence of 1 in 1,000 live births. It is the most common form of cystic disease of the kidney and the third most common cause of end-stage renal disease (ESRD) after diabetes mellitus (DM) and hypertension (HTN). This disease is usually asymptomatic until between age 30 and 40; however, <10% of cases present in the first decade of life. Extrarenal manifestations include cystic lesions of the liver, spleen, pancreas, and a higher incidence of cerebral aneurysms (10 versus 2% in the general population).

B There is a “two-hit” genetic hypothesis of cystogenesis. The two most commonly involved genes are located on chromosomes 4 and 16. It is inherited as autosomal dominant with variable penetrance. Embryologically, the underlying theory is a defect in the development of the renal collecting system, resulting in a progressive functional impairment.

C Grossly, the kidneys are enlarged with various-sized cysts scattered on the surface and within the parenchyma. Calcification within the cyst wall is possible, with cyst fluid usually being amber colored. Microscopically, there is peritubular fibrosis, a decreased number of glomeruli, and renal arteriolar thickening.

D Common presenting symptoms include pain, hematuria, or infection. Flank pain is the earliest and most common symptom. It can be due to the sheer weight of the kidneys, obstruction, cyst hemorrhage, or infection. Hematuria can be microscopic or gross and can be severe. Urinary tract infection can present as pyelonephritis or cyst infection. The important physical examination findings are hypertension, abdominal mass, and abdominal tenderness. HTN is found in 60 to 70% of patients and is a predictor of renal functional decline. Angiotensin-converting enzyme inhibitors (ACE-I) are usually the first-line treatment. Palpable kidneys on abdominal examination also occur in approximately 60% of patients. Tenderness is less common and usually occurs if there is infection. Laboratory evaluation is significant for anemia, proteinuria, microhematuria, and decreased creatinine clearance.

E There are multiple modalities that may aid in diagnosis. On plain abdominal radiographs, enlarged renal shadows can be seen bilaterally. Intravenous (IV) and retrograde pyelography illustrate a “spider deformity” of the calyces. These studies can also localize a possible area of obstruction. However, if possible, avoid retrograde pyelography, owing to the increased risk of introducing an ascending infection. Ultrasonography is the preferred method for the diagnosis of ADPKD because of its availability, sensitivity (100% in patients > age 30), and lack of exposure to radiographic material. Overall, contrast-enhanced computed tomography (CT) scans are the most sensitive diagnostic procedures, which can also detect possible complications such as stones, infection, and hemorrhage. Nuclear imaging studies show multiple cold avascular spots. Renal arteriograms demonstrate a classic “C” appearance of the vessels around the cysts. They can also demonstrate renal cell carcinoma, which can develop in polycystic kidneys.

As intracranial aneurysm (ICA) rupture is a potentially life-threatening manifestation of extrarenal ADPKD, we recommend radiographic imaging of the brain. In those patients with either a family history of ICA or a previous aneurysm rupture, screening with magnetic resonance angiography is usually started in the third decade of life.

F ADPKD must be distinguished from other disorders that have a similar constellation of renal findings. These include bilateral hydronephrosis, bilateral renal tumors, von Hippel-Lindau disease, and tuberous sclerosis. Most of these can be differentiated based on radiographic studies and the presence of other associated conditions.

G These patients generally receive supportive and nonoperative treatment. The goal is to manage the ESRD that inevitably develops and to manage the possible complications before and after developing renal failure. A low-sodium and low-protein diet has been noted to be beneficial. The clinician can manage severe pain and obstruction with decompression via a percutaneous aspiration and sclerosis or open drainage. Stones are treated with extracorporeal shock wave lithotripsy (ESWL) or percutaneously, with a > 80% success rate. Options for severe hematuria include embolization or nephrectomy. Manage infections with either IV antibiotics or drainage (percutaneous or open). Once renal failure develops, the only treatment options are dialysis or transplantation. The first sign of renal failure is an inability to maximally concentrate urine. Dialysis in these patients has a similar risk–benefit profile as the general population. Cadaveric transplantation is usually successful, that is, the cysts do not recur. Pretransplant bilateral nephrectomies have limited indications secondary to the high morbidity. The indications for pretransplant nephrectomies in ADPKD are recurrent infections, persistent bleeding, or that the size of the native kidneys precludes successful transplantation.
Adults with this disease have a more favorable prognosis than do children. Although uncommon in children, the progression to renal failure is much more rapid in those diagnosed with ADPKD within their first year of life. Adult patients generally do not live longer than 5 or 10 years after the onset of renal failure unless dialysis or renal transplantation occurs. The mean age of death is about age 50 years.16

**References**

Antenatal detection of hydronephrosis has led to the early identification of suspected ureteropelvic junction (UPJ) obstruction.1–3 Infants can present with a palpable abdominal mass or, occasionally, urosepsis. Symptomatic presentation of UPJ obstruction owing to intermittent episodes of abdominal or flank pain or nausea and/or vomiting is also noted in older children.4 Minor trauma contributing to hematuria can lead to the detection of a hydronephrotic kidney.5

The mainstay in detecting a suspected UPJ obstruction is ultrasonography of the kidneys and the bladder.6 I recommend a voiding cystourethrogram (VCUG) study to rule out vesicoureteral reflux, reported to occur in 13 to 42% of infants who are detected with hydronephrosis.7,8 In addition, this study is warranted in those children who present with a urinary tract infection. In the past, an intravenous pyelogram (IVP) was performed to diagnose a UPJ obstruction; however, currently diuretic renography has replaced the fluoroscopic imaging.9

MAG III diuretic renography has become the preferred method, allowing differential renal function and assessing washout from the individual kidney. Even so, controversy still exists about the interpretation of this study and the actual criteria used to define obstruction.10,11 Interpret cautiously diuretic renography performed in infants under age 6 weeks because of the transitional nephrology that exists in these developing kidneys. In the face of an equivocal study, repeating diuretic renography in 6 to 8 weeks can help establish a trend with respect to differential function, as well as washout from the affected kidney. The IVP helps in a situation wherein a symptomatic UPJ obstruction exists. Because this obstruction tends to be intermittent in nature, an IVP performed at the time the patient has symptoms can show the anatomy that may not be apparent at other times.

The Anderson-Hynes pyeloplasty is the most commonly employed open surgical procedure for the repair of UPJ obstruction.12 This technique that dismembers the ureter has widespread applicability owing to preserving anomalous vessels, excising the pathologic UPJ, allowing for appropriate repositioning, and finally incorporating successful reduction pyeloplasty. The surgeon prefers the placement of a JJ stent at the time of a dismembered pyeloplasty. Moreover, this may prove beneficial in a difficult anastomosis or with an infant pyeloplasty where poor peristalsis of the ureter can lead to persistent drainage from the anastomotic site postoperatively. Laparoscopic innovations include the repair of the UPJ obstruction.13 This technique is still primarily used in a handful of academic centers, but more widespread application is forthcoming.14–21 Table 15-1 provides the pyeloplasty results.

The endoscopic approach to UPJ obstruction has been successful, both in an antegrade and a retrograde fashion.22–24 Antegrade endopyelotomy can be performed under direct visualization, using a cold knife or electrocautery or the Acucise® device. Retrograde endopyelotomy is most easily accomplished in adolescents and adults and may require placement of a 6 or 7 French stent at least 1 week before the endopyelotomy to allow for passive dilation of the ureter. Postoperatively, the endopyelotomy stent (14F/7F) is maintained for 6 to 8 weeks. Table 15-2 provides the results of endopyelotomy.

The use of a nephrostomy tube for urinary diversion, with or without a ureteral stent across the anastomosis, is employed in certain situations.31 The repair of a solitary kidney in an infant or a redo pyeloplasty may warrant using a nephrostomy tube. The use of a nephrostomy tube without a ureteral stent across the anastomosis might permit apposition of the edges of the anastomosis immediately postoperatively, but, in reality, this is rarely seen. With the use of a nephrostomy tube, the Penrose drain can usually be removed in the first 48 hours following surgery. If a ureteral stent is employed, this, too, is removed soon following surgery. A nephrostogram is performed 10 to 14 days following surgery, using a low-pressure, gravity-drip nephrostogram on an outpatient basis. The use of intramuscular (IM) antibiotics prior to the procedure can limit the chances of a transient bacteremia. With evidence of good drainage, the nephrostomy tube can be removed. If there is inappropriate drainage initially, then the

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Patients or Kidneys</th>
<th>Success (%)</th>
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<tbody>
<tr>
<td>Poulson et al14</td>
<td>1987</td>
<td>35</td>
<td>100</td>
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<tr>
<td>O’Reilly15</td>
<td>1989</td>
<td>30</td>
<td>83–93</td>
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<tr>
<td>MacNeily et al16</td>
<td>1993</td>
<td>75</td>
<td>85</td>
</tr>
<tr>
<td>Shaul et al17</td>
<td>1994</td>
<td>32/33(&lt; age 2 mo)</td>
<td>97</td>
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<tr>
<td></td>
<td></td>
<td>30/33(&gt; age 2 mo)</td>
<td>93</td>
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<tr>
<td>Salem et al18</td>
<td>1995</td>
<td>100</td>
<td>98</td>
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<tr>
<td>McAleer and Kaplan19</td>
<td>1999</td>
<td>79</td>
<td>90</td>
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<tr>
<td>Austin et al20</td>
<td>2000</td>
<td>135/137</td>
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<tr>
<td>Houben et al21</td>
<td>2000</td>
<td>186/203</td>
<td>93</td>
</tr>
<tr>
<td>Jarrett et al13</td>
<td>2002</td>
<td>100</td>
<td>96*</td>
</tr>
</tbody>
</table>

*Laparoscopic.
Patient with URETEROPELVIC JUNCTION OBSTRUCTION

A History and physical examination

B Ultrasoundography, VCUG

C Diuretic renography

Equivocal

Positive

Negative

D Dismembered pyeloplasty (with/without JJ stent or nephrostomy tube)

E Endopyelotomy with JJ stent

Repeat ultrasoundography

F Nephrostogram

Without Drainage

With Drainage

Continue nephrostomy drainage

Remove nephrostomy tube

Stent removal 6–8 weeks

Follow-up ultrasonography 6–8 weeks

Stable hydronephrosis

Improved hydronephrosis

Follow-up ultrasonography 2 months

Diuretic renogram 6–12 months

Stable/worsening hydronephrosis

Diuretic renography

Improvement

No improvement

Observe

H Percutaneous nephrostomy tube/antegrade nephrostogram

Endopyelotomy

Redo pyeloplasty versus ureterocalicostomy

G Reoperation
nephrostomy tube should be left simply to gravity drainage for a period of time to allow for complete resolution of anastomatic edema. It is important to maintain patience because most cases with initial lack of drainage will show appropriate drainage by 4 months postoperatively. In the situation whereby there is significant drainage from the Penrose site, the Penrose should be left in place until the drainage subsides. Alternatively, retrograde placement of a ureteral stent in situations wherein a major anastomotic leak occurs can lead to prompt resolution of this drainage.

G The open repair of a UPJ obstruction has a very high success rate. In those rare situations whereby the degree of pyelocalyctasis does not improve and the furosemide (Lasix) renogram fails to show improvement, then reoperation is warranted. Clinicians sometimes see a failure owing to extrinsic compression secondary to a lower-pole crossing vessel. An intraperitoneal approach to the kidney facilitatesredissection around the renal pelvis. A ureterocalicostomy, whereby the ureter is anastomosed to a lower-pole calix, may benefit in this situation. To facilitate anastomosis between the calix and the ureter, it is imperative that the parenchyma of the lower pole be amputated.

H A nephrostomy tube placement in stable or worsening hydronephrosis or poor washout following a pyeloplasty can help to delineate the anatomy. The opening pressure at the time of the nephrostomy tube placement can predict the degree of obstruction that exists. An antegrade nephrostogram will determine if the anastomosis is in a dependent position and whether there is evidence of a focal narrowing. Then an antegrade endopyelotomy may be the ideal approach. Alternatively, if the anastomosis is not in an ideal location or if a long stricture is present, an open surgical approach may be necessary.

References
Anomalies of renal development may be discovered on prenatal ultrasound examination during serendipitous imaging of the kidneys; during urinary tract imaging initiated to evaluate urinary tract infection (UTI), hematuria, hypertension, and renal failure or other urinary symptoms; and during screening for sibling uropathy. When performing renal imaging in children, it is important to compare renal lengths to published standards. Without attention to this detail, the significance of symmetric but abnormally small kidneys may be overlooked. Although unilateral anomalies of development may be asymptomatic, oligohydramnios and perinatal death or renal failure may accompany bilateral lesions. Older children may present with chronic renal failure. Many factors may be responsible for diminished renal size or renal growth failure. Radiographic and even pathologic examination can fail to disclose the exact nature of the original insult.

In cases without obstruction or vesicoureteral reflux, clinicians often assume that a misadventure of ureteral bud development resulted in abnormal renal parenchyma. Renal hypoplasia and dysplasia are known to associate with several genetic syndromes, including those described by Turner, Drash, and Beckwith-Wiedemann. In 1973, Buchta and colleagues described the syndrome of hereditary renal adysplasia as an autosomal dominant trait with incomplete penetrance and variable expression. The literature shows many families with this syndrome, with varying presentations of unilateral and bilateral renal agenesis and cystic and noncystic renal dysplasia, and without apparent phenotypic difference from that found in sporadic cases. This suggests that many cases of renal agenesis are transmitted by autosomal dominant inheritance and that families of individuals with unilateral or bilateral renal agenesis (and perhaps dysplasia) should receive ultrasound screening examinations.

Image small or dysmorphic kidneys with two primary purposes in mind. The first is to document the presence or absence of vesicoureteral reflux (VUR) and the second is to determine relative differential renal function. Perform a voiding cystourethrography (VCUG) to detect and grade VUR. In addition, valuable information about bladder configuration and function may be obtained. Avoid using nuclear cystography in the initial evaluation of any patient; this technique is capable only of detecting the presence or absence of VUR without offering an assessment of bladder anatomy and dynamics, urethral anatomy, and accurate reflux grading. Differential renal function may be evaluated by radionuclide imaging using Tc 99m dimercaptosuccinic acid (DMSA). Diuresis renography is more appropriate when a functional assessment of obstruction is required in the presence of hydronephrosis or hydroureteronephrosis. In patients with renal failure, radionuclide imaging may not provide useful functional information.

The term hypoplasia is generally used to describe a small, architecturally and histologically normal kidney, usually associated with normal ureteral orifice configuration and position. These kidneys have fewer nephrons than do normal kidneys; thus, the term, “oligonephronia” has been used. “Dwarf” kidneys generally require observation only if VUR is absent and if the patient is normotensive. When vesicoureteral reflux is present, determine management by globally assessing the patient’s renal status, including the state of the contralateral renal unit and the total renal function. Hypertension or VUR into a poorly functioning kidney (differential function < 15%) may merit nephroureterectomy if UTIs are a concern, whereas ureteral reimplantation may be more appropriate if the kidney has reasonable function. In the absence of hypertension or UTI, observation may be appropriate, although the risks of infection are greater in younger females, and reflux management may be of primary concern.

In the same way, renal injury may cause small kidneys. Vascular insult (renal venous thrombosis) and infection (pyelonephritis) are common causes. If hypertension occurs, nephrectomy is indicated. Small kidneys associated with VUR may be congenitally small or may have been damaged by pyelonephritis. In many cases, a combination of factors is thought to be causative (eg, anomalous ureteral bud development and reflux nephropathy). Good kidney function may
warrant ureteral reimplantation. If function is poor, however, nephrectomy or nephroureterectomy may be appropriate.

Renal parenchymal dysplasia, a developmental anomaly that results in a pathologically distinct appearance of the renal parenchyma, is characterized by the presence of disorganized tissue composed of primitive ducts and ductules surrounded by fibromuscular collars and by embryonic mesenchymal tissue, with microcysts or macrocysts and nests of metaplastic cartilage. Normal nephrons may be present to a variable degree, interspersed among the dysplastic elements. Because nephron development is hindered in these cases and the number of normal nephrons is diminished, some authors use the term hypodysplasia. Kidneys with
dysplasia may be large or small, depending, in part, on whether microcysts or macrocysts are present and whether VUR or obstruction is associated with dilation of the collecting system.

Renal dysplasia is frequently associated with developmental or structural anomalies of the urinary tract, including high-grade VUR and severe obstructive uropathies, including ureteropelvic junction obstruction, urethral valves and atresia, prune-belly syndrome, ureteral ectopia, megaureter, and ureterocele.41–45 In these severe uropathies, the unanswered question is whether the dysplasia is an embryologic consequence of anomalous ureteral bud development, which also leads to the collecting system abnormality or whether the collecting system abnormality, (VUR or hydronephrosis) resulted in renal injury.4 Although the clinician must examine each case as a unique situation, many consider that both factors play a role in most situations.

A scheme to manage dysplastic kidneys must be developed after assessing multiple factors, specifically, the configuration and function of the kidney and its collecting system, and considering confounding factors, such as hypertension and the presence of UTI or incontinence. Clinicians may treat dysplasia associated with ureteropelvic junction obstruction by pyeloplasty when renal function is adequate or by nephrectomy when function is poor.46 In kidneys with borderline renal function, temporary percutaneous nephrostomy drainage may be used to relieve obstruction.47 This permits a secondary assessment of renal function after a period of observation. If function remains poor, nephrectomy is performed, and if function improves, pyeloplasty may be appropriate. In other cases of obstructive uropathy, repair is indicated unless renal function is poor or absent, in which case, nephrectomy may be more appropriate. Treat refluxing renal units by doing either ureteral reimplantation or by performing nephroureterectomy.

Give special consideration to boys with posterior urethral valves and unilateral VUR associated with a poorly functioning ipsilateral kidney and a functional contralateral kidney. In many cases, the refluxing system is associated with renal dysplasia (VURD syndrome [VUR and renal dysplasia]).48,49 If the refluxing renal unit is removed, pressures generated by the poorly compliant bladder, even after ablation of the urethral valves, may be forced upon the solitary remaining ureter and kidney, resulting in hydronephrosis or reflux and secondary renal injury. In a sense, the refluxing dysplastic kidney, acting as a pop-off mechanism, protected the contralateral kidney from high-pressure injury. Ureterocystoplasty or enterocystoplasty may be indicated to improve bladder compliance and to prevent initiation of injury to the solitary kidney.50–52

D Unilateral renal agenesis is one of the most common anomalies of the genitourinary tract. When clinicians think renal agenesis is present, they should perform a complete ultrasound examination of the retroperitoneum and of the lower abdomen. If there is a possibility that a small ectopic kidney might be present (ie, in cases of an ipsilateral ectopic ureter with incontinence), a nuclear medicine scan using DMSA may help in locating the ectopic kidney.53,54 In rare cases of presumed ureteral ectopia and with a small dysplastic kidney, cystoscopy and retrograde pyelography may localize the kidney.55

When unilateral renal agenesis is confirmed, give special consideration to evaluation and long-term follow-up in females. The close developmental relation of the wolffian and müllerian systems during embryogenesis means that, in a significant number of patients with unilateral renal agenesis, müllerian anomalies will be discovered, including vaginal and uterine duplication, uterus didelphys, uterus didelphys with an imperforate or dysplastic uterine horn, as well as other similar anomalies, which may be the consequence of a unilateral müllerian developmental anomaly.56,57 Because many of these anomalies will be undetectable by imaging the infant uterus, carry out serial pelvic ultrasonography in preadolescents and adolescents. There is evidence to link hereditary renal adysplasia with müllerian anomalies on a genetic basis. It has also been well documented that spontaneous involution of multicystic renal dysplasia occurs not uncommonly, and the remnant kidneys may be invisible on imaging studies.58,59 In these cases, wolffian and müllerian development is presumably normal, and müllerian anomalies should not be expected to be present.

References


Acute renal failure (ARF) is characterized by progressive azotemia over hours to days and by elaboration of a urine isosmolar with plasma. Oliguric renal insufficiency (urine volume < 400 mL/24 hours) is the most common form of ARF. However, in recent years, nonoliguric ARF has been increasingly recognized and now accounts for 35 to 40% of all ARF cases. The distinction is important because nonoliguric ARF probably represents a less severe form of ARF and has a substantially lower mortality than the oliguric variety. The differential diagnosis of ARF is classically divided into prerenal causes, renal parenchymal disease, and postrenal (obstructive) etiologies. Using this approach, the list of disorders associated with ARF is extensive. Table 17-1 shows the principal causes of ARF. Hospital-acquired ARF is not only a common problem (2 to 4% of all admissions) but is frequently multifactorial and iatrogenic. Decreased renal perfusion, aminoglycoside administration, exposure to nonsteroidal anti-inflammatory drugs (NSAIDs), use of angiotensin-converting enzyme (ACE) inhibitors, and infusion of radiocontrast media are the most common causes of ARF in the hospital setting.

The differential diagnosis of ARF begins with a thorough history and a physical examination. Patients with obvious hypotension, volume depletion, or obstructive uropathy must be identified. In addition, a careful review of medications will often reveal a temporal relation between drug administration and declining renal function in cases of drug-induced ARF.

Serial determinations of kidney function document the progressive rise in creatinine and blood urea nitrogen (BUN). Monitor electrolytes, including calcium and phosphorus, twice daily to assess the tempo of ARF and the response to any therapeutic maneuvers.

Several urinary indices are helpful in distinguishing pre-renal azotemia from intrinsic renal disease in oliguric ARF, especially when the history and physical examination provide equivocal information (Table 17-2). Patients with prerenal azotemia generally demonstrate a

### Table 17-1  Principal Causes of ARF

<table>
<thead>
<tr>
<th>Prerenal</th>
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<tbody>
<tr>
<td>Volume depletion</td>
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<tr>
<td>Hemorrhage</td>
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<td>Gastrointestinal fluid loss</td>
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<tr>
<td>Third-space losses</td>
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<tr>
<td>Diuretics</td>
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<tr>
<td>Congestive heart failure</td>
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<tr>
<td>Myocardial infarction</td>
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<tr>
<td>Sepsis</td>
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<td>Hepatorenal syndrome</td>
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<td>Vascular—renal artery or vein occlusion</td>
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<thead>
<tr>
<th>Renal</th>
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<tbody>
<tr>
<td>Acute glomerulonephritis</td>
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<tr>
<td>Poststreptococcal</td>
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<tr>
<td>Collagen vascular disease</td>
</tr>
<tr>
<td>Small vessel vasculitis</td>
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<tr>
<td>Acute interstitial nephritis</td>
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<tr>
<td>β-Lactam antibiotics</td>
</tr>
<tr>
<td>Sulfonamides</td>
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<tr>
<td>Sarcoïdosis</td>
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<tr>
<td>Acute tubular necrosis</td>
</tr>
<tr>
<td>Ischemia—hypotension owing to volume depletion, sepsis, myocardial infarction</td>
</tr>
<tr>
<td>Nephrotoxins</td>
</tr>
<tr>
<td>Aminoglycosides</td>
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<tr>
<td>Amphotericin</td>
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<tr>
<td>Radioiodinated contrast media</td>
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<tr>
<td>Hemepigments</td>
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<tr>
<td>Myoglobin</td>
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<tr>
<td>Hemoglobin</td>
</tr>
<tr>
<td>NSAIDs</td>
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<tr>
<td>Altered vascular reactivity</td>
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<tr>
<td>ACE inhibitors</td>
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<tr>
<td>Angiotensin receptor blockers</td>
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<td>Myeloma</td>
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</table>

<table>
<thead>
<tr>
<th>Postrenal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bilateral ureteral obstruction</td>
</tr>
<tr>
<td>Infravesical obstruction</td>
</tr>
</tbody>
</table>

\[ U_{\text{Na}} < 20 \text{ mEq/L} , \text{ a fractional excretion of sodium (FE}_{\text{Na}}) < 1 , \text{ a U/P creatinine} > 40 , \text{ and a U/P osmolality} > 1.5 . \]

On the other hand, subjects with intrinsic renal disease usually have a \( U_{\text{Na}} > 40 \text{ mEq/L} , \text{ a FE}_{\text{Na}} > 1% , \text{ a U/P creatinine} < 20 , \text{ and a U/P osmolality} < 1.1 . \)
Acute Renal Failure

Patient with ACUTE RENAL FAILURE

Progressive increase in BUN, creatinine

A History and physical examination

B Serial BUN, creatinine, electrolytes

Oliguric patient

Nonoliguric patient

C Urine and serum sodium, creatinine, and osmolality

D Prerenal disease

Volume depletion

Congestive heart failure

Saline (colloid)

Diuretics

Afterload reduction

E Renal ultrasonography

Normal-size kidneys

Hydronephrosis

Bilateral small kidneys

Relieve obstruction

F Urinalysis

Renal parenchymal disease

G Supportive management

H Unresponsive fluid overload, acidosis, hyperkalemia

Signs and symptoms of uremia BUN > 100 mg/dL

Dialysis
The two most common causes of prerenal azotemia in hospitalized patients are intravascular volume depletion and congestive heart failure. Prerenal azotemia owing to volume depletion should respond promptly to fluid resuscitation with isotonic saline or colloid administration. Treat patients with oliguric prerenal azotemia consequent to systolic dysfunction with afterload reduction, diuretics, and digoxin. If renal function does not improve with appropriate therapy, consider superimposition of prerenal azotemia on chronic renal parenchymal disease.

Renal ultrasonography is critical in patients with both oliguric and nonoliguric renal failure. It excludes hydronephrosis, making the diagnosis of obstructive uropathy extremely unlikely. In addition, it assesses renal size and symmetry. In patients with bilateral obstruction or obstruction in a solitary kidney, the site of obstruction must be identified and treated appropriately. Bilateral small kidneys (less than 8 cm in length) indicate a long-standing, most likely irreversible, parenchymal or vascular process. If ultrasonography demonstrates unobstructed normal-size kidneys, further evaluation for treatable causes of ARF is essential.

Perform a careful urinalysis in all patients with ARF. Renal tubular cells, renal tubular cell casts, and pigment-ed casts suggest acute tubular necrosis (ATN). Differential diagnostic considerations would then include prolonged renal ischemia, contrast nephropathy, sepsis, or nephrotoxic drugs, such as aminoglycosides (see Table 17-1). Eosinophiluria and white blood cell (WBC) casts are characteristic of allergic interstitial nephritis, which usually resolves with discontinuation of the offending drug. If renal function does not improve, a trial of glucocorticoid therapy may be warranted. Persistent renal failure, unresponsive to steroid therapy, is an indication for renal biopsy. Red blood cell (RBC) casts and/or proteinuria > 3 g/24 h suggest glomerulonephritis, vasculitis, or multiple myeloma. In cases of suspected glomerulonephritis or vasculitis, percutaneous renal biopsy is usually required to establish a specific diagnosis. When multiple myeloma is suspected, perform both serum and urine immunoelectrophoresis to include or exclude this diagnostic consideration. If the urine is positive for blood but no RBCs are found on microscopic examination, myoglobinuria or hemoglobinuria should be considered. Rhabdomyolysis resulting in myoglobinuria can be consequent to crush injuries, burns, seizures, or drug overdoses. An elevated serum creatine kinase is characteristic; a urine that is positive for myoglobin confirms the diagnosis. Appropriate therapy for myoglobinuric acute renal failure consists of aggressive fluid administration, administration of mannitol, and alkalinization of the urine.

With prompt recognition of the precipitating event and appropriate therapy, most ARF cases are self-limited and do not require renal replacement therapy. Nevertheless, these patients require careful monitoring and correction of electrolyte disturbances, fluid imbalance, and acid-base disturbances until renal function improves. Sodium polystyrene sulfonate (Kayexalate®) may be required for mild-to-moderate hyperkalemia. Sodium bicarbonate or its equivalent can be given if the serum bicarbonate concentration falls below 15 mEq/L. Both measures should be employed judiciously because they can worsen fluid overload. Review medications and make appropriate dose adjustments for the patient’s level of renal function. Finally, place the patient on a diet that is restricted in sodium, potassium, and protein (ie, a renal diet).

<table>
<thead>
<tr>
<th>Table 17-2 Characteristic Urinary Indices in Oliguric ARF</th>
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<tbody>
<tr>
<td>Urine sodium (mEq/L)</td>
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<tr>
<td>&lt; 20</td>
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<tr>
<td>Fractional excretion of sodium</td>
</tr>
<tr>
<td>Urine/plasma creatinine</td>
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<tr>
<td>Urine/plasma osmolality</td>
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</table>
Fluid overload, metabolic acidosis, or hyperkalemia that is unresponsive to conservative medical management, as well as signs and symptoms of uremia, such as nausea, vomiting, asterixis, or pericarditis, indicates renal replacement therapy. Although the data are inconclusive, it is probably best to institute early, prophylactic renal replacement therapy when the BUN reaches 100 mg/dL or the creatinine 10 mg/dL rather than allow clinical indications or uremic complications to develop. When renal replacement therapy is required, the choice between intermittent hemodialysis and continuous modalities will depend on the patient’s hemodynamic status and local expertise. Despite major diagnostic and therapeutic advances, mortality in patients with ARF who require dialysis has declined little over the past several decades and remains at about 50% for postoperative ARF, 35% for nephrotoxin-induced ARF, and 20% for postpartum renal insufficiency.

References
Chronic renal failure (CRF), eventually resulting in end-stage renal disease (ESRD) that requires dialysis or transplantation, is a major health problem worldwide. In a patient with an elevated serum creatinine, first the physician must determine whether the renal dysfunction is acute or chronic. The initial diagnostic approach to CRF includes determining whether the renal disease is glomerular, interstitial, or vascular based on a careful history, urinalysis, and measurement of 24-hour protein excretion. Establishing a specific diagnosis requires additional serologic studies, renal biopsy, renal ultrasonography, or imaging of the renal arteries. Once a diagnosis is made, management considerations begin with identification and correction of any acute reversible causes of renal dysfunction that may be superimposed on CRF. In patients with established CRF, for whom specific treatment is unavailable, several therapeutic maneuvers (eg, excellent blood pressure control and dietary protein restriction) have been shown to retard the progression of renal disease. After implementing these therapeutic strategies, the physician must anticipate and treat the multiple manifestations of CRF, including hypertension, anemia, hyperkalemia, metabolic acidosis, and fluid overload. Because most forms of chronic renal disease ultimately culminate in ESRD, patients should be educated with respect to dialysis and transplantation well in advance of the need for renal replacement therapy.

A The initial challenge is to determine whether the renal dysfunction is acute or chronic. A slow progressive increment in serum creatinine over months or years is best documented by reviewing previous laboratory values. Not infrequently, these data are unavailable, and the physician must rely on clinical evaluation, laboratory studies, and radiologic features to make this critical distinction. In patients with acute renal failure (ARF), a precipitating event (ie, volume depletion, administration of nephrotoxic drugs) is often temporally related to the increment in serum creatinine. Patients with ARF tend to be more symptomatic at any level of renal dysfunction compared with patients with CRF. In addition, anemia, hypocalcemia, and hyperphosphatemia are frequent in CRF but less marked in ARF. Finally, bilateral small kidneys on ultrasonography are diagnostic of chronic irreversible renal insufficiency.

B It is important to determine the cause of CRF once the chronic nature of renal dysfunction is established. From a diagnostic perspective, CRF can be broadly grouped into glomerular disease and interstitial or vascular disease (Table 18-1) on the basis of several laboratory and clinical features. Red blood cell casts on urinalysis, proteinuria > 3.5 g/24 h, or the presence of a systemic disease associated with a glomerulopathy (eg, diabetes, lupus) are predictive of glomerular disease. On the other hand, a bland urinalysis, minimal proteinuria, and the absence of a systemic illness associated with a glomerulopathy indicate chronic interstitial or vascular disease. Except for diabetic nephropathy and lupus nephritis, definitive diagnosis of glomerular disease requires a renal biopsy. A biopsy, however, is of limited help in determining the etiology of chronic interstitial disease; an accurate diagnosis generally requires a careful history and renal imaging studies (see Table 18-1).

C Renal disease of any cause impairs autoregulation of renal blood flow and enhances the nephrotoxic potential of various pathophysiologic states and pharmacologic agents. Hence, patients with CRF are susceptible to develop further acute decrements in renal function owing to various insults (Table 18-2). Volume depletion, congestive heart failure, urinary tract obstruction,
nephrotoxic drugs, and administration of radioiodinated contrast material are frequently responsible for acute declines in renal function in the setting of CRF.

D Unfortunately, there are no specific effective therapies for most renal diseases. Nevertheless, several nonspecific maneuvers have been shown to slow renal disease progression. The most effective among these includes controlling blood pressure, applying drugs that interrupt the renin-angiotensin-aldosterone (RAA) system, restricting dietary protein, and controlling blood glucose.\(^2\)\(^-\)\(^5\) Reducing blood pressure slows the decline in renal function. Reduce blood pressure to at least 130/80 mm Hg and to 125/75 mm Hg in patients with proteinuria > 1–2 g/24 h.\(^1\)\(^-\)\(^3\) Angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) are more renoprotective than are other classes of antihypertensive agents and thus should be first-line therapy in hypertensive patients with CRF.\(^4\) The National Kidney Foundation recommends a restriction of dietary protein to a level of 0.6 g/kg body weight for patients with a glomerular filtration rate (GFR) less than 25 mL/min.\(^5\) This maneuver has a small but statistically significant effect to slow the rate of renal function loss. Finally, excellent blood sugar control with glycohemoglobin < 7% retards the progression of diabetic nephropathy.\(^1\)\(^,\)\(^2\)

E Progressive CRF results in multiple clinical manifestations, the more common of which are outlined in Table 18-3.\(^1\)\(^,\)\(^5\) Salt retention with consequent fluid overload occurs as GFR declines and should be treated by restricting dietary sodium and diuretic administration. Loop-blocking diuretics in a twice-daily regimen are generally required to achieve the requisite natriuresis. Treat hypertension to achieve the previously outlined goal blood pressures. ACE inhibitors or ARBs should be first-line drugs unless contraindications exist (ie, hyperkalemia, bilateral renal artery stenosis). Limit dietary potassium to 60 mmol/day to minimize the development of hyperkalemia.\(^1\) Kayexalate may be required if hyperkalemia occurs despite dietary restriction. To minimize the development of renal osteodystrophy, give the patient sodium bicarbonate or Shohl’s solution to achieve a bicarbonate concentration of 22 to 24 mmol/L. Because secondary hyperparathyroidism can lead to osteodystrophy, serum calcium and phosphorus should be normalized with calcium-containing phosphate binders and, if necessary, oral vitamin D.\(^5\) Most patients with CRF develop anemia owing to decreased erythropoietin production. It is important to ensure adequate iron stores and administer erythropoietin to maintain a hematocrit of 33 to 36%.\(^1\)\(^,\)\(^3\)

F Despite excellent supportive care in patients with CRF, renal function generally declines, albeit at a slower pace. Anticipating this, refer patients for transplant evaluation and education with respect to treatment modalities for their impending ESRD when GFR is 20 to 25 mL/min.\(^1\)\(^,\)\(^5\) Hemodialysis or peritoneal dialysis may be selected as the treatment of choice or used as a bridge to renal transplantation. Ideally, referral for transplantation can be accomplished well in advance of the need for dialysis.

G Once the patient has decided on the preferred form of dialysis, make the appropriate referral for access placement when creatinine clearance is 15 to 20 mL/min in diabetics and 10 to 15 mL/min in nondiabetics. Importantly, this lead time allows for maturation of vascular access for hemodialysis and for technical training in the case of peritoneal dialysis.

H Fluid overload, hyperkalemia, and acidosis refractory to medical management or uremic symptoms, such as anorexia, nausea, vomiting, and lethargy, are clear-cut indicators for instituting dialysis. Even in an asymptomatic patient, dialysis should be instituted in patients with diabetes when the GFR is < 15 mL/min and nondiabetics when the GFR is < 10 mL/min.\(^1\)\(^,\)\(^5\) Preferably, begin dialysis at these earlier stages to minimize the morbidity associated with the abrupt onset of serious uremic complications such as pericarditis or neuropathy.

I The choice among treatment modalities for ESRD depends on the patient’s preference, age, and associated comorbidity. Transplantation is the treatment of choice in infants and children. On the other hand, patients older than age 72 years are usually not transplant candidates. In most patients, absolute contraindications to hemodialysis or peritoneal dialysis are few, and selection between the two is often based on patient preference.

### Table 18-2 Causes of Acute on Chronic Renal Failure

<table>
<thead>
<tr>
<th>Volume depletion</th>
<th>Congestive heart failure</th>
<th>Urinary tract obstruction</th>
<th>Nephrotoxic drugs</th>
<th>Nonsteroidal anti-inflammatory drugs</th>
<th>Radioiodinated contrast media</th>
</tr>
</thead>
</table>

### Table 18-3 Consequences of CRF

<table>
<thead>
<tr>
<th>Cardiovascular</th>
<th>Fluid overload</th>
<th>Hypertension</th>
</tr>
</thead>
<tbody>
<tr>
<td>Electrolyte/acid base</td>
<td>Hyperkalemia</td>
<td>Metabolic acidosis</td>
</tr>
<tr>
<td>Hematologic</td>
<td>Anemia</td>
<td>Platelet dysfunction</td>
</tr>
<tr>
<td>Endocrine</td>
<td>Calcium, phosphorus, vitamin D abnormalities</td>
<td>Gonadal dysfunction</td>
</tr>
</tbody>
</table>

65
Patient with SUSPECTED CHRONIC RENAL FAILURE

A. Acute vs chronic renal failure

Chronic renal failure

B. Etiology of chronic renal failure

C. Exclude causes of acute on chronic renal failure

- Volume depletion
  - Volume repletion
- Congestive heart failure
  - Diuretics, vasodilators
- Urinary tract obstruction
  - Relieve obstruction
- Nephrotoxic drugs
  - Discontinue nephrotoxic drugs
- Radioiodinated contrast media
  - Prevention: hydration, nonionic contrast

D. Retarding the progression of renal disease

- Control of blood pressure
  - Blood pressure: 130/80 mm Hg in general; 125/75 mm Hg in those with heavy proteinuria
- Inhibit RAAs
  - ACE inhibitors or ARBs
- Restrict dietary protein
  - Protein restriction to 0.6 g/kg when GFR < 25 mL/min
- Glycemic control
  - Glycohemoglobin < 7%
References

The diagnosis of renal artery aneurysm (RAA) is often suspected when ring-like calcification in or near the renal hilus is found on a plain abdominal radiograph (KUB), occurring in about 50% of cases. Most RAAs are asymptomatic. The most common clinical manifestation that prompts an evaluation is hypertension. Other symptoms and signs include flank pain, hematuria, and an abdominal bruit.

**A** Renal arteriography is the definitive diagnostic study to establish presence, configuration, size, and location of an RAA. There are three primary types of RAAs: saccular, fusiform, and dissecting (Figure 19-1).

**B** The most common type of RAA is a saccular aneurysm. This is characterized by an outpouching from the renal artery, usually at the bifurcation of the main artery or one of its branches. Such aneurysms may occur in association with renal arterial fibrous dysplasia or neurofibromatosis. There may be secondary atherosclerotic involvement with calcification of the aneurismal wall and intraluminal mural thrombus formation. Complications of saccular aneurysms include peripheral renal embolization, erosion into the renal vein or renal pelvis, direct involvement or extrinsic compression of renal artery branches, and spontaneous rupture. Rupture is most likely to occur with aneurysms that are not well calcified and that are less than 2 cm in size. There is also an increased risk of aneurysmal rupture during pregnancy. Surgical excision of a saccular aneurysm is indicated, either for significant related hypertension or to obviate the risk of rupture associated with the above features.

**C** A fusiform aneurysm occurs as a uniform dilatation of an entire segment of the renal artery to as much as three or four times its normal diameter. These aneurysms are generally not calcified and are typically found in young hypertensive patients with stenosing fibrous renal arterial disease. Most patients with this type of aneurysm require surgical treatment because of significant associated renal ischemia and hypertension.

**D** A dissecting aneurysm results from a tear in the internal elastic membrane of the renal artery, and as blood flows through the opening, the intima is separated from the remainder of the arterial wall. Such aneurysms are most often complications of renal arterial involvement with atherosclerosis, intimal fibroplasia, or perimedial fibroplasia. The clinical presentation of this lesion is often dramatic, with acute onset of severe flank pain, and surgical intervention is usually indicated for attempted renal salvage.

**E** If necessary, surgical treatment—aneurysmectomy with preservation of the involved renal unit—is possible in most cases. In situ revascularization techniques include aneurysmectomy with patch angioplasty, segmental arterial resection with reanastomosis, and aortorenal bypass with an autogenous vascular graft. Extracorporeal aneurysmectomy with microvascular reconstruction and autotransplantation are employed in patients with complex intrarenal aneurysms.

**Additional Readings**

Patient with SUSPECTED RENAL ARTERY ANEURYSM

Hypertension → Renal artery aneurysm confirmed

Renal arteriography

B. Saccular aneurysm
- < 2 cm in size
  - Asymptomatic
  - Normotensive
- > 2 cm in size
  - Asymptomatic
  - Normotensive

C. Fusiform aneurysm
- Any of the following regardless of aneurysm size:
  - Hypertension
  - Local symptoms
  - Young female
  - Renal artery stenosis
  - Peripheral renal embolism
  - Serial radiographic expansion

D. Dissecting aneurysm
- Absent or incomplete calcification
- Well calcified

E. Surgical treatment

Yearly follow-up with magnetic resonance angiography or CT scan

Ring-like calcification on KUB
A True renal vein thrombosis (RVT) is a relatively uncommon condition that may exist in two distinct forms: acute and chronic. The chronic variety may be more common and, owing to the slow development of collateral circulation, may be asymptomatic. The classic presentation for the acute variety tends to be more dramatic and may be associated with severe flank pain, gross hematuria, proteinuria, and possibly azotemia. Because of the variable nature of the rate of thrombus development, not all patients have such a dramatic presentation. Associated caval thrombus may lead to edema of the lower extremities. RVT more likely leads to unilateral involvement. Bilateral involvement is much less common but is likely to associate with oliguric renal failure with flank pain. Similarly, RVT may lead to sudden graft tenderness and hematuria after renal transplantation.

B The most common cause of RVT in adults is nephrotic syndrome, typically associated with membranous nephropathy. Hypercoagulable states such as protein C and S deficiency, oral contraceptive use, malignancy, and congestive heart failure may also lead to RVT. Less common causes include trauma, renal transplantation, amyloidosis, autoimmune vasculitis, diabetic nephropathy, and sickle cell nephropathy. RVT following renal transplantation may occur secondary to technical complications from surgery or to a relative hypercoagulable state induced by immunosuppressants, such as cyclosporine or muromonab-CD3 (OKT3). The thrombus typically starts in the smaller intrarenal vessels and main venous occlusion; when it occurs, it is a secondary phenomenon owing to antegrade spread from the site(s) of initial thrombosis.

C Many different options are available to evaluate patients with suspected RVT. Computed tomography (CT) scan with intravenous contrast may be the procedure of choice for noninvasive imaging. One may see a low attenuation clot within the renal vein and perhaps even the vena cava. The renal vein itself may be enlarged owing to obstruction. Further, the scan may reveal an enlarged kidney with evidence of decreased function and perinephric inflammation, suggested by thickening of Gerota’s fascia. Ultrasonography is less reliable, and gray-scale findings, such as renal enlargement and interstitial edema, are nonspecific. Doppler evaluation of the renal vasculature may help but can be misleading for segmental thrombosis. Often, intravenous pyelography is the first study obtained in a patient with flank pain and with hematuria but usually leads to nonspecific findings, specifically, a poorly functioning inflamed kidney. “Ureteral notching,” a sign of collateral vessel development, may be seen in more chronic forms of RVT. Venography with selective renal vein catheterization may be diagnostic but is usually not necessary. A venacavogram demonstrating no evidence of “dilution” of contrast near the expected location of the renal vein could provide indirect evidence of RVT. In the future, magnetic resonance (MR) angiography may become the diagnostic modality of choice.

D The mainstay of RVT treatment is systemic anticoagulation. After initial heparinization and stabilization, consider converting patients to long-term oral warfarin therapy. Vena caval filter placement may be needed for recurrent pulmonary emboli. Surgery is rarely needed, but consider nephrectomy in a patient with infection or unremitting hypertension. Although case reports that demonstrate marked improvement in renal function after thrombectomy exist, most patients will show no demonstrable improvement with surgical intervention. However, consider thrombectomy for patients not responding to anticoagulation, significant bilateral involvement, or RVT involving solitary kidney. Successful use of fibrinolytics, such as streptokinase or urokinase, has also been described.

E Historically, RVT has been associated with a high mortality rate, but today long-term outcome is largely dependent on the degree of renal function prior to the thrombotic event. Anticoagulation may allow recanalization, and even complete disappearance of the clot may be possible. The patient may need long-term anticoagulation to prevent recurrent thromboembolic events.

F Compared with adults, RVT in children generally is a different entity and is even more uncommon. Although older children with nephrotic syndrome or cyanotic heart disease may develop RVT in a manner analogous to adults, most children with RVT are neonates with profound hypovolemia. Volume depletion may be secondary to shock, dehydration, diarrhea, or sepsis. Spontaneous RVT may also occur rarely in infants of mothers with diabetes. Prenatal RVT detection has been described. Thrombi originate in the smaller intrarenal veins and propagate distally and proximally. Endothelial cell injury, in conjunction with diminished blood flow and/or a hypercoagulable state, lead to thrombus formation.

G Infants with RVT may present with gross hematuria, a flank mass, and thrombocytopenia. This classic triad, however, is present only in a minority of patients. Often, children also have microangiopathic hemolytic anemia. There may be clinical and biochemical evidence of a consumptive coagulopathy. Bilateral involvement may lead
to renal insufficiency. Older children may present with either microscopic or gross hematuria and flank pain.

**H** Ultrasonography (US) with Doppler evaluation is the procedure of choice in children because it is noninvasive, can simultaneously evaluate the inferior vena cava (IVC), and involves no contrast or any ionizing radiation. US findings include an enlarged kidney with loss of corticomedullary differentiation. The thrombus itself may be seen as an echogenic focus within the renal vein. Doppler evaluation will confirm the lack of blood flow. Nuclear renography will demonstrate little function of the involved kidney. Invasive studies such as venography and angiography may confirm the diagnosis but are rarely required.

**I** For unilateral involvement, supportive therapy, emphasizing fluid and electrolyte replacement, is usually all that is required. Unlike the case with adults and RVT, avoid anticoagulation unless the child has a coexisting consumption coagulopathy. Because of the risk of renal failure, one may consider a more aggressive approach with bilateral involvement, although reports of renal functional recovery in children with bilateral RVT with conservative management alone exist. Aggressive therapy in this setting includes either systemic fibrinolytic therapy or surgical thrombectomy.

**J** Unilateral RVT in an infant typically leads to an atrophic kidney. Removal of this unit is required only if infection or hypertension occurs. Bilateral involvement is more ominous; however, isolated reports of functional recovery exist.

**Additional Readings**
A There is no single clinical manifestation that can reliably distinguish renovascular hypertension from essential hypertension. Nevertheless, certain clinical manifestations strongly suggest a renovascular basis for hypertension. The greater the number of these clinical clues that are present, the greater the chance of identifying a lesion upon renal vascular imaging.

B Screening for renal artery stenosis with a noninvasive imaging study is indicated in patients with suggestive clinical signs or symptoms. Duplex ultrasonography, magnetic resonance angiography, and spiral computed tomographic (CT) scanning have all demonstrated utility in this regard. These studies can reliably demonstrate the presence of > 50% main renal artery stenosis but cannot quantify higher degrees of stenosis or reliably demonstrate branch renal artery disease.

C Intra-arterial digital subtraction angiography (IA-DSA) is the gold standard renal vascular imaging test in patients whose initial clinical evaluation and screening suggest renal artery stenosis.

D The functional significance of renal arterial occlusive disease as a cause of hypertension can be evaluated by differential renal vein plasma renin assay. This test is reliable in diagnosing renovascular hypertension when it is positive; however, its usefulness is limited by a high incidence of false-negative results. The peripheral plasma renin response to a single dose of oral captopril has proved to be a useful, less invasive screening test for renovascular hypertension. Isotope renography performed after a single dose of oral captopril is another useful noninvasive screening test for this disease.

E Available data concerning the natural history of atherosclerotic renal artery disease indicate that progressive obstruction occurs commonly and is accompanied by loss of renal function. The risk of renal functional impairment from progressive vascular disease is greatest in patients with high-grade (> 75%) arterial stenosis present bilaterally or in a solitary kidney.

F Treatment of fibrous dysplasia is based upon the specific type of renovascular disease, angiographic findings, and the associated natural history. Renal artery stenosis owing to intimal fibroplasia, perimedial fibroplasia, or true fibromuscular hyperplasia generally progresses, and ischemic renal atrophy is the unfortunate outcome in many cases. Renal revascularization or angioplasty is indicated in these patients both to preserve renal function and to minimize the need for long-term antihypertensive medication.

G In contrast to other fibrous disorders, medical management of hypertension is initially preferred for patients with medial fibroplasia because loss of renal function is uncommon with this disease. Surgery or angioplasty for progressive obstruction is reserved for patients whose blood pressure is difficult to control with multiple-drug antihypertensive therapy.

H Revascularization of the kidney can be successfully accomplished in most patients with renal artery disease. Percutaneous transluminal angioplasty is the treatment of choice for patients with main renal artery disease because of fibrous dysplasia; patients with branch renal artery disease are managed with extracorporeal microvascular surgical reconstruction and renal autotransplantation. Endovascular stenting has become the initial treatment of choice for most patients with atherosclerotic renal artery disease; surgical revascularization is the initial treatment for occasional younger patients with good longevity but more often is employed when endovascular stenting has been unsuccessful. The options for surgical revascularization in such cases include aortal renal bypass, hepatorenal bypass, splenorenal bypass, and iliorenal bypass.

Additional Readings


Renal Artery Stenosis

Medical therapy

Revascularization or endovascular stenting to preserve renal function

Medical therapy

Revascularization or endovascular stenting, or angioplasty for treatment of hypertension

Medical therapy

Onset of high blood pressure (HPB) before age 30 or after age 50

A systolic-diastolic bruit

Short duration (< 5 yrs) of HPB or recent exacerbation of existing mild HPB

Accelerated retinopathy

Unexplained azotemia (serum creatinine > 2.0 mg/dL)

Duplex ultrasonography

Magnetic resonance angiography

Spiral CT scan

Renal IA-DSA

Differential renal vein renin assays

Oral captopril test

Captopril renography

Atherosclerosis

Fibrous dysplasia

Intimal fibroplasia

Perimedial fibroplasia

Fibromuscular hyperplasia

Medial fibroplasia

HBP well controlled

HBP poorly controlled

> 75% RAS unilaterally

< 75% RAS bilaterally

< 75% RAS solitary kidney

HBP poorly controlled

HBP well controlled

> 75% RAS bilaterally or in solitary kidney

< 75% RAS bilaterally or in solitary kidney

Medical therapy

Medical therapy

HBP poorly controlled

Medical therapy
SECTION 3
INFECTION AND INFLAMMATION
Acute Pyelonephritis

Culley C. Carson, MD

A Pyelonephritis is an infection and associated inflammation of the renal parenchyma with secondary involvement of the renal pelvis and collecting system. Although gram-negative bacterial pathogens cause most of these infections, gram-positive organisms, viruses, and fungi can produce pyelonephritis. Pyelonephritis most commonly is suspected in patients presenting with fever from 38°C to 40°C that is associated with flank or abdominal pain, most often identified at the ipsilateral costovertebral angle. Patients may complain of severe ipsilateral flank and abdominal tenderness with guarding to light palpation. These symptoms are often associated with nausea, vomiting, and abdominal bloating. Preexisting irritative lower urinary symptoms may also be identified. These symptoms—frequency, urgency, dysuria, and even gross hematuria—are sometimes identified immediately prior to or remotely prior to onset of systemic symptoms. Nausea, vomiting, dehydration, and lethargy may accompany severe pyelonephritis.

B Laboratory findings usually include pyuria on urinalysis but may also include hematuria, bacteriuria, and proteinuria. Urine Gram’s stain may or may not reveal bacteria. A dipstick-positive evaluation for urinary tract infection on urinalysis may include positive results of leukocyte esterase and nitrite indicators. Nitrite may be positive in the presence of gram-negative organisms that are likely to change nitrate to nitrite in the urine. In patients for whom pyelonephritis is caused by uropathogens other than gram-negative organisms, such as enterococcus and Staphylococcus saprophyticus, leukocyte-esterase dipstick testing may be negative. The definite diagnosis is based on clinical features associated with urine culture—positive findings of uropathogens > 10^5 colonies per mL. Uropathogens should be single cultures, not multiple, and should be derived from a catheterized or well-collected midstream urine. The most common uropathogen remains Escherichia coli; however, Staphylococcus saprophyticus and Staphylococcus epidermidis are also seen. Pyelonephritis caused by urea-splitting organisms should suggest possible renal calculi. These organisms in culture require upper tract imaging studies. Urease-producing organisms associated with struvite calculi include Proteus mirabilis, Klebsiella pneumoniae, Enterococcus facialis, Pseudomonas aeruginosa, and some strains of staphylococcus including S. saprophyticus.

Although nitrofurantoin is an excellent choice in urinary tract infections in pregnancy, its use in pyelonephritis may be less effective, owing to low concentrations in the renal parenchyma. Nitrofurantoin may be chosen in patients sensitive to beta-lactam agents and in whom gentamicin offers significant risk. Sulfonamides with and without trimethoprim produce folate deficiency in the fetus and should not be used. Sulfonamides may also increase the risk of hyperbilirubinemia in the third trimester. Similarly, avoid fluoroquinolones because of concerns for cartilage and bone uptake. Tetracyclines are contraindicated owing to dental discoloration in the fetus.

Evaluation in most patients may be limited to history, physical examination, and urine studies. Reserve imaging studies for patients with complicated pyelonephritis or for those who do not respond well to adequate antibiotic treatment. Chosen antibiotics should focus on the most likely uropathogen, based on community, hospital, and medical suspicion. In community-acquired pyelonephritis in young women who are not pregnant, fluoroquinolones continue to be the standard of care. Owing to its high incidence of community-based resistance, reserve trimethoprim sulfa as a second-line agent. Other alternatives include beta-lactam agents such as cefixime and cefpodoxime. Ampicillin—namely, trimethoprim sulfamethoxazole—is associated with a high prevalence of resistant
organisms in most communities. Resistance to these antibiotics from community-acquired *E. coli* may be in excess of 25% and above 50% in some areas.

**D** Most cases of acute pyelonephritis respond rapidly to oral fluoroquinolones; however, patients with severe or complicated pyelonephritis may require more aggressive treatment. Patients who are toxic, dehydrated, or with intravenous fluid, resuscitation and parenteral antibiotics should be considered. In these patients, an aminoglycoside antibiotic, combined with a beta-lactam agent or parenteral fluoroquinolone, should be the agents of first choice. Clinicians may modify this regimen at 48 to 72 hours, after culture and sensitivity (C & S) results are available to guide antibiotic choice. Once the patient has stabilized and fever has resolved, use oral antibiotics to complete the 7- to 14-day course of treatment.

In nonpregnant patients who do not respond to oral antibiotics after 72 hours, consider imaging studies.

These studies may include abdominal ultrasonography, computed tomography (CT) scan, or IVP. These studies are performed to evaluate the possibility of ureteral obstruction, renal calculus disease, perinephric abscess, emphysematous pyelonephritis, or other upper tract abnormalities that limit the effectiveness of antibiotic treatment.

**Additional Readings**
Symptomatic urinary tract infections (UTIs) in women are exceedingly common, resulting in about 8 million office visits yearly in America, most representing cystitis. Diagnosis requires combining the clinical syndrome that may include dysuria, frequency, urgency, and suprapubic pain, along with identifying the offending microbe in a properly obtained urine specimen. Further, noninfectious causes of these symptoms, including malignancy, must be considered in the appropriate clinical context. In simple cystitis, 3 days of antimicrobial therapy has been shown to be adequate; 1-day therapy is inadequate, and 7 days of treatment is unnecessary except in the presence of pregnancy, diabetes, over age 65 years, or if symptoms have been present for more than 1 week. Women who have had UTI in the past are more likely to experience re-infection in the future. Factors that can interfere with eradication infection include infection with a resistant microbe, renal insufficiency, presence of a large calculus, and noncompliance with therapy. Bacterial persistence—the documentation of the same species in the urine after appropriate antimicrobial therapy. Thus, susceptibility testing is required to select the drug capable of sterilizing the urine. If unresolved bacteriuria is sensitive to the initial agent and the patient is compliant, consider insufficient drug concentration, owing to azotemia, papillary necrosis, or the presence of staghorn calculus. It is important to be aware of the antimicrobial resistance patterns of uropathogens in your region. Over the past decade, E. coli resistance to beta-lactams has reached about 30% in some locales and trimethoprim-sulfamethoxazole (TMP-SMX) resistance as much as 20%. Further, 7% of E. coli isolates demonstrated multidrug resistance in a recent survey. Resistance to nitrofurantoin and the fluoroquinolones has remained uncommon at about 2%. The use of fluoroquinolones may, in some settings, be more cost-effective owing to their higher therapeutic effectiveness despite higher drug costs.

Recurrent infections are caused by organisms that either persist within the urinary tract between episodes of infection or that re-infect the urinary tract from an outside reservoir (ie, bowel flora). We recommend 3 days of therapy with a drug that is not likely to cause resistance in the bowel flora (nitrofurantoin, TMP-SMX, fluoroquinolone). Recurrence with the same organism at short intervals suggests bacterial persistence.

The most common cause of bacterial persistence is infected renal calculi (usually associated with urea-splitting organisms such as Proteus mirabilis) and infected anatomic abnormalities of the urinary tract.

More than 95% of all recurrent infections in women are re-infections. We usually perform cystourethroscopy but limit intravenous urography (IVU), cystography, or cystometry to patients with risk factors such as hematuria, acute pyelonephritis, obstructive symptoms, neurogenic bladder, renal calculi, analgesic abuse, severe diabetes mellitus, or urea-splitting bacteria. Women with two or more UTIs in 6 months or three or more in 1 year usually benefit from nightly low-dose prophylaxis with TMP-SMX (½ regular-strength tablet), nitrofurantoin (50 mg), or cefalexin (250 mg).

Women with frequent UTIs and no demonstrable urologic abnormality may be managed by several regimens, depending on the pattern of infection. Self-start therapy has emerged as a powerful tool that allows immediate therapy with appropriate documentation of infectious agent. Following the patient’s detection of symptoms, collect midstream urine for culture in a pre-provided dip slide urine culture kit. Next, the patient initiates therapy immediately, with oral antimicrobials (generally, fluoroquinolone), and delivers the specimen the following day to the clinician’s office.
Cystitis in the Adult Female

References


Urinary tract infection (UTI) occurs in approximately 2% of all girls and 1.4% of all boys (0.4% of circumcised boys) before age 3 years. Neonates often experience hematogenous dissemination of bacteria with subsequent renal involvement, but infants older than 2 months most often develop urine infection by the ascending route. The distinction between cystitis and pyelonephritis in older children is based on clinical symptoms, but for infants and young children, this is often impossible. An anatomic distinction may be moot in infants because epidemiologic studies suggest that systemic symptoms predominate (implying renal involvement) in early infancy and that, for both boys and girls, the incidence of pyelonephritis decreases with age and that of cystitis increases. Unfortunately, the most significant sequela of UTI (ie, renal scarring) is also inversely related to patient age. Young infants—the very population at risk for damage—often show few signs and symptoms that directly refer to the urinary system, even with significant upper tract involvement. All studies suggest that timely therapy with appropriate antibiotics has utmost importance in decreasing the likelihood of permanent renal damage. The clinical challenge is to have a high index of suspicion that an ill infant may be at risk for a UTI. Fundamentally important in the diagnosis of UTI is to acquire and then to properly assess the urine specimen. With findings that suggest a significant infection, whereas 10^4 to 10^5 col/cc on urine culture will confirm the diagnosis, but this test is best interpreted in statistical terms. Any number of colonies (HPF) on a spun urine and positive Gram’s stain for bacteria on unspun urine all suggest a UTI diagnosis, thus allowing for prompt therapy. The quantitative urine culture will confirm the diagnosis, but this test is best interpreted in statistical terms. Any number of colonies in pure culture obtained by SPA provide a > 99% probability of infection. A transurethral catheterization that results in > 10^6 colonies/cc has a 95% probability of significant infection, whereas 10^4 to 10^5 col/cc on urine similarly obtained concludes only that infection is possible. A colony count of > 10^8 from voided urine has an 80% probability of infection. The statistical uncertainty deriving from the quantitative urine culture does not negate widespread utility.

A The problems with diagnosing UTI in infants and young children are legion. Young infants with significant renal involvement may not demonstrate fever (> 39°C), but the clinician must consider the possibility of a UTI with any signs of systemic toxicity such as lethargy, tachycardia, poor feeding, vomiting, diarrhea, and irritability. Nonspecific laboratory indications for systemic inflammation, such as elevations in the white blood cell count, C-reactive protein concentration, and sedimentation rate, all suggest the occurrence of a significant clinical event but are obviously not specific to the urinary system.

B Properly obtained urine for assessment is key in managing young patients who are suspected of having a UTI. Suprapubic aspiration (SPA) to obtain bladder urine is reliable but invasive. Although neonatologists are quite comfortable with this procedure, most other clinicians are not well practiced in the technique. The catheterized urine specimen is therefore the preferred method of urine procurement in both boys and girls. Compared with SPA, transurethral catheterization has a 95% sensitivity and a 99% specificity. Bagged urine specimens can provide useful information if the patient has a low likelihood of UTI and if the urine proves negative. The rate of contamination, as well as the attendant unacceptably high rate of false-positives, however, convinces most to abandon bagged specimens when evaluating an ill child for possible UTI. Once obtained, the urinalysis provides useful information that enables the clinician to initiate therapy appropriately in patients with a likely UTI. A positive nitrite, leukocyte esterase positivity, and more than 5 WBCs/high-power field (HPF) on a spun urine and positive Gram’s stain for bacteria on unspun urine all suggest a UTI diagnosis, thus allowing for prompt therapy. The quantitative urinary culture will confirm the diagnosis, but this test is best interpreted in statistical terms. Any number of colonies in pure culture obtained by SPA provides a > 99% probability of infection. A transurethral catheterization that results in > 10^6 colonies/cc has a 95% probability of significant infection, whereas 10^4 to 10^5 col/cc on urine similarly obtained concludes only that infection is possible. A colony count of > 10^8 from voided urine has an 80% probability of infection. The statistical uncertainty deriving from the quantitative urine culture does not negate widespread utility.

C Oral therapy for UTI has long been practiced in older children and adults. Because of the vulnerability of young infants and the pyelonephritic character of their infections, admission to the hospital for treatment with intravenous (IV) antibiotics until afebrile has long been the standard of care. A recent study by Hoberman and colleagues, however, found that infants and young children who experience their first UTI with fever and who were well enough for management at home (oral cefixime for 14 days ) had no greater rate of subsequent renal scarring (9%) than did infants admitted to the hospital and treated with parental cefotaxime for 3 days and then oral cefixime for 11 days (7%). Compliance with oral medication is always an issue, and it should be noted that in this well-controlled study, 15% of patients were found to have no evidence of antibiotic in the urine when assessed as outpatients.

D If the child is too ill for outpatient management, this necessitates admission to the hospital for hydration with
Patient is YOUNG CHILD AGE 2 MONTHS TO 4 YEARS

Acute unexplained febrile illness or illness with signs and symptoms that suggest UTI, with or without systemic toxicity. Consider UTI.

Catheterized if not potty trained or systemically ill

Clean catch midstream if potty trained and well

Collect urine for urinalysis (U/A) and quantitative culture with antibiotic sensitivity testing

U/A positive

UTI

C/S positive

UTI possible. Await culture and sensitivity (C/S) if patient condition warrants.

C/S negative

UTI. Treat according to sensitivity × 7 days.

Well enough for oral therapy

Ill patient

PO antibiotics for 7 days and PA until renal ultrasonography (RUS) and VCUG

Admit for IV antibiotics. RUS while hospitalized.

Await C/S to plan to discontinue on appropriate PO therapy when well to complete 10-day course

PA until VCUG

parenterl administration of broad-spectrum antibiotics. Timely assessment with renal sonography will often disclose anatomic abnormalities that require attention—if not immediately (duplication anomalies, hydronephrosis, and thick bladders, suggestive of posterior urethral valves), then certainly in the long term.

With both outpatient therapy and hospital admission, it is important to check the culture sensitivities when available to ensure appropriate antibiotic administration. I recommend reducing therapeutic dosing to prophylactic levels until follow-up radiographic assessment of the bladder.
E Universally, 30 to 40% of infants and young children affected with UTI will be found to have anatomic abnormalities, most commonly vesicoureteral reflux (VUR), on subsequent testing. Young infants with VUR often have high-grade abnormalities, which surprisingly do not seem to prejudice against ultimate resolution. Although surgical repair of VUR does minimize febrile morbidity, the operation has not been found to affect the occurrence of renal scarring. For these reasons, some argue against obtaining a voiding cystourethrogram (VCUG), given that renal sonography shows normal renal size and no hydronephrosis in a child with no UTI history. Sophism aside, the practical value of diagnosing VUR far outweighs the negative aspects of the diagnostic inquiry. Although the radionuclide cystogram exposes the patient to less radiation, it does not provide anatomic information about the bladder, bony structures, and abdominal contents. For the marginal cost of radiation, the benefits of routine VCUG seem compelling enough to warrant routine application. Treatment with PAs protects the patient from re-infection in the already inflamed urinary tract until the bladder assessment is accomplished.

F Approximately one-third of the patients with known VUR on a PA will develop “breakthrough” UTIs. However, not all of these infections will be threatening to the kidney. Although fever is an unreliable sign for renal involvement in young infants, in older infants and young children, fever will invariably be present if the patient has a urine infection localized to the renal parenchyma. It is reasonable to diagnose a UTI not localized to the kidney (in spite of VUR) in patients with lower-tract symptoms who lack fever and demonstrate a positive urinalysis. The bacteria responsible for such infections are always resistant to the antibiotic used for prophylaxis. Switching to a different oral antibiotic and awaiting the final culture could result in a reasonable chance that the infection can be treated effectively with oral medication with no renal consequence.

G A breakthrough infection with fever and systemic toxicity can also occur in children with VUR on PA. Such occurrences should be aggressively managed to avoid the development of new renal scarring. Admission to the hospital and the initiation of therapy, with a combination of IV gentamicin and ampicillin, will cover almost all uropathogens, except for the very resistant species. The admission allows acute imaging of the kidney, as well as effective therapy of the infection, regardless of resistance patterns. Additional assessment of parental compliance, risk factors for UTI, and discharge planning can be accomplished while awaiting the final culture and sensitivity report.

H Acute assessment of the kidneys for renal parenchymal involvement with infection, using either dimercaptosuccinic acid (DMSA) scintigraphy or computed tomography (CT) assessment (with and without contrast), provides accurate information about the extent of renal involvement. Kidneys that demonstrate normal renal uptake of contrast or isotope lack renal involvement and therefore are not at risk for subsequent scarring. Children with no renal parenchymal involvement can be safely switched to oral medication and discharged home when well, even if still febrile.

I On the other hand, some patients with documented renal swelling will develop a subsequent scar in the area of the kidney involved with the acute changes. Ample literature exists to suggest that VUR, particularly high-grade VUR, places the patient at greater risk for this outcome. Although sensitivities often show that oral medication is effective against the infecting bacteria, intravenous administration ensures delivery of the medication to the involved kidney. Similarly, parenteral administration of antibiotics in the hospital or in the home (using widely available home health services) intuitively has fewer issues of lack of compliance with the prescribed medication regimen. All studies of renal scarring suggest that renal damage occurs in the setting of patients with VUR and poorly treated infections. Given these facts, it is prudent to be aggressive in the recommendation for a full 10-day course of parenteral antibiotics, despite alternatives suggested by the results of the sensitivity testing that demonstrate acceptable oral antibiotics. Following therapy completion, it is best to choose a different PA than the one used when the patient developed the breakthrough UTI.

J Breakthrough infections generally indicate surgical intervention in patients with VUR. Interval UTIs may warrant re-evaluation with repeat cystography. It is also necessary to stratify the infection according to severity. A cystitic event with lower-tract symptoms differs from a febrile event with renal swelling in that it does not have near the consequences. Most new renal scars occur in the setting of not only VUR but also ongoing risk factors for infection. We now view voiding dynamics and bowel habits to be of utmost importance in the development of UTIs. With or without surgical intervention, to lessen the threat to renal well-being, these well-recognized factors for infection demand management.

Additional Readings
Urinary Tract Infection in Young Children

Patient with KNOWN VESICOURERETAL REFUX ON PA

Acute unexplained febrile illness or illness with signs and symptoms that suggest UTI, with or without systemic toxicity. Consider UTI.

If potty trained, clean catch midstream specimen
If toxic or not potty trained, catheterize

U/A and C/S

U/A positive and patient well

Choose antibiotic different than PA and treat with therapeutic. Check C/S and confirm patient improvement on optimal antibiotic. After a 7-day course, reduce to PA dose.

U/A positive and patient febrile and ill

Admit for IV ampicillin and gentamicin

Image kidneys for renal parenchymal involvement (DMSA or CT scan with and without contrast)

Renal involvement demonstrated

Follow for clinical improvement. Await C/S to allow for more specific IV therapy. Plan for home health maintenance of IV therapy for 10 days total

No renal involvement demonstrated

Await sensitivities to allow for oral therapy when well enough to discontinue

Select different PA if possible

Re-evaluate causes for UTI and status of VUR

DMSA scan in 6 months to assess for new renal scanning

U/A negative

Follow patient and await C/S

Change to appropriate oral antibiotics

Not UTI

Re-evaluate causes for UTI and status of VUR
The overall mortality of patients presenting with septic shock ranges from 10 to 90%. Evaluation and appropriate early treatment decrease the frequency of shock and improve survival rates. Evaluation of the patient who presents to the physician with complaints of fever, chills, and other symptoms suggestive of urinary tract infection, with a differential diagnosis of sepsis or septic shock, includes the following:

A careful questioning of previous urinary tract infections, urinary stones, previous urinary tract surgery, history of neurogenic bladder, and diabetes is important. If the patient is not able to give a full history, a family member may be able to help.

Physical examination should include vital signs; abdominal and flank examination noting any areas of tenderness; a careful examination of the genitalia noting any signs of epididymo-orchitis, scrotal redness or fluctuance, or Fournier’s gangrene; and a digital rectal examination to note possible prostatitis or a perirectal abscess.

Laboratory examination should include urinalysis, urine culture, aerobic and anaerobic blood cultures, and serum electrolytes, as well as complete blood count and chemistries. In addition, all potential sources of bacteremia should be identified and cultured (urine, wound, and sputum). Make a thorough attempt to identify the source of the infection as this will help in selecting the most appropriate antibiotic regimen.

Immediate antibiotic therapy is indicated for the patient with the suspected diagnosis of septic shock. The patient should be started empirically on broad-spectrum antibiotics that cover the majority of urologic pathogens until the offending organisms are identified. Aminoglycosides are generally effective, but care must be exercised in regard to renal function.

B If there are no obstructive processes identified and no abscess present, then supportive measures are indicated. If a urinary obstruction or retroperitoneal abscess is identified, then open surgical drainage, a ureteral stent, a percutaneous nephrostomy, or percutaneous drainage of the abscess (depending on the comfort level and expertise of the radiologist) is indicated. A general surgical consultation may be indicated for a perirectal abscess or an intra-abdominal process.

C Fluid resuscitation is mandatory. If a patient remains hypotensive despite fluid resuscitation and antibiotics, vasopressors (eg, dopamine, vasopressin) should be added to the patient’s regimen. Adult respiratory distress syndrome (ARDS) may develop in spite of optimal medical management, and patients may require mechanical ventilatory support.

If imaging studies confirm an obstructing stone or pyonephrosis, a percutaneous nephrostomy or ureteral stent may be emergently required to drain the kidney. Percutaneous drainage of a perinephric abscess may be required or open surgical drainage of a large abscess of the kidney, scrotum, or rectum.

If no abscesses or obstructive phenomena are identified, then supportive measures are indicated. A second series of cultures and imaging studies may be needed to identify any processes that may have developed in the course of therapy.

Additional Readings
Patient with presumptive or established diagnosis of septic shock

**A**
- Diagnosis
  - History, vital signs
  - Physical examination
  - Imaging studies
  - Institute antibiotic therapy

**B** Patient normotensive
- Obstruction or abscess
  - Surgery, ureteral stent, percutaneous drainage, nephrostomy
- No obstruction or abscess
  - Supportive measures

**C** Patient hypotensive
- Fluid and respiratory support as indicated
Perinephric Abscess

Culley C. Carson, MD

Since the advent of systemic antibiotics for remote infections, the incidences of perinephric and renal abscesses have declined. Abscesses, however, still occur in clinical practice and are often indolent, requiring clinical diagnostic acumen for their early identification and adequate treatment. Signs and symptoms are usually nonspecific and do not suggest the diagnosis until adequate imaging has been carried out. As a result of the delay in diagnosis and treatment, as many as 50% of those affected may die from unidentified abscesses.

Prior to widespread antibiotic use, most perinephric abscesses resulted from hematogenous spread of gram-positive organisms, most often Staphylococcus aureus. These abscesses, previously termed carbuncles, are still occasionally identified in patients with immune compromise, individuals who abuse intravenous substances, and patients with dermatologic infectious conditions. Currently, however, most perinephric abscesses are from more virulent uropathogens and often occur in immunocompromised patients with a urinary portal of entry. The most common infectious agents include gram-positive uropathogens, such as Escherichia coli, Proteus mirabilis, Pseudomonas aeruginosa, and Klebsiella pneumoniae. Gram-positive organisms including enterococci and fungi, such as Candida, may also be cultured in some patients. Most perinephric abscesses occur as a result of erosion into the perirenal space from intrarenal infected calculus, ureteral obstruction, or poorly treated chronic pyelonephritis.

A Signs and symptoms of perinephric abscesses are usually nonspecific. They may, however, include features of systemic infections such as fever, chills, and abdominal or flank pain. Patients may also have nausea, vomiting, diarrhea, weight loss, or malaise. Those abscesses preceded by lower urinary tract infections may also be associated with irritative voiding symptoms or with gross hematuria. Most patients have associated medical conditions that predispose them to severe renal infections. These conditions include immunosuppression in patients with human immunodeficiency virus (HIV) or alcoholism, diabetes mellitus, urinary tract calculi (usually struvite), previous genitourinary surgery, obstruction, or underlying renal disease.

B Physical examination may demonstrate scant findings or flank or abdominal pain associated with a flank or abdominal mass. As many as one-half of patients with perinephric abscesses will have abdominal mass lesions. In patients with large perinephric abscesses in the posterior portion of the kidney, psoas muscle irritation may be identified. In these patients, physical examination will yield a positive iliopsoas rigidity test similar to that seen in patients with acute appendicitis.

C Laboratory tests may not help, but most patients will demonstrate leukocytosis with a left shift, pyuria, and a positive urine culture. Renal abscesses with sterile urine cultures may occur, especially with a hematogenous gastrointestinal origin. Many patients may also have elevated serum creatinine and decreased hemoglobin.

There is a high index of clinical suspicion in patients with renal calculi or urinary infections who are treated with appropriate antibiotics but who remain febrile for more than 72 hours following initiation of appropriate treatment.

D It is important for definitive imaging in these patients, and it is best to begin with a renal ultrasound or a computed tomography (CT) scan. Magnetic resonance imaging (MRI) may help in some patients wherein contrast media cannot be given because of limited renal function. A CT, both with and without contrast, is excellent for identifying abscesses. Abscesses associated with xanthogranulomatous pyelonephritis may have associated calcification, diffuse pyonephrosis, and renal mass. This imaging modality may demonstrate purulence, gas within the lesion that is pathognomonic for abscess, or a low attenuation mass with rim enhancement after contrast administration. Perinephric changes with these abscesses may include the obliteration of perinephric tissue planes, of stranding, and of mass effect. Although less specific in diagnosing abscesses, renal ultrasonography may be an adequate screening technique and may assist in drain placement for patients requiring percutaneous drainage.

E Patients are unlikely to improve or respond to antibiotic treatment without abscess drainage. In past years, open surgical drainage was the treatment of choice. Currently, however, imaging-guided percutaneous drainage is effective in most patients with low expected morbidity. Prior to drainage, however, patients should undergo Gram’s stain and culture of urine, blood, and any remote infections to guide the choice of antibiotic coverage. Start patients on a presumptive combination of aminoglycoside antibiotic for gram-negative coverage and a beta-lactam antibiotic, such as ampicillin for gram-positive cocci. In patients for whom beta-lactam
allergy is identified or resistant organisms are suspected, vancomycin can be substituted. Similarly, if anaerobic bacteria are possible, such as in perinephric abscesses with gastrointestinal etiologies, add an agent such as clindamycin or metronidazole to the antimicrobial therapeutic program.

**F** Once adequately cultured and treated with predrainage antibiotics, abscess drainage is best carried out with CT or ultrasound-guided needle aspiration to avoid nearby organs and to adequately drain all portions of the abscess. Submit abscess fluid for aerobic and anaerobic cultures and sensitivities (C&S). Following placement of an 8- to 12-French drainage catheter, perform a repeat CT scan or ultrasonography to rule out further abscess cavities, fluid collections, or undrained loculations. Provide follow-up with continued antibiotic coverage and tube drainage until drainage has resolved. If fever continues despite seemingly adequate drainage and antibiotics, carry out additional imaging studies to identify any occult abscesses.

**G** If abscess drainage is inadequate after multiple attempts with imaging and percutaneous approaches, consider an open surgical procedure. Perform an open surgical drainage to adequately eliminate all collections and to allow drainage. To protect these areas from contamination, ensure that care is taken to avoid entry into the peritoneal or the pleural cavities. After adequately draining and identifying abscesses, carry out antibiotic irrigation of the cavity and then place multiple Penrose drains through separate stab wounds to permit continuous drainage. Keep infected wounds open for healing by secondary intention and perform tissue closure with monofilament absorbable sutures, such as chromic catgut. Initially, skin sutures may be placed left open and then tied for skin healing at 7 to 10 days postoperatively once drainage has ceased and fever has resolved. Prior to wound closure, pack the wound, ensure that dressing changes occur daily to permit adequate healing, and carry out infection drainage two to three times daily.

Relief of associated ureteral obstruction or treatment of obstructing stone with ureteral stenting or percutaneous nephrostomy tube may facilitate recovery. These procedures may be performed simultaneously with abscess drainage and may improve renal function once infection resolves.

### Additional Readings


SECTION 3  Infection and Inflammation

Patient with RENAL ABSCESS

Fever, chills
Abdominal pain
Flank mass
Fever > 3 days after appropriate treatment of UTI

History and physical examination

Electrolytes
Urine C&S
Blood C&S, CBC
Creatinine

Upper tract imaging
Renal ultrasonography
CT scan

Empiric antibiotics prior to diagnostic studies

Acute pyelonephritis
See Chapter 22

Fluid collection or Perinephric abscess

Antibiotics based on most likely pathogen (community antibiogram, comorbid conditions)
Perinephric Abscess

Percutaneous aspiration

Diagnosis confirmed

Insertion of percutaneous drain

Drainage failure
Continued fever

Repeat CT
Repeat aspiration

Open surgical drainage
if failure to resolve fever and fluid collection

Follow-up imaging
Continued antibiotics for 14–21 days

Antibiotics continue until drainage resolves

Appropriate antibiotics
14–21 days after drainage resolution

Maintain drains until fever resolves
Drainage ceases

Follow-up imaging
Continued antibiotics for 14–21 days
Genitourinary Tuberculosis
Culley C. Carson, MD

Despite new and innovative antimicrobial treatment options, the incidence and prevalence of tuberculosis have risen throughout the world. This can be traced to progression in resistant organisms, as well as to the advent of widespread immunosuppression caused by human immunodeficiency virus (HIV) infections and acquired immune deficiency syndrome (AIDS). Genitourinary tuberculosis is rising, along with the total incidence of tuberculous infections worldwide.

Genitourinary tuberculosis is usually a late sequela of tuberculous infections in other parts of the body, most often pulmonary. It is rarely either an acute disease or an isolated infection. Most often, genitourinary tuberculosis is a urinary manifestation of late pulmonary disease resulting from hematogenous mycobacterial dissemination. The usual cause of genitourinary tuberculosis continues to be Mycobacterium tuberculosis. In patients with HIV and other immunosuppression syndromes, other pathogens such as Mycobacterium bovis, Mycobacterium avium, and Mycobacterium kansasii may be encountered. Because these latter organisms have different antituberculin drug sensitivities, careful culture is essential prior to initiation of definitive therapy.

A To diagnose genitourinary tuberculosis, the clinician performs a urinary evaluation. Acid-fast smears of morning urine—the previous standard—may be misleading. Urine cultures from three morning voids are important but require days or weeks to provide diagnosis. Using the recently introduced BACTEC radiometric system from Becton, Dickinson and Company of Franklin Lakes, NJ, culture results can now be available in 10 to 14 days. This radiolabeled carbon-14 system has high specificity and sensitivity for all mycobacteria. Nucleic acid amplification (NAA) techniques for identifying deoxyribonucleic acid (DNA) and ribonucleic acid (RNA) from mycobacterium in clinical specimens can also be used in urines. These rapid, accurate studies can provide a diagnosis in 6 to 8 hours.

Renal tuberculosis is the most common extrapulmonary infection, occurring in up to 4% of tuberculous infections. Most renal infections occur in middle-aged adults and also occur in patients with HIV or other immune compromise (eg, renal transplant has a higher incidence). Because tuberculosis usually reaches the genitourinary system by hematogenous spread, renal infection predominates in current genitourinary tuberculosis. If renal infection is identified, both kidneys are at risk and should be investigated. Renal infection can result in severe parenchymal inflammation and infection and, ultimately, in destruction of the entire renal unit. Later tuberculous infections are marked by scarring and cicatrization with infundibular stenosis, ureteral stenosis, and calcification of affected organs. Once established as a renal infection, the tubercle bacilli produce downstream infections from ureter, bladder, prostate, seminal vesicles, and epididymis. Of male genital tuberculosis, 50% is associated with previous renal infection. Female genital tuberculosis that usually affects ovaries, fallopian tubes, and uterus is almost always hematogenous and is rarely associated with renal infection. These patients usually respond well to antituberculous drugs but usually suffer persistent infertility.

B The clinical features of genitourinary tuberculosis or of other urinary infections may be absent. Recurrent Escherichia coli infection may be associated with genitourinary tuberculosis, and tuberculosis infection should not be overlooked in patients with these recurrent infections. More than 70% of patients present with urinary symptoms, whereas 20% of patients are asymptomatic. Dysuria, frequency of urination including nocturia with a sterile urine culture, and significant pyuria are common. Although hematuria can be identified as a late sign, it is rarely a presenting symptom. In patients with seminal vesical, epididymal, or vasal tuberculosis, hematospermia may be identified. These men often present with enlarging masses of prostate, seminal vesicles, or epididymis, and diagnosis is made on biopsy. In these cases, the clinician may also identify scrotalgia and testicular swelling. Often, patients will have few symptoms, even when extensive renal involvement has taken place to the level of autonephrectomy.

C Following a high index of suspicion, the history and physical examination should include questions about the exposure of patients to friends and family members with active tuberculosis, immune deficiency syndromes, and previous tuberculous infections. Urinalysis is abnormal in 95% of patients. Examine the urine for red and white cells and carry out a culture for tuberculous bacilli. In addition, perform urine-sediment staining for acid-fast bacilli; however, it is less accurate than the newer NAA or BACTEC techniques.

D These culture techniques should include three to five consecutive, early morning urine specimens cultured
Patient with GENITOURINARY TUBERCULOSIS

Suspicion of tuberculosis
Risk factors (HIV positive, tuberculosis exposure)
Sterile pyuria, painless nocturnal frequency

History, physical examination

Tuberculin test

Positive test in patient with previously negative test

Urine studies

Urine cultures
5 first am urines
(Löwenstein-Jensen medium, pyruvic egg medium)
BACTEC culture

Positive cultures for
*M. tuberculosis*
Atypical mycobacterium

Blood studies
CBC
ESR
Creatinine

Imaging studies

Chest radiographs
Plain abdominal film for calcifications
IVP
Other imaging as required for obstruction

Antituberculous chemotherapy

INH
Pyrazinamide
Rifampicin

Nephrectomy if necessary 4–6 wk after start of medication

Ureteral obstruction

Corticosteroids if fails to resolve 3 weeks after medications

Follow-up for all genitourinary tuberculosis

Calcification
No calcification

Surgical treatment

KUB with/without IVP every 12 months

IVP at 3, 6, 12 months
Again only with symptoms
on pyruvic egg medium and Löwenstein-Jensen medium or the BACTEC system where available. These two culture techniques will identify nontuberculous mycobacteria and *M. tuberculosis*, respectively, as well as drug sensitivities of the mycobacteria species. Obtain blood count, creatinine, and electrolytes, as well as an erythrocyte sedimentation rate (ESR). The ESR, if elevated, can be an excellent method for following treatment response in patients with active tuberculosis.

**E** Intravenous pyelogram (IVP) or a computed tomography (CT) scan is an important imaging modality for evaluating patients who are suspected of genitourinary tuberculosis. A triphasic CT or even a magnetic resonance (MR) urogram may help in patients for whom IVP is difficult to obtain or evaluate. The latter is especially effective in those patients with significant renal failure that is secondary to active tuberculosis and for whom radiographic contrast cannot be used. For patients who can tolerate an IVP, this imaging study can be invaluable in identifying areas of cavitation, stricture formation, hydronephrosis, calcifications in the upper and lower urinary tract, and the progression of bladder changes to small, poorly compliant contracted bladder. Nonspecific urographic signs may include papillary necrosis, parenchymal scarring, and lobar calyceal dilatation. Because many imaging changes involve segmental scarring, renal ultrasonography is less valuable than IVP or CT scans.

Radioisotope investigations can be useful in identifying renal function and relative renal dysfunction. These studies may assist in stratifying obstructive uropathy and may help in making the decision for surgical intervention, including nephrectomy or medical therapy. Renal changes evolve with medical treatment; thus, early surgical intervention based on imaging studies should be avoided.

**F** Medical management should initially include triple antitubercular medical treatment. Because of the emergence of multidrug-resistant *M. tuberculosis* and other mycobacteria with resistance to isoniazid (INH) and rifampin, new combinations of agents may be required in many patients with HIV. For current drug-susceptible tuberculous infections, continue a three-drug combination for 2 months, specifically, INH, rifampin, and pyrazinamide (PZA). Patients with susceptible organisms can then be transitioned to daily INH and rifampin for 4 months. In communities with INH resistance above 4%, add a fourth agent, either ethambutol or streptomycin. Additional first-line agents include rifabutin, rifapentine, ethionamide, and ethambutol. Because second-line antitubercular agents have less effectiveness, are frequently not bactericidal, or have higher toxicity, they are reserved for resistant organisms in combination programs. These agents should be chosen based on clinical experience and the guidelines for multidrug-resistant tuberculous infections published by the Centers for Disease Control and Prevention. Owing to the rapid evolution of antitubercular treatment, recommend infectious-disease consultation in treating these complex patients.

**I** Iatrogenic tuberculosis may occur in patients treated with intravesical bacille Calmette-Guérin (BCG) for superficial bladder cancer. In patients with persistent malaise, low-grade fever, hematuria, and signs or symptoms of systemic infection, suspect active tuberculosis. For patients with persistent low-grade fever without symptoms of systemic infection, recommend treatment with INH (300 mg daily for 3 months). With associated pulmonary or hepatic infection, multidrug therapy including INH, rifampin, and ethambutol in severe cases should be carried out for 4 to 6 months. If INH is used for long periods, pyridoxine 25 to 50 mg daily must be added to the combined treatment to prevent neuropathy. Although systemic disease from BCG treatment occurs in less than 5% of patients receiving BCG, it is clearly a life-threatening, high-morbidity condition that must be actively, acutely, and aggressively treated.

**G** Surgical treatment for tuberculosis has declined significantly because of effective medical antitubercular treatment. Patients must, however, continue to be considered for tuberculous surgical treatment for complications of infections that do not respond to medical treatment. In patients with nonfunctioning kidneys or extensive involvement of an entire kidney associated with ureteropelvic junction (UPJ) obstruction, hypertension, or coexisting renal cell carcinoma, consider nephrectomy. Any surgical intervention, however, should be preceded by 4 to 6 weeks of antituberculous medical therapy based on cultures and sensitivities. Partial nephrectomy may be considered in the small subset of patients for whom a localized polar lesion or localized calcification is associated with progressive renal damage.

Other genitourinary surgical procedures for tuberculosis include epididymectomy in patients with scrotal abscesses not responding to chemotherapy or with continued pain, obstruction, and difficult medical management.

Most surgical procedures required for genitourinary tuberculosis are reconstructive. These include ureteral substitution for stenosis and fibrosis and UPJ repair for UPJ obstruction and usually require specific ureteral bypass including psoas hitch, Boari flap, or ileal interposition. Lower urinary tract reconstruction may include augmentation cystoplasty in patients with contracted, poorly compliant, hypertonic bladders that associate
with symptoms such as pain, frequency, urgency, nocturia, and bladder instability. Augmentation cystoplasty can be carried out with ileum, colon, cecum, or stomach. Patients with severe bladder dysfunction, however, may require urinary diversion with ileal or colonic bladder substitutions.

Because of progressive scarring and cicatrization, even following adequate medical management, provide continuous follow-up after completing medical therapy. Follow-up should include annual IVP to evaluate the possibility of progressive calcification, cicatrization, or obstruction. Urinalysis should focus on resolution of pyuria, and the ESR should be monitored to identify recurrences in infection.

### Additional Readings
Renal papillary necrosis (RPN) is not a specific disease but rather a clinicopathologic syndrome characterized by ischemic necrosis of the inner medulla or papillae. Papillary necrosis is usually asymptomatic and discovered incidentally by excretory urography or at autopsy. A minority of patients present with acute, life-threatening sepsis or with recurrent episodes of RPN of varying severity over a period of months to years. Fever and chills are the most common manifestations in symptomatic patients. Renal colic, dysuria, and gross hematuria occur less frequently (Table 28-1). The most frequent laboratory features include proteinuria, leukocyturia, positive urine culture, macroscopic hematuria, leukocytosis, and azotemia (see Table 28-1).

There are several groups of patients at increased risk to develop RPN. In a recent, large series from the Mayo Clinic, urinary tract infection (UTI) (41%), analgesic abuse (36%), urinary tract obstruction (29%), and diabetes mellitus (22%) were the most frequently associated risk factors. However, it is important to note that, in most instances, one or more risk factors are present (Figure 28-1). Analgesics linked to RPN include aspirin and phenacetin combinations, nonsteroidal antiinflammatory drugs, and, to a lesser extent, aspirin and acetaminophen. In addition, RPN has also been reported in sickle cell disease, sepsis, pancreatitis, and chronic alcohol abuse.

Urinalysis reveals fragments of sloughed papillae in only a few cases. However, the finding of papillary fragments establishes the diagnosis. In all cases of suspected papillary necrosis, UTI and obstruction must be excluded.

More often, the urinalysis is nonspecific and demonstrates only red blood cells (RBCs), white blood cells (WBCs), and/or a small amount of protein. Obtain a urine culture and, if positive, prescribe appropriate antimicrobial therapy.

In the presence of RBC casts, nephrotic range proteinuria, or a normal excretory urogram, parenchymal diseases such as glomerulonephritis or acute interstitial nephritis would be important diagnostic considerations.

Intravenous pyelography (IVP) with nephrotomograms is the best way to establish the diagnosis if papillary fragments are not demonstrated by urinalysis. In RPN, the calyces may appear irregular, fuzzy, or clubbed; there may be sinus formation in the medulla. A “ring shadow” can be present if the papilla actually separates from the medulla. Although RPN has characteristic features on both computed tomographic and ultrasound examination, there are only limited comparisons with IVP. If any radiologic study demonstrates coexistent obstruction, prompt drainage is essential to avoid further renal damage and to minimize the risk of infection.

Once the diagnosis of RPN is established and after any infection or obstruction has been adequately treated, there is little specific therapy available. Because the only potentially reversible cause of RPN is analgesic abuse, question patients carefully with respect to analgesic ingestion. Once an episode of RPN has been documented, follow the patient closely for development of recurrent episodes, urinary tract infection, and obstruction.

### Table 28-1 Symptoms and Laboratory Features in Papillary Necrosis

<table>
<thead>
<tr>
<th>Feature</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever/chills</td>
<td>67%</td>
</tr>
<tr>
<td>Flank pain/dysuria</td>
<td>40%</td>
</tr>
<tr>
<td>Gross hematuria</td>
<td>20%</td>
</tr>
<tr>
<td>Proteinuria</td>
<td>80%</td>
</tr>
<tr>
<td>Leukocyturia</td>
<td>70%</td>
</tr>
<tr>
<td>Positive urine culture</td>
<td>70%</td>
</tr>
<tr>
<td>Microscopic hematuria</td>
<td>40%</td>
</tr>
<tr>
<td>Leukocytosis</td>
<td>60%</td>
</tr>
<tr>
<td>Azotemia</td>
<td>60%</td>
</tr>
</tbody>
</table>

Adapted from Eknoyan G et al.¹
References
Prostatitis has long been a poorly understood and poorly characterized entity. Prostatitis represents over 2 million medical office visits yearly in the United States, and its overall prevalence has been estimated at 5 to 15%. Patients report a sickness impact of prostatitis that is similar to myocardial infarction or Crohn’s disease. Less than 10% of cases of prostatitis have a bacterial cause that responds to conventional antimicrobial treatment. The etiology, pathogenesis, and optimum treatment of the remaining 90% of cases of prostatitis (ie, chronic pelvic pain syndrome) are unclear. Empiric therapy is frequently used with unpredictable efficacy. Two important advances in the study of prostatitis—the development of the National Institutes of Health (NIH) consensus definition of the prostatitis categories (Table 29-1) and the validation of the NIH chronic prostatitis symptom index (NIH-CPSI) (Figure 29-1)—have facilitated assessment, diagnosis, and management of patients.1 A carefully performed Meares-

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**Table 29-1**

<table>
<thead>
<tr>
<th>Domain</th>
<th>Scoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td>4</td>
</tr>
<tr>
<td>Urinary Symptoms</td>
<td>4</td>
</tr>
<tr>
<td>Quality of Life</td>
<td>4</td>
</tr>
</tbody>
</table>

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**Figure 29-1** The National Institutes of Health chronic prostatitis symptom index.

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1. In the last week, have you experienced any pain or discomfort in the following areas?
   - Area between rectum and testicles (perineum)
   - Testicles
   - Tip of the penis (not related to urination)
   - Below your waist, in your pubic or bladder area

2. In the last week, have you experienced:
   - Pain or burning during urination?
   - Pain or discomfort during or after sexual climax (ejaculation)?

3. How often have you had pain or discomfort in any of these areas over the last week?
   - Never
   - Rarely
   - Sometimes
   - Often
   - Usually
   - Always

4. Which number best describes your AVERAGE pain or discomfort on the days that you had it, over the last week?

   0 1 2 3 4 5 6 7 8 9 10

   NO PAIN

   PAIN AS BAD AS YOU CAN IMAGINE

5. How often have you had a sensation of not emptying your bladder completely after you have finished urinating, over the last week?
   - Not at all
   - Less than 1 time in 5
   - Less than half the time
   - About half the time
   - More than half the time
   - Almost always

6. How often have you had to urinate again less than two hours after you finished urinating, over the last week?
   - Not at all
   - Less than 1 time in 5
   - Less than half the time
   - About half the time
   - More than half the time
   - Almost always

**Impact of Symptoms**

7. How much have your symptoms kept you from doing the kinds of things you would usually do, over the last week?
   - None
   - Only a little
   - Some
   - A lot

8. How much did you think about your symptoms, over the last week?
   - None
   - Only a little
   - Some
   - A lot

**Quality of Life**

9. If you were to spend the rest of your life with your symptoms just the way they have been during the last week, how would you feel about that?
   - Delighted
   - Pleased
   - Mostly satisfied
   - Mixed (about equally satisfied and dissatisfied)
   - Mostly dissatisfied
   - Unhappy
   - Terrible

---
Patient with SUSPECTED PROSTATITIS

History and physical examination
Midstream urine culture (UC)

Not acutely ill

Urinary tract infection, site unknown

Exclude nonprostatic site of infection

Stop any antimicrobial. Repeat UC off-therapy with four-glass cultures

Urine culture (positive)

Leukocyte (positive)

Culture (positive)

NIH Category II

Leukocyte (positive)

Culture (negative)

NIH Category IIIB

Leukocyte (negative)

Culture (negative)

NIH Category I

NIH Category IIIA

Signs of systemic infection, sepsis; tender, boggy prostate

Defer expressed prostatic secretions

Inadequate/retention

Voiding

Adequate

Expressed prostatic secretions or VB3

Antimicrobial therapy

Antimicrobial therapy

Good response

A

Continued 4–12 weeks

Poor response

Antimicrobial therapy

Effective

CT to evaluate for prostatic abscess

Ineffective

No further treatment

Suppressive therapy

Radical transurethral resection of the prostate

Antimicrobial therapy

Appropriate evaluation to exclude other pathology

Serial NIH-CPSI to assess response

Treatment options include

Antimicrobials
Alpha-blockers
Anti-inflammatories
Finasteride
Phytotherapy
Biofeedback
Trigger point therapy
Prostatic massage

Consider enrollment in multi-institutional trial
Stamey four-glass urine test (Figure 29-2) is a cornerstone of the thorough evaluation of the infected male urinary system. The patient diagnosed with prostatitis who is referred for urologic evaluation can require careful consideration to interpret the influences of prior treatments and diagnostic studies in the context of this quite complicated disease process.

A Urinary retention may accompany acute bacterial prostatitis. Attempt the gentle passage of a small Foley catheter; if unsuccessful, insert a suprapubic drainage tube.

B Antimicrobial selection in acute prostatitis should be guided in part by the institutional and regional microbiologic sensitivity profiles. As the incidence of trimethoprim-sulfamethoxazole (TMP-SMX) resistance is about 15% in many parts of the country, initial treatment with a fluoroquinolone or aminoglycoside-beta-lactam combination is appropriate until culture and susceptibility data are available.

C Antimicrobial therapy of chronic bacterial prostatitis should be carefully directed against the microbiologic species identified, should consist of a prostate-penetrating agent such as a fluoroquinolone, and should continue for a minimum of 6 weeks. To identify bacterial persistence, follow-up cultures after completing therapy are important to obtain.

D Careful evaluation is crucial before assigning the diagnosis of chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) to exclude other causes of pelvic symptomatology. Use urine cytology to exclude transitional cell malignancy in the setting of microhematuria or significant irritative symptoms. Other tests to consider in the appropriate setting include prostate-specific antigen (PSA), semen analysis and culture, urethral swab and culture, pressure flow or urodynamic studies, cystoscopy, transrectal ultrasonography (TRUS), and computed tomography (CT) or magnetic resonance imaging (MRI).

E The optimal treatment of the CP/CPPS patient is quite unclear at present. Many different therapies have been used with varied success; most of these have been in the context of poorly controlled studies. Multi-institutional, randomized trials are currently under way, comparing a few of the more common therapies. Treatments including alpha blockade, finasteride, anti-inflammatory medication, Elmiron, bioflavinoids such as Quercetin, and prostatic massage may all have some value. These are acceptable therapy when applied carefully to patients who have not been found to have a more easily treatable affliction. An excellent summary of the state of the art was written by McNaughton Collins and coworkers.2,3

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Table 29-1 National Institutes of Health Classification and Definition of Prostatitis Categories

<table>
<thead>
<tr>
<th>Category I: acute bacterial prostatitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute infection of the prostate gland</td>
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</table>

<table>
<thead>
<tr>
<th>Category II: chronic bacterial prostatitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrent urinary tract infection</td>
</tr>
<tr>
<td>Chronic infection of the prostate</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Category III: chronic abacterial prostatitis/chronic pelvic pain syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discomfort or pain in the pelvic region (for at least 3 months) with</td>
</tr>
<tr>
<td>variable voiding and sexual symptoms</td>
</tr>
<tr>
<td>No demonstrable infection</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Category IIIA: inflammatory chronic pelvic pain syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>White blood cells in semen/expressed prostatic secretion/VB3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Category IIIB: noninflammatory chronic pelvic pain syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>No white blood cells in semen/expressed prostatic secretion/VB3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Category IV: asymptomatic inflammatory prostatitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Evidence of inflammation in biopsy, semen/expressed prostatic secretion</td>
</tr>
<tr>
<td>No symptoms</td>
</tr>
</tbody>
</table>

Adapted from data from the National Institutes of Health summary statement. Presented at the National Institutes of Health/National Institute of Diabetes and Digestive and Kidney Disease Workshop on Chronic Prostatitis, National Institutes of Health, Bethesda, MD, December 1995. VB3 = initial 10 mL of voided urine after prostatic massage.

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Figure 29-2 The classic Meares-Stamey four-glass urine test. VB1 is the initial 10 cc of the urinary stream and represents the urethral specimen. VB2 is a midstream from the bladder itself. EPS and voided bladder-3 (VB3, the first 10 cc of urine after prostatic massage) are representative of the prostatic microbiologic environment.
References


Epididymitis is a common urologic diagnosis. The most important decision is the differentiation of this infectious entity from the ischemic emergency of testicular torsion. In younger patients, especially those under age 20 years, a high degree of clinical suspicion should prompt immediate scrotal exploration without delay for confirmatory studies such as ultrasonography or radionucleotide imaging. In epididymitis, the microbiology is generally that of urethritis in sexually active men under 35, that is *Neisseria gonorrhoeae* and *Chlamydia trachomatis*. In patients over age 35 years or those practicing insertive anal intercourse, coliforms predominate. Tuberculosis, *Brucella*, and *Cryptococcus* infections are documented infrequently, and ultrasonographic evaluation for testicular tumor should be obtained in the absence of a clear etiology for pain or mass. Finally, the antiarrhythmic amiodarone has been shown to cause a sterile inflammation in the head of the epididymis that generally responds to a decrease in dosage of the drug.1,2

A Patients with acute scrotal pain, epididymal and testicular tenderness, and swelling or induration require a complete history and physical examination. Testicular torsion is more common than is epididymitis as a cause of acute scrotal pain in young men and boys. In the absence of evidence of urinary tract infection or urethritis, emergency exploration to rule out torsion of the testes merits serious consideration.

B A history of straining or heavy lifting occasionally precedes acute epididymitis. In preschool children, it is frequently associated with coliform or *Pseudomonas* infection and structural or neurologic abnormalities of the urinary tract. Sexually transmitted organisms (*N. gonorrhoeae, C. trachomatis*) are the most common cause of acute epididymitis in men under age 35 years. In men older than 35 years, sexually transmitted pathogens are less common, and epididymitis is usually secondary to coliform bacteriuria associated with underlying genitourinary pathology.3 All patients with acute epididymitis require scrotal support and bed rest.

C If the midstream urinalysis shows bacteria, the epididymitis is due to coliform, coccal, or *Pseudomonas* infection. Initial empiric therapy with a broad-spectrum antimicrobial is appropriate, with modification based on sensitivity results. A complete urologic evaluation to rule out underlying structural abnormalities is warranted.

D In the absence of bacteriuria or gonococcal urethritis, the clinician may presume *C. trachomatis* infection. The appropriate therapy is azithromycin (1 g orally in 1 dose) or a 10-day course of either doxycycline or erythromycin. The sexual partner of patients with gonococcal or chlamydial epididymitis should also receive antimicrobial therapy.

E If the urethral smear shows intracellular diplococci, *N. gonorrhoeae* is most likely the cause of the epididymitis. The appropriate therapy is ceftriaxone, 125 mg intramuscularly once; treatment for chlamydial infection as outlined above is also warranted because the incidence of *C. trachomatis* co-infection is 25% in men with gonorrhea.4 Check for suspect tumors, tuberculosis, or other etiology if the patient fails to improve.

F If the patient has a negative midstream urine, urethral smear, or culture and/or fails to improve on appropriate therapy, other diagnoses, such as testicular tumors, tuberculosis, or intermittent torsion, should be considered.

References
Patient with ACUTE SCROTAL PAIN

History, physical examination

Epididymal induration
Swelling
Tenderness

Acute epididymitis

No induration, swelling or tenderness

Age ≤ 20, suspect testicular torsion
Age > 20, suspect testicular tumor

Scrotal exploration or ultrasonography as appropriate

Midstream urine
Gram's stain
Culture

Urethral smear
Gram's stain
Culture

Positive
Negative

Patient ≤ 20 yr
Suspect torsion
Bed rest
Scrotal support

Patient > 20 yr
Bed rest
Scrotal support

Bed rest
Scrotal support

Evaluate for:
Chronic bacterial prostatitis
Structural abnormalities

Treat urinary tract infection

Therapy for gonorrhea
Treat sexual partners

Treat for C. trachomatis
Treat sexual partners

Follow
Etiology
Retroperitoneal fibrosis was first described by Albarran in 1905 and further characterized by Ormond in 1948. Approximately two-thirds of cases have no specific etiology and are classified as idiopathic retroperitoneal fibrosis. Table 31-1 summarizes other etiologic factors. Drugs, most notably methysergide and other ergot alkaloids, are associated with retroperitoneal fibrosis (RPF). Graham noted a 1% incidence of RPF with prolonged methysergide use, possibly through inhibition of serotonin receptors. Drugs may also act as haptens, causing a hypersensitivity reaction. Malignancy causes RPF in 7.9% of cases. Lymphoma is the most common, with carcinoid, multiple myeloma, sarcoma, and metastatic carcinomas also in the differential diagnosis.

There is growing evidence that idiopathic RPF is related to a chronic immune response to ceroid, an oxidized lipid and protein component of atherosclerotic plaques. Anticericoid antibodies and similarities in histopathologic features and anatomic distribution have led some authors to categorize idiopathic RPF, inflammatory abdominal aortic aneurysm, and periaorternal RPF together as “chronic periaortitis.”

RPF may also be associated with other disease processes associated with fibrosis, including mediastinal fibrosis, Riedel’s thyroiditis, and systemic lupus erythematosus.

Pathology
Grossly, RPF is a tan or white plaque that may envelop the great vessels from the renal hilum to the sacral promontory and extends laterally to involve the ureters and psoas muscles. On rare occasions, the process extends proximally into the mediastinum or invades the ureters, although pelvic extension is not uncommon. Histologically, active inflammation characterized by lymphocytes, plasma cells, macrophages, and polymorphonuclear leukocytes is interspersed with fibrous scar tissue. Although heterogeneity exists even within the same mass, fibrous tissue tends to predominate in late-stage disease. These findings have been used to support an immune etiology of RPF and also to differentiate the symptoms of early-stage versus late-stage disease.

The incidence of RPF is approximately 1 in 200,000. There is no racial predominance, but the disease is two to three times more common in men than in women and most commonly presents in the fourth to sixth decade. Symptoms in the early stage relate to inflammation, including malaise, weight loss, anorexia, and low-grade fever. Most patients have back and abdominal pain, often in a girdle-like distribution, originating in the back and radiating to the lower abdominal quadrants and groin. The pain is usually dull and noncolicky and is classically relieved by anti-inflammatories but not by narcotics. The erythrocyte sedimentation rate (ESR) is elevated in 90% of patients. Moderate leukocytosis, anemia, and hypertension are common, even in early-stage disease. Late-stage disease shows progressive ureteral obstruction with azotemia, uremic symptoms, and flank pain. Venous thromboembolism may occur in up to 25% of cases owing to vena cava compression. Approximately one-half of patients present with late-stage disease (Table 31-2).

Laboratory studies should include complete blood count (CBC), blood urea nitrogen (BUN), serum creatinine, urinalysis, and urine culture. Although largely supplanted by computed tomography (CT) scan, intravenous pyelogram (IVP) may be the initial study in patients who present with flank pain, with early-stage

### Table 31-1 Etiologies of Retroperitoneal Fibrosis

<table>
<thead>
<tr>
<th>Aortitis</th>
<th>Drugs</th>
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<tbody>
<tr>
<td>Aortic aneurysm</td>
<td>Methysergide</td>
</tr>
<tr>
<td>Inflammatory reaction to atherosclerosis</td>
<td>β-Blockers</td>
</tr>
<tr>
<td>Collagen vascular disease</td>
<td>Hydralazine</td>
</tr>
<tr>
<td></td>
<td>Haloperidol</td>
</tr>
<tr>
<td>Retroperitoneal tumors</td>
<td>Methylidopa</td>
</tr>
<tr>
<td>Retroperitoneal hemorrhage</td>
<td>Reserpine</td>
</tr>
<tr>
<td>Radiation</td>
<td>Phenacetin</td>
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<table>
<thead>
<tr>
<th>Infection</th>
<th></th>
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<tbody>
<tr>
<td>Tuberculosis</td>
<td></td>
</tr>
<tr>
<td>Gonorrhea</td>
<td></td>
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<tr>
<td>Chronic UTI</td>
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</table>

### Table 31-2 Common Symptoms of Retroperitoneal Fibrosis

<table>
<thead>
<tr>
<th>Symptom</th>
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<tbody>
<tr>
<td>Flank pain</td>
</tr>
<tr>
<td>Back pain</td>
</tr>
<tr>
<td>Abdominal pain</td>
</tr>
<tr>
<td>Weight loss</td>
</tr>
<tr>
<td>Nausea or vomiting</td>
</tr>
<tr>
<td>Edema</td>
</tr>
<tr>
<td>Malaise</td>
</tr>
</tbody>
</table>
History (including medication use)
Physical examination

CBC, serum chemistry, ESR, urinalysis, and urine culture
Stop suspect medications

CT scan (MRI if renal impairment)

Drugs suspected
Mild/no renal impairment
Minimal hydronephrosis

Observation with/without steroids

Improve ment or no progression?

Yes

Continued observation

No

Steroids

Improvement?

Yes

Percutaneous nephrostomy or ureteral stents

No

Continue medical management

Elevated ESR
Mild/no renal impairment

Steroids

Improvement?

Yes

Ureterolysis (laparoscopic or open)
Biopsy of mass

Renal impairment
Severe hydronephrosis

Yes

No

Stent or percutaneous nephrostomy

Leaf
disease and little or no impairment of renal function. The classic IVP finding is medial deviation of the ureters at L4–L5, although this is neither an invariable finding nor pathognomonic because 20% of normal patients have a similar medial deviation. In contrast, abdominal aortic aneurysm and retroperitoneal neoplasms tend to cause lateral displacement of the ureters. Retrograde pyelograms demonstrate similar findings; however, the ureters will typically allow passage of a 5- or 6-French ureteral catheter, which supports the hypothesis that the pathogenesis of ureteral obstruction in RPF is due to interruption of ureteral peristalsis by inflammation.

CT is the radiologic examination of choice in evaluating suspected RPF. The lesion appears as a periaortic soft tissue mass with variable contrast enhancement, mostly in areas of active inflammation. The mass in RPF typically lies anterior and lateral to the aorta. Complete encirclement of the great vessels, anterior displacement of the aorta from the spine, local bone destruction, and discrete enlarged periaortic lymph nodes raise the suspicion of malignancy (Figure 31-1).

Magnetic resonance imaging (MRI) allows multiplanar imaging, provides better delineation of the relation of adjacent structures to the mass, and may be performed in patients with renal insufficiency. RPF is typically of low signal intensity compared with muscle on T1-weighted images and has variable intensity on T2-weighted images based on disease stage. The active inflammation of early stage disease has a high T2 signal intensity, whereas late-stage disease is typically low intensity. Malignancy, however, also exhibits variable T2 signal intensity; therefore, this finding is nonspecific.

MRI may also be able to assess the response to medical therapy for RPF: a decrease in tissue edema from steroids and other drugs may be reflected as decreased T2 signal intensity.

Ultrasoundography is not commonly used to evaluate RPF but may be the initial study obtained in a patient presenting with elevated serum creatinine and flank pain. Sonographic findings may include an anechoic, irregular, well-marginated extrarenal mass and hydronephrosis.

Although radiologic evaluation can suggest a diagnosis of idiopathic RPF, the true diagnosis can be made only after eliminating malignancy or other etiologies with a tissue diagnosis. This is typically done with multiple deep biopsies at the time of open or laparoscopic ureterolysis. A recent report in a small series of patients suggests that fine-needle aspiration may be sufficient for diagnosis, but the authors note the possibility of a false-negative diagnosis. Another series suggests that this approach is best reserved for patients unable to undergo operative intervention.

Initial RPF management is determined by the patient’s renal function and clinical status, with emphasis on providing adequate drainage of the urinary tract with ureteral stents or percutaneous nephrostomy tubes and correcting electrolyte abnormalities. If drug-induced RPF is suspected, discontinuing the drug alone has allowed improvement in a few patients with only mild hydronephrosis; however, disease progression may also occur.

Some authors advocate treating patients with mild or no renal impairment with an initial trial of steroid therapy without biopsy, arguing that a delay in diagnosing a retroperitoneal malignancy by 2 or 3 weeks will not impact the overall clinical outcome. Failure to respond in this time period is an indication for biopsy. Steroids are most effective in treating patients with signs of acute inflammation: elevated erythrocyte sedimentation rate (ESR), leukocytosis, and evidence of active inflammation on biopsy. There is no consensus on dose or length of therapy if improvement is noted.

Other immunosuppressive drugs have been used in treating RPF. Azathioprine, tamoxifen, cyclophosphamide, and cyclosporine have been used in selected cases with success, although steroid therapy remains the mainstay of medical therapy.

Given the progressive nature of RPF, most urologists recommend surgical exploration with biopsy of the mass and ureterolysis. Open ureterolysis is performed through a midline transabdominal incision. As generally, the process is bilateral, bilateral ureterolysis is recommended, even if hydronephrosis is unilateral. After
the ureters are completely lysed, they may be transposed laterally with retroperitoneal fat or omentum interposed between the ureters and the fibrosis. Alternatively, the ureters may be intraperitonealized, again with the possibility of an omental wrap. A recent study noted no difference in the outcome with either approach, each with > 90% success.16

Laparoscopic ureterolysis was initially described by Kavoussi and colleagues in 1992.17 A subsequent study comparing unilateral laparoscopic with unilateral open ureterolysis showed no difference in efficacy.18 Bilateral laparoscopic ureterolysis has also been described.19

Postoperative steroids are often employed to prevent progression of the fibrosis. Nevertheless, this remains controversial because they do not prevent recurrent obstruction in all patients and may not influence the restenosis rate, even in disease with a predominance of inflammatory tissue.

### Outcome and Follow-Up

Disease recurrence is possible, even in the years following initial treatment. We recommend follow-up radiologic studies, such as IVP, ultrasonography, or renal scan, along with monitoring of renal function and ESR at regular intervals.

### References

SECTION 4

VENEREAL DISEASE
Primary Syphilis

Durwood E. Neal Jr, MD

In the years leading up to the onset of the epidemic of human immunodeficiency virus (HIV) infection, the incidence of syphilis had been gradually increasing. This change likely did not relate to changes in reporting because syphilis has been consistently reportable worldwide for decades. There is, however, one obfuscating issue: physicians and those in training may underrecognize the disease. Nonetheless, after the initial acquired immunodeficiency syndrome (AIDS) cases were reported, syphilis cases began to diminish, even though there was a heightened awareness (and thus recognition) of the disease. Much of this was attributable to the fear of contracting AIDS and the subsequent practice of “safe sex,” as well as reduced needle sharing among the drug addict population. In the last few years, as more and more medications have become available to treat HIV infection, concomitant with a fall in the death rate from the disease, the incidence of syphilis, as well as other sexually transmitted diseases, has been on the rise. As a result, physicians need to be vigilant about the manifestations of syphilis. With the relative paucity of cases, the physicians’ experience may wane, and, consequently, the disease may go unrecognized. In addition, with the reduction in routine testing for syphilis, patients discovered by screening will diminish, giving a greater opportunity for spread of the infection.

A. Syphilis may take many forms, although only the primary type will be reviewed here. It manifests itself by a single, painless, usually indurated ulcer (chancre) noted at the portal of entry of the organism *Treponema pallidum*. This is usually on the genitalia, mouth or pharynx, or at the rectum. On rare occasions, the chancre may be located on the cervix or vaginal wall in women or in the anal canal in either sex and may be less recognizable in those locations. The incubation period varies from 1 week to 3 months and usually lasts about 4 weeks (3 to 8 weeks). The time course may be shortened if antibiotics are administered, even if a dosage or time course is insufficient to completely eradicate the spirochete. There is usually lymphadenopathy that lasts several weeks, but intervening with antibiotic therapy may shorten the time course. The lymph node enlargement frequently is bilateral and rarely tender or suppurative and is otherwise indistinguishable from other inflammatory processes. A confusing aspect of primary syphilis is the high likelihood of concomitant infection with other agents causing sexually transmitted diseases (STDs). Further, the chancre may serve to increase the infectivity of other STDs by breaking the integumentary barrier. Because of this, the diagnosis may be clouded, so screening for multiple STDs is mandatory to completely treat each entity. It is also important to examine the cerebrospinal fluid if the patient had the primary form for more than 1 year. This is to rule out early neurosyphilis.

Another type of primary syphilis is congenital syphilis. The organism freely crosses the placenta and occurs in the primary or secondary forms. The child begins to manifest the disease by the end of the fourth month. Generally, the earlier the symptoms and signs occur, the worse the prognosis. A myriad of clinical findings may be manifest. One of the best known is Hutchinson’s triad, which is interstitial keratitis, eighth nerve deafness, and Hutchinson’s teeth, which are deformities of two central incisors of the permanent teeth, spacing the deciduous teeth. Clutton’s joint is manifested by hydrarthrosis of the knee. The classic nasal appearance is due to flattening of the nasal bridge from cartilage destruction from nasal syphilis, called *snuffles*.

B. The laboratory diagnosis of syphilis has changed over the years, from the classic darkfield microscopy examination or fluorescent antibody to one of molecular diagnosis. Serology, however, remains an important method of screening patients and contacts. The Venereal Disease Research Laboratory (VDRL) is one of the most common tests and is considered to be a nontreponemal test, measuring nonspecific antibodies. Most clinicians use this laboratory determination for following the patient’s recovery and illness. It will revert to a negative result after disease resolution. It is a flocculation test, and the measurement standards have been set by the World Health Organization. Some of the problems associated with this test are that it may be read as negative when truly positive, owing to an excess of antibody (referred to as a prozone phenomenon). In addition, certain disease processes—most notably those that involve antibody production or malignancy—may result in false-positive VDRL tests. The treponemal tests, such as fluorescent treponemal antibody absorption test (FTA-ABS), which is an indirect fluorescent antibody test, may be used for both screening and following patients with the disease. Unfortunately, other treponemal diseases, such as pinta or yaws, may cause a false-positive FTA-ABS. This test usually remains positive for life, irrespective of treatment. It also becomes positive earlier in the infection than does the VDRL.

C. The goals of treatment of primary syphilis involve three main aspects. The first is eradication of the primary infection. The organism is fairly fastidious and sensitive.
Primary Syphilis

The most commonly used agent is benzathine penicillin, typically given as a single intramuscular injection of 2.4 million units. This is sufficient to eliminate the spirochete in > 98% of the cases. Most patients who are adequately treated for syphilis will experience the Jarisch-Herxheimer reaction. This is manifested by fever, rash, malaise, and headache. It is likely due to the death of spirochetes, but this is unclear. It resolves in 24 hours or less in virtually all cases. The patient must have follow-up serology to determine whether further therapy is required. The second part of therapy is to reduce transmission to other individuals. The single penicillin injection does help in that arena in that the patient’s infectivity is all but completely eliminated in a few days. Third, prevent the effects of secondary or tertiary syphilis, which may be fatal or irreversible. If the patient is appropriately followed, this should not occur. Even in the noncompliant patient, almost all patients who receive the prescribed treatment will not progress to the lethal complications.

There are other treatments that may be used that are effective, especially for patients who are allergic to penicillin. One of these is tetracycline, which is given as an oral preparation for 2 weeks (500 mg four times daily). Although this is quite effective, it does require more compliance from the patient and more diligence on the part of the health care provider or system. Oral macrolides may be used as well. The absorption of both of these agents may be affected by certain over-the-counter medications, especially antacids. Thus, the patient needs to be informed about these issues. All the treated patient’s primary sexual contacts must be treated and tested; even those patients who initially test negative should probably be treated. To ensure eradication, all treated patients must have follow-up quantitative VDRL tests periodically for 2 years. Keep in mind, however, that prevention is the first line of therapy in all circumstances.

Additional Readings

Chancroid is one of the ulcerative sexually transmitted diseases. Chancroid is characterized by painful genital ulcers, often with regional lymphadenitis, but not by systemic infection. The disease is caused by a bacterial infection with *Haemophilus ducreyi*, a short, nonmotile, gram-negative bacillus.

Chancroid is common in developing countries and is also endemic in some areas of the United States. In addition, the disease occurs in discrete outbreaks. Chancroid is well established as a cofactor for human immunodeficiency virus (HIV) transmission; high rates of HIV infection among patients who have chancroid have been reported in the United States and other countries. Therefore, counseling and testing for HIV infection should be recommended for patients with chancroid or any other ulcerative genital disease.

**A** Probable clinical diagnosis depends on the presence of all of these four criteria: (a) one or more painful genital ulcers; (b) no evidence of *Treponema pallidum* infection (ie, syphilis) by darkfield examination of ulcer exudates or by a serologic test for syphilis performed at least 7 days after the onset of symptoms; (c) the clinical presentation, ulcer appearance, and regional lymphadenopathy, if present, are typical for chancroid; and (d) a negative test for genital herpes simplex virus (HSV) infection. The combination of a painful ulcer plus tender inguinal adenopathy is said to be pathognomonic for chancroid. Unfortunately, this combination of clinical signs occurs in only about one-third of patients.

**B** Definitive diagnosis of chancroid can be challenging. *H. ducreyi* can be isolated in culture using special media. Unfortunately, such media are not widely available from commercial sources, and the sensitivity of optimal cultures remains ≤ 80%. Molecular diagnostic testing for *H. ducreyi* might become available soon.

After a short incubation period (3 to 5 days), a maculopapular lesion develops that progresses rapidly to ulceration. Multiple lesions often ensue, frequently by autoinoculation. The most common sites of lesions in men are the prepuce, glans, and coronal sulcus. Serpiginous ulceration of the coronal sulcus is said to be highly typical of chancroid. In women, the most common sites are the fourchette and labia. The ulcers are erosive, ragged, and painful. Suppurative, unilateral, painful, inguinal lymphadenitis may develop within 1 to 2 weeks. With delayed or ineffective treatment, the inguinal ulceration may progress to form a pus-filled bubo that may eventually rupture through the skin to form a deep, ragged crater. Untreated disease remains regional but does not spread systemically.

**C** An estimated 10% of patients who have chancroid also have coinfections with *T. pallidum* or HSV; therefore, it is important to test patients for these infections even if the clinical appearance is characteristic.

**D** Successful treatment cures chancroid, resolves the clinical symptoms, and prevents transmission to others. In extensive cases, scarring can progress despite successful therapy.

Antimicrobial therapy is the cornerstone of treatment. Recommended regimens are summarized in Table 33-1. All four regimens are also effective for chancroid in HIV-infected patients. The azithromycin and ceftriaxone regimens offer the advantage of single-dose therapy. Worldwide, several isolates have been reported with intermediate resistance to either ciprofloxacin or erythromycin.

Some data suggest that uncircumcised men and HIV-infected persons do not respond as well to treatment as do circumcised men or HIV-negative persons. Patients should be tested for HIV infection at the time chancroid is diagnosed and then retested 3 months later if the initial test results for syphilis and HIV were negative.

The time required for healing depends on the size of the ulcer and the patient’s immunologic status. Large ulcers may require several weeks of appropriate therapy before healing is complete. Some authorities also suggest that healing of chancroidal ulcers is slower in uncircumcised men with ulcers under the foreskin. Clinical resolution of fluctuant lymphadenopathy is slower than that of ulcers and may require drainage, even during oth-

<table>
<thead>
<tr>
<th><strong>Table 33-1</strong> Recommended Antimicrobial Regimens for Chancroid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azithromycin 1 g orally in a single dose OR Ceftriaxone 250 mg intramuscularly in a single dose OR Ciprofloxacin 500 mg orally twice a day for 3 days* OR Erythromycin base 500 mg orally four times a day for 7 days</td>
</tr>
</tbody>
</table>

*Ciprofloxacin is contraindicated in pregnant or lactating women and persons < 18 years old.
erwise successful therapy. Incision and drainage of buboes is preferred to needle aspiration because there is less need for subsequent drainage procedures.

Patients should be reexamined 3 to 7 days after therapy is initiated, at which time substantial clinical improvement should be apparent. A number of possibilities must be considered if there is minimal or no improvement after this period: (a) the diagnosis may be incorrect; (b) the patient may be coinfected with another sexually transmitted infection; (c) the patient may be immunosuppressed owing to HIV infection; (d) the patient may not be compliant with the recommended regimen; or (e) the infecting *H. ducreyi* strain may be resistant to the prescribed antimicrobial.

Patients should be strongly encouraged to refer their sex partners for examination and treatment. Because the duration of infectiousness appears to be relatively short, anyone who has had sexual contact with the patient during the 10 days before the onset of symptoms in the index case should be evaluated. Evaluation is recommended whether or not the sex partners have urogenital symptoms.

### Additional Readings

With respect to sexually transmitted diseases (STDs), lymphogranuloma venereum (LGV) is relatively uncommon. It is classified among the STDs that are manifested by genital ulceration. The others are primary syphilis, genital herpes, chancroid, and granuloma inguinale. LGV is found in about 11% of the patients who are seen with genital ulcer disease. In this same population, 75% were found to be infected with the human immunodeficiency virus (HIV). The differential diagnosis of this group is critical because of the differences in treatment for each. The disease tends to occur in those at risk for STD, so the population demographics are the same. The most important association is with HIV infection; the sexual act may be the precipitating event in both cases, and even mild genital trauma may facilitate the transmission of all STDs. Serologic studies show that STDs frequently coexist.

A The organism responsible for LGV is *Chlamydia trachomatis*, serotypes L1, L2, and L3. The serovars of this organism that cause nongonococcal urethritis, were in a state of decline. Most authors considered the heightened awareness brought on by the acquired immunodeficiency syndrome (AIDS) epidemic as the basis for the decline. Unfortunately, this was short-lived, and the incidence has reversed itself and has been increasing for the past year or so. The educational priorities on safe sexual practices seem to be failing, possibly owing to some improvements in treating AIDS, which avoid the worst of the complications.

B The diagnosis of LGV usually involves serology to detect antibodies against chlamydia. The most common tests are complement fixation and immunofluorescence. There are several tests that can detect chlamydial deoxyribonucleic acid by polymerase chain reaction (PCR). It is possible to culture chlamydia from vaginal secretions, urethral swabs, or even urine.

C Treating most chlamydial infections, including LGV, involves the use of the tetracycline class of antibiotics. A 2-week course of therapy is considered to be sufficient to eradicate the infection. For patients who are unable to take this class of medication, clinicians use erythromycin. Some of the newer tetracyclines, such as novomycin or doxycycline, as well as the newer macrolides, such as clarithromycin and azithromycin, are better tolerated and have better tissue penetration than some of the more generic preparations. Secondary infection of the enlarged lymph nodes with suppuration may substantially alter the treatment course. In addition, consider the degree of immunosuppression because most patients are probably HIV infected, along with having infection and fistula formation.

Note that many STDs coexist in the same patients. This may complicate the therapy by adding other medications or altering the treatment course. It seems prudent to keep LGV in the differential diagnosis of genitourinary ulcer disease, as well as inguinal lymphadenopathy.

Additional Readings

Patient with GENITAL ULCER

A

B

Confirmatory laboratory analysis (eg, serology, direct culture, PCR) lymphadenopathy

Positive Negative

C

Consider secondary infection: aspirate

Positive Negative

Secondary organism No secondary organism

Treat as appropriate

Treat 14 d tetracycline or macrolide

Positive Negative

Secondary organism No secondary organism

Treat as appropriate

Treat 14 d tetracycline or macrolide
Granuloma inguinale is an ulcerative sexually transmitted disease characterized by progressive, painless lesions without regional adenopathy. The disease is caused by the intracellular, nonmotile gram-negative bacillus *Calymmatobacterium granulomatis*. Granuloma inguinale is also known as donovanosis and granuloma venereum.

Granuloma inguinale is rare in the United States. The disease is endemic in certain tropical and developing areas, including India, Papua New Guinea, central Australia, and southern Africa.

**A** Granuloma inguinale presents with painless, progressive, ulcerative lesions without regional lymphadenopathy. Characteristic lesions are highly vascular (ie, “beefy red” appearance) and bleed easily on contact. The lesions expand slowly and then undergo necrosis and fibrosis. Both phimosis and penile lymphedema develop commonly during the active phase of infection. Secondary bacterial infection of lesions is common. Coinfection with another sexually transmitted disease pathogen is also common.

The incubation period ranges from 8 to 80 days. Single or multiple subcutaneous nodules develop and then erode through the skin to produce clean, sharply defined, painless ulcers. Secondary infection is common, but frank cellulitis is rare. Development of extragenital granuloma inguinale is rare.

**B** *C. granulomatis*, the causative organism, cannot be cultured on standard microbiologic media. Diagnosis requires visualization of dark-staining Donovan bodies on a tissue-crush specimen or biopsy prepared with Wright’s stain or Giemsa stain. Donovan bodies are bipolar, encapsulated bacilli lying mainly within vacuoles in large macrophages. Both extracellular and intracellular forms are found, and each form may or may not be encapsulated.

**C** Other ulcerative sexually transmitted infections must be excluded, especially syphilis (by darkfield microscopy or an immunofluorescence test plus serology) and genital herpes virus infection (by culture or an antigen detection test). Patients with granuloma inguinale should be counseled and tested for human immunodeficiency virus infection. Biopsies may also prove helpful to exclude the diagnosis of penile carcinoma.

**D** Treatment appears to halt progressive destruction of tissue, although prolonged duration of therapy is often required to enable granulation and re-epithelialization of the ulcers. Recommended antimicrobial regimens and alternatives are summarized in Table 35-1. Relapse can occur 6 to 18 months later despite effective initial therapy.

Patients with granuloma inguinale should be reevaluated during the first few days of therapy. If lesions have not responded by this period, addition of an aminoglycoside (gentamicin 1 mg/kg IV every 8 hours) should be considered. Follow-up should continue until clinical signs and symptoms have resolved completely.

Sex partners of patients with granuloma inguinale should be examined and treated if they (a) had sexual contact with the patient during the 60 days preceding the onset of symptoms in the patient and (b) have clinical signs and symptoms of the infection. Surgical drainage is rarely necessary.

Pregnancy is a relative contraindication to the use of sulfonamides. Both pregnant and lactating women should be treated with the erythromycin regimen. The addition of a parenteral aminoglycoside (eg, gentamicin) should be strongly considered for pregnant women or HIV-infected patients with granuloma inguinale.

**Table 35-1 Antimicrobial Treatment Regimens for Granuloma Inguinale**

<table>
<thead>
<tr>
<th>Recommended regimens</th>
<th></th>
<th>Alternative regimens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trimethoprim-sulfamethoxazole one double-strength tablet orally twice a day for a minimum of 3 weeks OR Doxycycline 100 mg orally twice a day for a minimum of 3 weeks. Therapy should be continued until lesions have healed completely.</td>
<td>Ciprofloxacin 750 mg orally twice a day for a minimum of 3 weeks OR Erythromycin base 500 mg orally four times a day for a minimum of 3 weeks.</td>
<td></td>
</tr>
</tbody>
</table>

**Additional Readings**
Granuloma Inguinale (Donovanosis)

Patient with GENITAL ULCER

Granuloma inguinale suspected

A History
  Physical examination
  Clinical features

B Biopsies, stained smears (crush prep)
  Exclude carcinoma
  Culture and polymerase chain reaction testing (if available)

C Excluded other ulcerative sexually transmitted infections:
  Genital herpes
  Syphilis
  Lymphogranuloma venereum
  Chancroid

Genital lesions only or mild inguinal adenopathy
Secondary infection of lesions

D Antimicrobial therapy
  (Table 35-1)

Good response
Continue until resolution minimum of 3–4 weeks

Poor response
Add parenteral antibiotics


Disease that is caused by the herpes family of viruses is ubiquitous worldwide. For the purposes of characterization, there are two classes of herpes simplex to be considered as a sexually transmitted disease (STD): herpes simplex virus (HSV) types I and II. The disease is somewhat difficult to follow because it is not reportable to any of the tracking agencies. In fact, it depends on the definition of herpetic disease insofar as documentation of the specific infection is concerned. In several studies, the seroconversion rate is about 50 to 90% in most countries, when both types I and II are considered. Considering type II alone, which has shown a degree of tropism for the genitourinary organs, the range in incidence is 10 to 70% of genital infections, with about a 5% incidence of HSV infections in patients presenting to their primary care physician’s office with acute disease. The two types are distinguishable from one another by either monoclonal antibodies against viral capsid proteins or by differences in deoxyribonucleic acid (DNA) analysis. The virus may be transmitted by oral-genital contact, as well as genital-genital and genital-anal exposure, thus making this distinction somewhat more relevant. There is a definite opportunity for crossover of HSV types I and II. Hence, one may not necessarily assume that the location of the primary (or recurrent) disease dictates the exact etiologic type.

A The first episode of HSV infection tends to differ substantially from subsequent ones. In the former, there is a higher likelihood of systemic symptoms developing, such as fever, malaise, muscle pain, and arthralgias. Tender lymphadenopathy is typical in a first episode but much less common in recurrent disease. Likewise, bilaterality is very common in the primary infection rather than in the recurrent variety. If a recurrent infection resembles a primary one, the clinician should suspect immunosuppression. The primary infection is also more severe in women than in men and tends to cause urinary retention, hematuria, and other severe local symptoms. Severe symptoms are evident in both sexes when the primary lesions are in the anal region. Patients who are immunocompromised tend to have more frequent and much more severe recurrent episodes, which may lend confusion to the diagnosis. Further, it must be remembered that other STDs may coexist, thus causing ambiguity with respect to the specific diagnosis.

Recurrent HSV infections occur in patients who experience a primary lesion with an incidence of >80%. The vesicles tend to be unilateral, less numerous, and less painful. They rarely cause any degree of systemic symptomatology, if at all, and produce fewer and milder local reactions. The eruptions tend to be shorter in duration and are less susceptible to secondary bacterial infection. Nonetheless, they are still highly infectious and may cause autoinoculation with subsequent new lesions.

B The clinician reaches a diagnosis most frequently by obtaining a history, supplemented with physical examination. Many times the lesions are in a state of resolution, and the viral particles may be difficult to isolate. The clinician may perform a biopsy on the lesions or may take smears to look for intranuclear inclusion bodies, by either the Papanicolaou (Pap) test or the Tzanck smear technique. The HSV antigens may be detected by either immunofluorescence or immunoperoxidase, but all of these tests have false-negative and false-positive rates of 10 to 50%. If the lesions are within the first 5 to 6 days of eruption, the virus may be cultured, and these results are the most sensitive and specific. For clinical purposes, it may be unnecessary to perform expensive and labor-intensive laboratory determinations; however, when a group of vesicles on an erythematous base do not follow a neural distribution, this appearance is classic for herpes simplex infection.

C Several medications are available for treating genital herpes. The prototypical drug, acyclovir, has been supplanted by famciclovir and valacyclovir. This class of drugs blocks thymidine kinase by serving as an analog of guanidine. Its action inhibits DNA polymerase and also acts as a chain terminator. These drugs work to decrease the time course and severity of the symptoms, as well as to reduce viral shedding. In the same way, they have been used to prevent recurrences or to significantly reduce recurrent episode frequency in a daily prophylactic fashion. When recurrences occur, they are shorter in duration and are significantly reduced in severity. Patients need to take the drugs on a regular basis to consistently prevent infections. When the infections occur, the dosage is increased.

The treatment of primary herpes involves high dosages of the thymidine kinase inhibitors, which are taken until the lesions are greatly regressed or have disappeared. More importantly, clinicians should manage the other symptoms that accompany a primary herpetic infection. Frequently, the lesions are exquisitely painful and have the added dimension of referred pain along the neural distribution of the viral particles. Management may be undertaken best by using nonsteroidal anti-inflammatory agents or cyclo-oxygenase-2 inhibitors. Other agents may also help, but often narcotics become necessary because of the severe nature of the discom-
Urinary retention is a common sequela that occurs more often in women, which might be due to the pelvic floor spasm that results from the intense neural stimulation. Occasionally, catheterization is required, but because of the overwhelming inflammatory reaction, often a suprapubic tube is necessitated. Intermittent catheterization is the preferred method. For less severe cases, consider using alpha-blocking agents, such as terazosin or doxazosin, or possibly the selective agent tamsulosin. Theoretically, these agents may reduce the discomfort to a degree; they may block not only the sympathetic efferents (motor, smooth muscle) but also the sympathetic afferents. Some patients will require the use of corticosteroids to mitigate the inflammation. A dose of 100 mg of hydrocortisone three times daily is sufficient to blunt this process. Their use, however, may prolong the infection and the symptoms. Anal lesions may be severe enough to require fecal diversion by colostomy.

HSV is transmitted by direct contact. If the skin or mucous membrane is abraded, there is a higher likelihood of infection, as well as increasing the numbers of lesions. This is usually the result of oral-genital, genital-genital, or genital-anal contact. The virus is shed in very high numbers in the fluid from the vesicles but may be transmitted from the crusted lesions in amounts that are sufficient to cause infection. In fact, viral shedding has been shown to occur from grossly intact skin and mucous membranes, all of which leads to a very high infectivity rate. Using prophylactic antivirals may all but eliminate viral shedding. The virus is not transmitted across the placenta but may infect the newborn at parturition and during passage through the birth canal. In fact, this may be considered a criterion for performing a scheduled cesarean section. In infants, especially premature ones who require treatment for pulmonary immaturity, this infection may be fatal.

Herpes antibodies exist in most adults throughout the world, but HSV type I is more common than type II. Nonetheless, this viral family is extremely common. Individuals may enhance infection prevention by using barriers (condoms, etc) or possibly some of the lubricant preparations. Avoiding contacts when they have active or resolving lesions is the ideal method, but, as stated above, asymptomatic viral shedding has been known to occur.

### Additional Readings


Urethritis is defined as inflammation of the urethra, characterized by the presence of leukocytes (WBCs) and classic symptoms of urethral discharge and dysuria. Asymptomatic inflammation of the urethra is also common. The major cause is infection with urogenital pathogens, especially *Neisseria gonorrhoeae* and *Chlamydia trachomatis*. Patients infected with *N. gonorrhoeae* have gonococcal urethritis, or gonorrhea. Nongonococcal urethritis (NGU) is diagnosed in patients with urethral WBCs and negative tests for *N. gonorrhoeae*.

An estimated 600,000 new infections with *N. gonorrhoeae* occur each year in the United States. Chlamydial genital infections also occur frequently among sexually active persons. By any estimate, urethritis is a common and important clinical condition.

The key to managing patients with urethritis is to provide efficient and accurate diagnosis and prompt therapy to prevent complications and to limit the potential for spread to others.

Most infections in men cause symptoms that prompt patients to seek curative treatment soon enough to prevent serious sequelae. Often, this may not be soon enough to prevent transmission to others. Some infections in men are complicated by development of disseminated gonococcal infection, epididymitis, epididymo-orchitis, urethral stricture disease, or Reiter’s syndrome. In contrast, many infections among women do not produce recognizable symptoms until complications (eg, pelvic inflammatory disease) have occurred. Both symptomatic and asymptomatic cases of pelvic inflammatory disease result in tubal scarring leading to infertility or ectopic pregnancy. Potential complications in infants born to women with untreated genital tract infections include prematurity, low birth weight, eye disease, and neonatal pneumonia.

Gonococcal urethritis is diagnosed if gram-negative intracellular diplococci are seen on Gram’s stain or if testing demonstrates presence of *N. gonorrhoeae*. NGU is diagnosed when *N. gonorrhoeae* is not identified in a patient with objective evidence of urethral WBCs. *C. trachomatis* is the most frequent cause of NGU (ie, in 23 to 55% of cases); however, the prevalence differs by age group, with lower prevalence among older men. The proportion of NGU cases caused by chlamydia has been declining gradually. Documentation of chlamydial infection is important because partner referral for evaluation and treatment would be indicated.

The etiology of most cases of nonchlamydial NGU is unknown. *Ureaplasma urealyticum* and possibly *Mycoplasma genitalium* are implicated in as many as one-third of cases. Specific diagnostic tests for these organisms are not indicated in uncomplicated patients with urethritis. *Trichomonas vaginalis* and genital herpes virus infections sometimes cause NGU. Diagnostic testing and treatment procedures for these organisms are reserved for situations in which NGU is nonresponsive to therapy.

It is important to assess risk factors and anatomic sites that are exposed. Physical examination should include specific attention to the urethra, where discharge should be evaluated as occurring spontaneously or by milking the urethra. The urethra should also be palpated carefully for presence of strictures. Occurrence of inguinal adenopathy suggests the presence of other sexually transmitted disorders, such as lymphogranuloma venereum, granuloma inguinale, or human immunodeficiency virus infections. It is also important to exclude other causes of external genital pathology such as genital ulcer disease, herpes simplex virus infections, condyloma acuminate, and potential complications of genitourinary tract infections, such as epididymitis, prostatitis, or urethral stricture.
Patient with SUSPECTED URETHRITIS

A
History
Assess risk factors
Physical examination
Urethra:
Discharge
Stricture
Epididymitis
Inguinal nodes
Exclude external genital lesions
Epididymitis

B
Urethral smear with/without first-void urine

Gram-negative intracellular diplococci (GC) present

C
Test for GC and chlamydial infection (CT)
Positive GC
Treat for gonorrhea (Table 37-1)

C
Treat for chlamydial infection (Table 37-2)

D
Serologic test for syphilis
Counseling and testing for HIV infection
Recommend evaluation and testing of sex partners

Leukocytes (WBCs) present
No GC

C
Positive CT
Treat for chlamydial infection (Table 37-2)

D
Serologic test for syphilis
Counseling and testing for HIV infection
Recommend evaluation and testing of sex partners

No GC
No WBCs

No GC
No WBCs

Reliable patient
Empiric therapy if high risk

Unreliable patient
Reevaluate: urethral smear before first void of the day
B The initial diagnostic evaluation should address two issues: first, confirm the presence of urethritis; second, test for the most common pathogens.

Clinicians should document that urethritis is, indeed, the cause of the patient’s symptoms. Urethritis can be documented by the presence of any one of the following four signs:

- Mucopurulent or purulent discharge found on physical examination. The discharge may occur spontaneously or after stripping of the urethra.
- Gram’s stain of urethral secretions shows $\geq 5$ WBCs per oil immersion field. The Gram’s stain is the preferred rapid diagnostic test for documenting the presence of urethritis. This test has high sensitivity and high specificity for documenting both urethritis and the presence or absence of gonococcal infection. Gonococcal infection is established by documenting the presence of WBCs containing intracellular gram-negative diplococci.
- Positive leukocyte esterase test obtained on first-void urine. Examination of first-void urine has proven more acceptable than the traditional urethral swab in high-risk populations, such as adolescents or patients attending sexually transmitted disease clinics. In urologic patients, this test has lower sensitivity than the Gram’s-stained urethral smear.
- Microscopic examination of first-void urine shows $\geq 10$ WBCs per high-power field.

If none of these criteria is present, defer treatment if the patient is reliable. Such patients should be tested for \textit{N. gonorrhoeae} and \textit{C. trachomatis} and treated appropriately in the event of positive test results. Empiric treatment of symptoms without documenting urethritis is recommended only for patients at high risk and who are unlikely to return for follow-up. If empiric treatment is necessary, treat for both gonorrhea and chlamydial infection. Testing to determine the specific disease is recommended because both of these infections are reportable to state health departments, and a specific diagnosis may improve compliance and partner notification. New nucleic acid amplification tests enable detection of \textit{N. gonorrhoeae} and \textit{C. trachomatis} on first-void urine; in some settings, these tests are more sensitive than traditional culture techniques.

C Initiate treatment as soon as possible after diagnosis.

For gonorrhea (Table 37-1), the single-dose regimens are preferred because they offer the important advantage of improved compliance and the possibility of directly observed therapy. Each regimen recommended for treating gonorrhea includes dual therapy for possible coexisting \textit{C. trachomatis} infection. Treatment with any recommended regimen results in alleviation of symptoms and microbiologic cure of infection in the great majority of patients. Instruct patients to abstain from sexual intercourse until 7 days after therapy is initiated.

Cefixime has a spectrum similar to ceftriaxone, but the 400 mg oral dose does not provide as high or as sustained a bactericidal level as the 125 mg dose of ceftriaxone. In published clinical trials, the 400 mg dose cured 97.1% of uncomplicated urogenital and anorectal gonococcal infections. The advantage of cefixime is that it can be administered orally.

<table>
<thead>
<tr>
<th>Table 37-1 Treatment of Uncomplicated Gonococcal Infections$^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Recommended regimens</strong></td>
</tr>
<tr>
<td>Cefixime 400 mg orally in a single dose$^a$</td>
</tr>
<tr>
<td>OR</td>
</tr>
<tr>
<td>Ceftriaxone 125 mg IM in a single dose$^a$</td>
</tr>
<tr>
<td>OR</td>
</tr>
<tr>
<td>Ciprofloxacin 500 mg orally in a single dose$^a$</td>
</tr>
<tr>
<td>OR</td>
</tr>
<tr>
<td>Ofloxacin 200 mg orally in a single dose$^a$</td>
</tr>
<tr>
<td>PLUS</td>
</tr>
<tr>
<td>Azithromycin 1 g orally in a single dose$^a$</td>
</tr>
<tr>
<td>OR</td>
</tr>
<tr>
<td>Doxycycline 100 mg twice a day for 7 days</td>
</tr>
<tr>
<td>Alternative regimen</td>
</tr>
<tr>
<td>Spectinomycin 2 g IM in a single dose$^a$</td>
</tr>
</tbody>
</table>

$^a$Many other antimicrobials are also active against \textit{N. gonorrhoeae}. However, recommendations are based on the consensus of expert opinion incorporated in the most recent guidelines from the Centers for Disease Control and Prevention.

$^a$Single-dose cephalosporin regimens other than ceftriaxone and cefixime include cefuroxime 500 mg IM, cefotaxime 500 mg IM, cefotetan 1 g IM, and cefoxitin 2 g IM with probenecid 1 g orally. None of these injectable regimens offers any advantage in comparison with ceftriaxone, and clinical experience is limited.

$^a$Other single-dose quinolone regimens include enoxacin 400 mg orally, lomefloxacin 400 mg orally, and norfloxacin 800 mg orally. Data regarding these regimens are limited, but none appears to offer any advantage over ciprofloxacin or ofloxacin.

$^a$Spectinomycin is expensive and must be injected; however, it has been effective in published clinical trials, curing 98.2% of uncomplicated urogenital and anorectal gonococcal infections. Spectinomycin is useful for treatment of patients who cannot tolerate cephalosporins and quinolones.
Ceftriaxone in a single injection of 125 mg provides sustained, high bactericidal levels in the blood. Extensive clinical experience indicates that ceftriaxone is both safe and effective, curing 99.1% of uncomplicated urogenital and anorectal infections in published clinical trials.

Ciprofloxacin is a safe, relatively inexpensive, oral medication that has proven effective against most *N. gonorrhoeae* strains. The 500 mg ciprofloxacin dose provides a sustained bactericidal concentration. In published clinical trials, this dose has cured 99.8% of uncomplicated urogenital and anorectal infections.

Ofloxacin also is effective against most *N. gonorrhoeae* strains. The 400 mg oral dose has been effective for treatment of uncomplicated urogenital and anorectal infections, curing 98.4% of infections in published clinical trials.

Spectinomycin is preferred for patients who cannot tolerate cephalosporins or quinolones. Because spectinomycin is unreliable (ie, only 52% effective) against pharyngeal infections, patients who have a suspected or known pharyngeal infection should have a pharyngeal culture evaluated 3 to 5 days after treatment to verify eradication of infection.

If these regimens are unsuccessful, patients should be recultured. Antimicrobial resistance is responsible for a few treatment failures. However, most patients who have *N. gonorrhoeae* after one of the recommended regimens are noncompliant or are reinected from an untreated sexual partner, rather than treatment failures. Evaluation for other potential infectious causes of nongonococcal urethritis, such as *U. urealyticum*, *T. vaginalis*, or other infections, should be considered (see persistent urethritis, below) for patients who have continued urethral inflammation but do not have *N. gonorrhoeae*.

Strains of *N. gonorrhoeae* resistant to fluoroquinolones have been reported sporadically from many parts of the world, including North America, and are becoming widespread in certain areas of Asia. To date, such infections have been documented rarely in the United States: < 0.05% of 4,639 isolates evaluated by the Centers for Disease Control and Prevention. Thus, the fluoroquinolone regimens can be used with confidence. However, as importation of resistant strains will probably continue, this recommendation may change. Perform culture and susceptibility testing on patients who appear to be treatment failures.

Disseminated gonococcal infection (DGI) results from gonococcal bacteremia. DGI often presents with petechial or pustular skin lesions, asymmetric arthralgia, tenosynovitis, or septic arthritis. The infection is complicated occasionally by perihepatitis and rarely by endocarditis or meningitis. *N. gonorrhoeae* strains that cause DGI tend to cause minimal genital inflammation. Gonococcal infection often is asymptomatic in sex partners of patients with DGI. The recommended regimen is ceftriaxone, 1 g IM or IV every 24 hours until the patient improves. The patient should then complete a full week of therapy.

Initial treatment of NGU (Table 37-2) is directed primarily against *C. trachomatis*. Patients who have urethritis but no evidence of either *N. gonorrhoeae* or *C. trachomatis* may also benefit from treatment with one of the regimens listed in Table 37-2. Clinical trial results indicate that azithromycin and doxycycline are equally efficacious. Azithromycin offers the advantage of single-dose therapy, especially for patients for whom compliance is in question. Erythromycin is less effective than either azithromycin or doxycycline, and gastrointestinal side effects occur frequently. Ofloxacin is similar in efficacy to doxycycline, but it is more expensive to use and offers no advantage in duration of therapy. Other quinolones are either not reliably effective against chlamydial infection or have not been studied adequately.

To minimize transmission, patients treated for chlamydial infection should be instructed to abstain from sexual intercourse for 7 days after completion of treatment. To minimize the risk of reinfection, patients should also be instructed to abstain from intercourse until all of their sex partners are cured.

**Table 37-2 Regimens for Treatment of Nongonococcal Urethritis (Uncomplicated *C. trachomatis* Infections)**

<table>
<thead>
<tr>
<th><strong>Recommended regimens</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Azithromycin 1 g orally in a single dose</td>
<td>OR</td>
</tr>
<tr>
<td>Doxycycline 100 mg orally twice a day for 7 days</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Alternative regimens</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Erythromycin base 500 mg orally four times a day for 7 days*</td>
<td>OR</td>
</tr>
<tr>
<td>Erythromycin ethylsuccinate 800 mg orally four times a day for 7 days*</td>
<td>OR</td>
</tr>
<tr>
<td>Ofloxacin 300 mg twice a day for 7 days</td>
<td></td>
</tr>
</tbody>
</table>

*If erythromycin is the only agent that can be used and the patient cannot tolerate high-dose schedules, one of the following regimens can be used: Erythromycin base 250 mg orally four times a day for 14 days OR Erythromycin ethylsuccinate 400 mg orally four times a day for 14 days.
rheae infections. Some experts believe that the standard use of dual therapy has resulted in substantial decreases in the prevalence of chlamydial infection. Because most gonococci in the United States are susceptible to doxycycline and azithromycin, routine cotreatment might also hinder the development of antimicrobial-resistant \textit{N. gonorrhoeae}. Since the introduction of dual therapy, the prevalence of chlamydial infection has decreased in some populations.

Because the recommended regimens for gonorrhea have proven so effective, routine test-of-cure evaluation is no longer recommended. Patients should be instructed to return for evaluation only if symptoms persist or recur after completion of therapy. Symptoms alone, without documentation of signs or laboratory evidence of urethral inflammation, are not a sufficient basis for re-treatment.

Similarly, patients do not need to be retested for chlamydial infection after completing treatment with doxycycline or azithromycin unless symptoms persist or reinfection is suspected. The value of chlamydial cultures at $> 3$ weeks after completion of therapy to identify treatment failures has not been established. False-negative culture results can occur because of low numbers of chlamydial organisms. Nonculture chlamydial diagnostic tests for patients who were treated successfully may also remain false-positive because of continued excretion of dead organisms.

Reevaluate patients with persistent or recurrent symptoms following therapy. Specific attention should be directed to a history of noncompliance with recommended therapy or to sexual contact with an untreated partner. Objective signs of urethritis should be present before initiation of antimicrobial therapy. Patients who have persistent or recurrent urethritis should be re-treated with the initial regimen if they did not comply with the treatment regimen or if they were re-exposed to an untreated sex partner. Obtain culture and sensitivity testing for \textit{N. gonorrhoeae} to evaluate the possibility that antimicrobial resistance may be responsible for treatment failure. Otherwise, perform a wet mount examination and culture of an intraurethral swab specimen for \textit{T. vaginalis}. Other potential pathogens, such as the genital mycoplasmas, should be evaluated if diagnostic facilities are available.

The regimens listed in Table 37-3 should be considered pending test results. Effective regimens have not been identified for treating patients who do not have objective signs of urethritis but who have persistent symptoms or frequent recurrences after treatment. Urologic examinations usually do not reveal a specific etiology.

<table>
<thead>
<tr>
<th>Table 37-3 Recommended Regimens for Recurrent/Persistent Urethritis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metronidazole 2 g orally in a single dose</td>
</tr>
<tr>
<td>PLUS</td>
</tr>
<tr>
<td>Erythromycin base 500 mg orally four times a day for 7 days</td>
</tr>
<tr>
<td>OR</td>
</tr>
<tr>
<td>Erythromycin ethylsuccinate 800 mg orally four times a day for 7 days</td>
</tr>
</tbody>
</table>

Strongly encourage patients to refer all partners they have had sex with within the preceding 60 days for evaluation and appropriate treatment. Because a specific etiologic diagnosis may facilitate partner referral, testing for gonorrhea and chlamydia is encouraged, even for patients who are to receive empiric treatment. Instruct patients to abstain from intercourse until they and their sex partners have completed treatment.

**Additional Readings**


To evaluate a patient with a genital ulcer, assess the patient’s risk factors for infection, for the onset and duration of lesions, for whether the lesion is painful, and for the patient’s previous history of genitourinary tract disorders and procedures, urinary tract infection, and sexually transmitted diseases.

Five infectious diseases should be considered in the differential diagnosis: genital herpes simplex virus (HSV) infection, syphilis, chancroid, granuloma inguinale (donovanosis), and lymphogranuloma venereum (LGV). Table 38-1 summarizes the causative organisms and their microbiologic classification.

The relative frequency of each condition differs by geographic area and patient population. In the United States, most genital ulcers in sexually active persons are caused by genital herpes. Syphilis is the second most common infectious cause in most areas. Chancroid and LGV are important considerations in some areas and populations. Granuloma inguinale is a rare cause of genital ulcers in the United States.

### Table 38-1 Infectious Causes of Genital Ulcers

<table>
<thead>
<tr>
<th>Disease</th>
<th>Cause</th>
<th>Microbiologic Class</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genital herpes</td>
<td>Herpes simplex virus types</td>
<td>Virus (double-stranded DNA)</td>
</tr>
<tr>
<td></td>
<td>1 and 2</td>
<td></td>
</tr>
<tr>
<td>Syphilis</td>
<td>Treponema pallidum</td>
<td>Bacterium (treponeme)</td>
</tr>
<tr>
<td>Chancroid</td>
<td>Haemophilus ducreyi</td>
<td>Bacterium (gram-negative bacillus)</td>
</tr>
<tr>
<td>Lymphogranuloma venereum</td>
<td>Chlamydia trachomatis (LGV serovar)</td>
<td>Bacterium (chlamydial)</td>
</tr>
<tr>
<td>Granuloma inguinale</td>
<td>Calymmatobacterium granulomatis</td>
<td>Bacterium (gram-negative bacillus)</td>
</tr>
</tbody>
</table>

Two critical considerations determine the optimal clinical approach to patients with genital ulcers. First, more than one infection may occur simultaneously in any patient who has genital ulcers. Second, each infectious cause of genital ulcers has been associated with a two- to fourfold increased risk for human immunodeficiency virus (HIV) infection. Thus, HIV testing should be recommended for each patient with a genital ulcer.

Because diagnosis based only on the patient’s medical history and physical examination is often inaccurate, diagnostic testing is recommended for all patients presenting with genital ulcers. Minimal evaluation of all patients who have genital ulcers should include a serologic test for syphilis and diagnostic evaluation for genital HSV (viral culture and/or antigen detection). Other highly desirable tests include microscopic examination for *Treponema pallidum* by either a darkfield examination or by a direct immunofluorescence test.

If available, obtain a culture or molecular diagnostic test for *Haemophilus ducreyi*.

Counsel patients appropriately, and recommend diagnostic testing for HIV. Ideally, patients should be treated based on the results of specific diagnostic tests. However, treatment is often advisable before diagnostic test results are available. In this situation, direct therapy against both syphilis and chancroid. However, despite complete diagnostic evaluation, at least 25% of patients with genital ulcers have no laboratory-confirmed diagnosis.

Additional Reading
Genital Ulcers

History
- Risk factors
- Onset
- Prior genitourinary history
- Pain

Physical examination
- Characteristics of ulcer
- Inguinal adenopathy
- Systemic findings

Patient with GENITAL ULCER

Differential diagnosis
- HSV
- Syphilis
- Chancroid
- Granuloma inguinale
- Lymphogranuloma venereum

Initial diagnostic testing
- Serologic test for syphilis
- Microscopic examination for syphilis
- Testing for HSV
- Culture or other testing for chancroid, if available
- Counseling

HIV testing

Specific diagnosis
Treat appropriately

Empiric treatment necessary
Treat for syphilis and chancroid
SECTION 5
GENITOURINARY TRAUMA
Trauma is currently the leading cause of death and morbidity in young Americans. Approximately 10 to 15% of all patients with abdominal trauma have an associated urologic injury. It has been estimated that 1.1% of all trauma will involve the upper urinary tract. Blunt urologic injury is the most common form of trauma seen by practicing urologists and is responsible for 80 to 90% of all urologic injuries. The most common causes of injury are motor vehicle accidents, falls from heights, and direct blows to the flank. The kidney is the most commonly involved organ, followed by the bladder, urethra, and ureter. Although penetrating injuries account for only about 20% of all traumatic injuries, they represent 80 to 90% of all renal trauma cases that require exploration. Renal injury accounts for about 1 in 3,000 hospital admissions and should be suspected in anyone sustaining blunt or penetrating trauma to the lower chest, back, or abdomen. Over the past two decades we have seen a continued evolution in the diagnosis, evaluation, and treatment of urologic injuries. Urologic evaluation is no longer necessary in all patients sustaining blunt abdominal trauma because a subset of patients who are likely to have sustained a urologic injury have been well defined. Similarly, we have seen continued changes in the way patients with urologic injuries are being treated. With improved staging techniques, even patients with penetrating renal injuries are being selectively managed in a nonoperative manner.

Renal trauma should be suspected in anyone sustaining blunt or penetrating trauma to the lower chest, back, or abdomen. Emergency room evaluation includes the determination of cardiopulmonary status and the presence of life-threatening injuries. Once hemodynamic stability has been ensured and the pulmonary status stabilized, a detailed history, physical examination, and urinalysis are obtained. Falls from great heights or high-speed motor vehicle accidents with associated deceleration-type injuries may result in renal pedicle injuries in the absence of hematuria. Individuals with renal injuries may demonstrate costovertebral angle (CVA) or flank tenderness, a palpable flank mass, or flank ecchymosis. The presence of fractured ribs, pneumothorax, or vertebral body fractures suggests the possibility of renal injury. Patients presenting with the above findings undergo radiographic evaluation regardless of the findings on urinalysis. In patients who sustain penetrating trauma, it is helpful to determine the type of weapon used. Lacerations and entrance and exit wounds are also noted. Urinalysis is obtained in all trauma victims. It is well known that the degree of hematuria does not correlate with the severity of renal injury. Renal artery thrombosis, which may result in complete loss of renal function, may occur after a mild renal contusion. All patients with gross hematuria require radiographic evaluation. Patients with isolated microscopic hematuria determined by dipstick or by microscopic urinalysis do not require radiographic imaging. All patients with microscopic hematuria who present with shock (systolic blood pressure < 90 mm Hg) or who have multisystem injuries require urologic evaluation. Patients sustaining severe deceleration-type injuries are also evaluated.

A
Patient with SUSPECTED RENAL TRAUMA

Physical examination
Urinalysis

Stable

Unstable

Abnormal
Normal

Abdominal CT scan
Renal artery thrombosis

Minor renal injury (Grades I, II)
Major renal injury (Grades III, IV, V)

Bilateral injury
Solitary kidney

Observation
Unilateral

Observation

Attempted revascularization

Exploratory laparotomy; IVP

Renal exploration

Unstable

Unstable
B Computed tomography (CT) is the most accurate imaging study available to evaluate and stage the extent of renal trauma.\textsuperscript{17,18} CT scanners are readily available in all trauma centers. The study is noninvasive and has replaced intravenous pyelography (IVP) and renal arteriography as the gold standard in identifying and staging renal injuries. CT clearly defines parenchymal lacerations, hematomas, and the presence of urinary extravasation; it also allows accurate assessment for the presence of other associated injuries.\textsuperscript{19} CT is also highly accurate in identifying arterial injuries (Figure 39-1).\textsuperscript{20,21} The presence of the cortical rim sign signifies an acutely devascularized kidney with persistent capsular perfusion and is diagnostic of a renal artery thrombosis. The use of three-dimensional CT has been reported to be a noninvasive technique to accurately diagnose renal artery injuries. It provides image quality similar to that provided with angiography and may someday replace angiography as the imaging study of choice in patients with suspected renal artery trauma.\textsuperscript{22} Current helical CT scanners have been shown to occasionally underestimate the full extent of the injury. Modern-day scanners obtain images before intravenous contrast is excreted into the collecting system. To avoid understaging, it has been recommended that either a repeat scan be performed after completing the initial study or the initial scan be delayed for 5 to 20 minutes after contrast injection.\textsuperscript{23,24} The purpose of the CT scan is to not only identify the presence of a renal injury but also to help classify the extent of the injury using a system established by the Organ Injury Scaling Committee of the American Association for the Surgery of Trauma.\textsuperscript{25} This system classifies the renal injury into five groups. Grade I: contusion and nonexpanding subcapsular hematoma without laceration. Grade I injuries comprise 75 to 80\% of all renal injuries. Grade II: nonexpanding perirenal hematoma confined to the retroperitoneum or a laceration less than 1 cm without urinary extravasation. Grade III: greater than a 1 cm laceration extending into the renal parenchyma without collection-system rupture or extravasation. Grade IV: a renal parenchymal laceration extending through the corticomedullary junction and into the collecting system (Figure 39-2). (Urinary extravasation may or may not be present.) A Grade IV vascular injury consists of a main renal artery or vein injury with contained hemorrhage. Grade V: completely shattered kidney with multiple lacerations through the renal parenchyma or avulsion of the renal hilum with a devascularized kidney.

C Eighty-five to 90\% of all renal trauma will be classified as either Grade I or Grade II renal injuries. These patients are best treated with observation. Patients with gross hematuria are hospitalized and placed on bed rest until the urine becomes grossly clear. Complications are rare.

D Treatment of major renal trauma is controversial. Opinion is divided between those who favor immediate operative intervention and those who favor observation with exploration reserved for instances where complications arise or hemodynamic instability develops.\textsuperscript{26–30} Patients at risk for the development of complications include those with urinary extravasation and/or devitalized renal segments. Advancements in endourologic and percutaneous techniques have lessened the morbidity of these complications. Retroperitoneal urine collections and persistent urinary extravasation may be successfully managed endourologically with stents and/or drainage tubes negating the need for renal exploration in the majority of patients.\textsuperscript{31} In our experience, no patient who has initially stabilized has required surgical exploration for complications related to nonoperative management. We have found that patients with persistent hemodynamic instability require prompt sur-

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{fig39-1.png}
\caption{Trauma CT scan showing classic findings of left renal artery thrombosis. Note the abrupt cut-off of the left renal artery and nonfunction of the left kidney.}
\end{figure}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{fig39-2.png}
\caption{Trauma CT scan showing a Grade IV renal injury. Note the large right pleural hematoma and the presence of urinary extravasation.}
\end{figure}
All stable patients with major renal trauma are treated nonoperatively. Patients with gross hematuria are kept on bed rest until the urine clears. Vital signs and serial hematocrits are obtained. Broad-spectrum antibiotics are prescribed. Once the urine clears, the patient is allowed to ambulate. If the urine remains clear for 24 hours, the patient is discharged. A follow-up CT scan is obtained in 4 to 6 weeks. Complications are rare, and surgical exploration is reserved for those patients who manifest hemodynamic instability in spite of aggressive resuscitative efforts.

Traumatic renal artery thrombosis is an uncommon complication of blunt abdominal trauma and should be suspected in any patient presenting with severe deceleration-type injury. Since the initial description by von Recklinghausen in 1861, approximately 200 cases of traumatic renal artery occlusion have been reported in the literature.32–35 Traumatic renal artery thrombosis results from excessive stretching of the renal artery with subsequent tearing of the inelastic renal intima and occlusion of the renal artery. When the condition is bilateral, immediate surgical exploration and attempted revascularization are warranted (Figure 39-4). Treatment of unilateral renal artery thrombosis is controversial. Advocates of surgical exploration believe renal function can be preserved by prompt revascularization; however, in fact, renal function is rarely preserved and nephrectomy usually results. Recently, successful transluminal angioplasty with stent placement has been described as an alternative to open revascularization techniques.36 Advocates of the nonoperative approach believe that adequate renal function can rarely be restored and that elective nephrectomy can be performed if hypertension develops. It is our recommendation that all patients with either a solitary kidney or bilateral injuries undergo prompt surgical exploration and attempted revascularization. Patients with unilateral injuries are observed with nephrectomy performed if hypertension develops.33–35

Unstable patients require emergent laparotomy. Once the patient has been stabilized and life-threatening injuries have been repaired, an emergent single-shot excretory urogram is obtained on the operating table. A high-dose bolus infusion of 2 mL/kg of radiographic contrast is injected. A simple, plain abdominal radiograph is obtained 10 minutes after injection. Additional delayed studies may be obtained as deemed necessary.37 One goal of the trauma IVP is to determine the presence or absence of two functioning kidneys.

Patients with an expanding or pulsatile hematoma, absence of a nephrogram on the intraoperative IVP, (Figure 39-5) or a gunshot wound to the kidney undergo renal exploration. Scott and Selzman, in 1966, first described the technique of preliminary vascular control
before opening Gerota’s fascia. Carroll and associates described excellent results using this technique. Proponents of early vascular control believe nephrectomy rates can be reduced by limiting the blood loss and transfusion requirements. Others have found the technique to be time consuming, tedious, and rarely necessary. Once Gerota’s fascia has been opened, all devitalized tissue is débrided, the renal parenchyma is approximated, the collecting system is closed, and hemostasis is obtained. The kidney is drained. Follow-up imaging studies are obtained prior to patient discharge.

### References


Pelvic fractures frequently occur in association with other severe injuries and have a reported mortality rate of 10 to 30%. Mortality is usually due to hemorrhage, head trauma, sepsis, or multiple-organ system failure. More than one-half of patients with pelvic fracture present with a hemoglobin < 10 g/dL and in hypovolemic shock. Severe, unstable pelvic fractures may require > 10 units of blood to stabilize the patient. Bleeding from pelvic fractures may originate from raw bony surfaces or from ruptured retroperitoneal veins or arteries. Other potentially life-threatening bleeding sites include thoracic and intra-abdominal injuries. The urologist is called when genitourinary injuries are discovered and when treating and managing urologic injuries require a coordinated effort between the urologist and other members of the trauma and orthopedic teams.

About 15% of all pelvic fractures are associated with an injury to the bladder or urethra.¹ The incidence of lower urinary tract injury in adults with pelvic fractures is between 7.5 and 25%.² Genitourinary injury in pediatric population with pelvic injury has a lower incidence, ranging from 2.8 to 13.5%.³⁻⁶ Children have a lower incidence of urethral injuries because of the elastic nature of their pelvis.⁷ No association between the type of pelvic fracture and lower urinary tract injury can be made.

Motor vehicles striking pedestrians is the most common mechanism of injury to the pelvis, associated with lower genitourinary tract injury (range 59 to 90%, median 71%).³⁻⁵,⁸ Other causes of injury include motor vehicle accidents (range 10 to 32%, median 24%) and falls (range 2 to 9%, median 6.5%).³⁻⁵,⁹

A Although a frequent source of chronic morbidity, urologic injuries are seldom life-threatening and are therefore evaluated after more serious neurologic and intra-abdominal injuries have been ruled out. Patients with gross hematuria require evaluation of the lower urinary tract, as do those victims who are unable to void. Clinical findings that suggest a urinary tract injury include blood at the urethral meatus, perineal ecchymosis, and/or a nonpalpable or high-riding prostate gland.

Lower urinary tract imaging does not appear to be required in patients who are clinically stable, have a normal genitourinary examination, do not have gross hematuria, and do not have multiple associated injuries. In the adult population, only patients with gross hematuria and obvious urologic injuries need a complete work-up. Although traditionally, all pediatric patients with any degree of hematuria have a work-up, there have been several reports in recent years that challenge this recommendation and suggest that these pediatric patients with microhematuria may be managed in the same manner as adults.¹⁰ A recent study has shown a very low incidence of genitourinary injuries in the pediatric population and recommends evaluation in those with gross hematuria and/or multiple other associated injuries.⁶

B Posterior urethral tears are the most common urologic injury in males.¹¹ Usually, these injuries are associated with a displaced anterior pelvic arch fracture that ruptures the urethra directly by perforating it with a bony fragment or as a result of shearing forces that occur when the prostate is displaced from its normal anatomic position.¹¹,¹² Urethral injuries are rare in females, presumably owing to the lack of fixation of the urethra to the pubis. In males, retrograde urethrogram should be performed in the oblique position to ensure adequate visualization of the entire urethra. A small Foley catheter (10 to 12 French) may be placed into the urethral meatus and the balloon inflated in the fossa navicularis with 1 to 2 cc of saline. Appearance of contrast in the bladder, along with extravasation, indicates a partial urethral disruption diagnosis. Extravasation without bladder filling indicates a complete urethral disruption.¹¹,¹³,¹⁴

C A retrograde cystogram is obtained in all females and in males with a normal urethra. A Foley catheter is passed into the bladder, and under gravity pressure, 300 to 500 cc of water soluble contrast is instilled. Avoid false-negative examinations by filling the bladder with at least 300 mL contrast and obtaining films in both the oblique and anteroposterior projections.¹⁵ Attain a third film after draining the bladder. Fluoroscopy may help in the equivocal case or when a bladder injury is not clearly defined. Spiral computed tomography (CT) is less accurate than is retrograde cystography in diagnosing traumatic bladder rupture, and CT has significant diagnostic limitations, owing to inadequate bladder distention and to an inability to distinguish urine from ascites.¹⁶,¹⁷ However, when performed correctly, with adequate bladder filling and distention, CT cystography has been proven highly accurate in diagnosing traumatic bladder ruptures.¹⁸

References
The views expressed in this chapter are those of the authors and do not reflect the official policy or position of the United States Army, Department of Defense, or the US Government.

Ureteral injuries, although rare, present a major source of morbidity and potential mortality in the trauma victim. Although ureteral injuries from external violence account for only 1 to 3% of total genitourinary injuries,1,2 penetrating abdominal trauma leads to ureteral injury in a reported 2.3 to 17% of cases.3–6 Patients often have multiple associated injuries that require immediate attention, but early recognition and proper reconstruction of ureteral injury at the time of initial presentation generally lead to favorable outcomes. Accurate and timely diagnosis can be difficult; thus, a high index of suspicion for ureteral injury is required. Delays in diagnosis are common, occurring in up to 57% of patients, with resulting morbidity (sepsis, loss of renal function, and death) developing in 40 to 50% of patients.1,7,8 Delayed diagnosis leads to nephrectomy seven times more frequently than when ureteral injury is recognized at the time of initial presentation.9

Anatomy

The ureter lies well protected in the retroperitoneum and is not easily injured. Its narrow diameter, mobility, elasticity, and retroperitoneal position surrounded by the spine, major muscle groups, and peritoneal contents generally afford shelter from external trauma. The ureteral blood supply travels through the adventitial layer and arises from multiple sources, including the aorta and the renal, gonadal, iliac, uterine, middle hemorrhoidal, vaginal, and superior vesical arteries.10 A single artery runs the length of the ureter between the adventitial sheath and the ureteral musculature in 80% of ureters.11

Types of external ureteral injury include contusion, transection (complete or partial), avulsion, crush, and devascularization, owing to the blast effect of gunshot wounds. Any portion of the ureter can be injured in external trauma, and case series have demonstrated approximate equality in the location of ureteral injuries, with a slight predominance of midureteral injuries.4,12–16

Most external ureteral injuries are attributable to penetrating assault, with gunshot wounds and stab wounds accounting for approximately 81% and 16% of cases, respectively.12 Ureteral injuries occur in 2 to 3% of all gunshot wounds to the abdomen.4,5 Most gunshot wounds involve low-velocity missiles, but high-velocity injury warrants special consideration. Large missiles identified on radiographs are usually low velocity, but if the bullet is not seen or if there is extensive deformity of the bullet, high-velocity injury is likely.17 In addition to transection or laceration of the ureter, temporary cavitation that the bullet creates can cause significant tissue damage and delayed necrosis owing to an associated “blast effect” (Figure 41-1). High-velocity missiles (muzzle velocity > 2,500 feet per second), such as military assault rifles, can create a cavitation 30 to 40 times their original size and lead to thermal microvascular injury as the missile passes near the ureter.10,18–21

Figure 41-1 Blast effect in civilian gunshot wound. KUB, bullet fragments rest in right abdomen after shattering lumbar transverse process. Paper clip marks bullet-entry site. Empiric ureteral stent placement for presumed ureteral contusion facilitated prompt recovery.
Ureteral Injury from External Violence

Patient with SUSPECTED EXTERNAL URETERAL INJURY

A Risk Factors

Stable
Unstable

B Urinalysis CT with delayed films

Normal
Extravasation

C Exploratory laparotomy
Resuscitation
Direct inspection

Ureteral injury? No

Consider stent

Yes

Stable
Unstable

D Single-J stent diversion or ligation/nephrostomy

Stable

D Delayed repair

E Definitive repair

F Delayed diagnosis?

Stent/repair

Renal pelvis or UPJ

Primary closure with stent

Upper/mid ureter

Ureteroureterostomy with stent

Distal ureter

Reimplantation with psoas hitch and/or Boari flap
Delayed ureteral fistula can later occur if ischemic thrombosis causes sloughing of the ureteral wall. In addition, contusions from projectiles passing near the ureter can damage the intima of ureteral blood vessels, leading to ischemia with delayed necrosis and urinary leakage (Figure 41-2).

Blunt trauma to the ureter is relatively rare and accounts for only 8% of ureteral injury from external impact. Blunt trauma to the ureter is typically caused by rapid deceleration injuries, such as motor vehicle accidents or falls from a great height. Although ureteropelvic junction (UPJ) disruption is a relatively rare consequence of blunt trauma, the UPJ is the most commonly injured portion of the ureter in blunt trauma. Classic descriptions of blunt trauma leading to disruption or avulsion at the UPJ involve children in the setting of a rapid deceleration accident. It is theorized that the hyperextensible spinal columns of children allow for stretching and tearing of the ureter against the twelfth rib and lumbar vertebral transverse processes during rapid deceleration.

External ureteral injuries, especially UPJ disruptions, are usually accompanied by multiple organ system trauma, and concomitant visceral injury is frequently encountered. Associated injuries occur in > 90% of patients with penetrating ureteral injuries and > 70% of blunt injuries to the ureter. The most commonly co-injured structures include the small bowel, colon, rectum, liver, and iliac vessels. Patients with associated duodenal, pancreatic, and colonic injuries are at higher risk for complications. Although some authors advocate against performing primary ureteral repair when bowel resection or colostomy is required, others report that peritoneal contamination has no adverse effect on the ureteral reconstruction if the repair is isolated with omentum.

A high index of suspicion is required for the prompt recognition of ureteral injury and preservation of renal function. Accurate diagnosis is complicated by a lack of clinical laboratory findings specific for ureteral injury. A history of trauma to the flank or pelvis, rapid deceleration injury, flank pain, or ecchymosis may suggest ureteral injury, but physical findings are notoriously nonspecific. Hematuria (gross or microscopic) is an unreliable finding and is absent in approximately 30% of ureteral trauma. False-negative rates for urinalysis of 15 to 34% have been reported. Delayed recognition of ureteral injury can manifest as fever, flank pain, prolonged ileus, urinoma, persistent drainage from operative sites, fistula formation (most commonly to vagina, skin, and bowel), or sepsis, but these features often arise several days after injury. All trauma patients who have (1) gross or microscopic hematuria, (2) penetrating abdominal trauma, (3) lumbar transverse process fracture, or (4) major deceleration or extension injuries are at risk for damage to the ureters and should be evaluated accordingly.

Blunt trauma involving rapid deceleration (falls, motor vehicle accidents) or hyperextension of the thoracolumbar spine should also prompt evaluation for ureteral damage. Children are especially susceptible to ureteral injury owing to the tremendous level of spinal
flexibility in the pediatric population. Diagnosis of UPJ disruption is often obscure at initial presentation, and diagnostic delays > 36 hours occur in more than 50% of patients. Such long delays are usually secondary to comorbid multisystem trauma and nonresponsive hypovolemic shock requiring emergent celiotomy and thus precluding radiologic assessment. Likewise, patients with UPJ disruption can present without any physical signs or symptoms other than a history of blunt deceleration injury, and the physician must rely on a high index of clinical suspicion to prompt investigation for ureteral injury. A normal urinalysis must not preclude consideration of ureteral injury in patients at high risk. All children with significant blunt abdominal trauma should have radiographic ureteral assessment.

Historically, high-dose (2 mL contrast/kg body weight) intravenous urography (IVU) has been the initial study for evaluation of suspected upper urinary tract injury. Signs of contrast extravasation, delayed excretion, nonvisualization of the collecting system, or mild ureteral dilation or deviation may indicate ureteral damage. Whereas the reported sensitivity of IVU ranges from 78 to 100% for completed studies, the rate of detection falls to 20% when only a single flat-plate film of the abdomen is obtained 10 minutes after infusion in the setting of severe abdominal trauma requiring emergent intervention. Recent studies show the accuracy of IVU to be quite poor and characterize IVU as a very unreliable indicator of ureteral injury, much like urinalysis. Brandes and colleagues reported IVU as nondiagnostic in 75% of their cases, which is similar to the low sensitivity of 27% reported by Presti and colleagues. A more recent published series showed IVU to have a false-negative rate of 33%. Although extravasation is the hallmark of ureteral injury, IVU is typically normal with ureteral contusion. Recognizing these limitations, IVU remains a helpful study in hemodynamically stable patients, and delayed films appear to optimize its diagnostic yield (Figure 41-3).

Computed tomography (CT) is increasingly used as the initial evaluation of choice in multiple abdominal injuries at major trauma centers and is generally recognized as superior to IVU in identifying ureteral injury. Absence of ureteral filling distal to the site of ureteral injury is a sentinel CT finding of ureteral transection, along with medial perirenal contrast extravasation. Partial lacerations, however, may allow for distal filling of the ureter on CT, and the exact location of ureteral injury may be obscured if there is a large amount of urinary extravasation. With both CT and IVU, contrast excretion can be delayed, secondary to hypotension or coexisting renal trauma, resulting in incomplete opacification of the collecting system. The sensitivity of CT for ureteral injury detection is currently unknown but may be reduced by the rapid sequencing of modern helical CT scanners that provide images only during the nephrogram or early excretory phases. The use of delayed films at 5 and 8 minutes can help prevent a missed diagnosis that is caused by imaging prior to filling of the collecting system. UPJ disruption can be classified as complete avulsion or partial laceration. Both types of injury can be recognized by the CT findings of medial perirenal contrast extravasation with an intact calyceal system and renal parenchyma. Because partial UPJ injury allows for distal ureteral filling, nonvisualization of the ipsilateral ureter should raise suspicion for complete UPJ disruption. When contrast extravasation on CT scanning prevents accurate visualization of the ureter, delayed KUB can demonstrate distal ureteral filling and thus help distinguish incomplete UPJ laceration from avulsion (Figure 41-4A).

When emergent laparotomy is required in the acute trauma setting, radiographic studies are unnecessary prior to operative intervention; not only can both CT and IVP be falsely negative with delayed contrast...
SECTION 5 Genitourinary Trauma

excretion because of hypotension or coexisting renal trauma, but they may also cause an inordinate delay of treatment.46,47

The retrograde pyelogram (RPG) is the most sensitive and accurate ureteral imaging study but can rarely be obtained in acute trauma owing to the urgent need for surgical intervention. If the results of IVU and CT studies remain inconclusive in a stable patient, then obtain a retrograde pyelogram.48

C Most ureteral injuries (75%) are recognized intraoperatively.1,10 Direct visual inspection during the initial laparotomy is the most accurate and consistent diagnostic method in ureteral trauma.7,8,13,46 The missile’s path or knife track should be examined closely. Although obvious urinary extravasation can be seen, more common subtle findings of ureteral disruption include contusion, discoloration, lack of bleeding, and decreased peristalsis.12 However, the presence of ureteral peristalsis does not reliably exclude ureteral damage or ischemia.1 Intravenous injection, or intraureteral injection in the case of hypotension or concomitant renal injury, of indigo carmine or methylene blue can aid in recognizing the injury.1,10,12 Even without demonstrable urinary, dye, or contrast extravasation, ureteral injury can result from the “blast effect” from high-velocity weapons. Although bruising, thrombosis, or hemorrhage of the ureteral wall may be evident, subtle signs of blast effect can be overlooked and require a high level of suspicion.10,22 The most accurate method of assessing devascularization owing to blast effect is to incise the ureter and observe for a healthy bleeding edge.1

D In the hemodynamically unstable patient, the trauma surgery concept of “damage control” has recently been applied to ureteral injuries.49 Abbreviated laparotomy is
first performed to control active bleeding and contamination, followed by aggressive intensive care resuscitation and planned reoperation for definitive repair. Options for managing the ureteral injury at the first damage control laparotomy include the following: (1) a temporary cutaneous ureterostomy performed by exteriorizing a single-J ureteral stent or pediatric feeding tube placed into the renal pelvis,1,50 (2) rapid stenting of contusions or partial lacerations, or (3) intraoperative ureteral ligation with postoperative placement of a percutaneous nephrostomy tube.11 The surgeon can perform definitive repair at a planned second laparotomy when the patient is stable.

**E Treatment of external ureteral injuries involves considering the timing of recognition, the location of injury, the extent of damage, the mechanism of injury, and the presence of associated trauma. The timing of diagnosis generally dictates the timing of repair. If ureteral injury is identified at the time of initial presentation, or within 7 to 10 days in a stable patient, immediate repair should be performed through a midline transperitoneal incision. Reserve ureteral stent placement for contusion or partial lacerations.10,12,51 For an obviously bruised or contused ureter, place a double-J stent and a retroperitoneal drain to control delayed urinary leakage.1,22,52**

**Successful ureteral reconstruction requires careful ureteral mobilization with preservation of adventitia. Thorough débridement of nonviable tissue; creation of a watertight, spatulated anastomosis free of tension; internal ureteral stenting; isolation of the repair from associated injuries with omentum or fat in patients with a high risk for infection (concomitant bowel, vascular, or pancreatic injuries); and sufficient postoperative retroperitoneal drainage are required. Periureteral dissection should minimize handling of the ureter and carefully preserve the ureteral vasculature coursing through the adventitia. All gunshot wounds to the ureter require both proximal and distal resection until a clean bleeding edge is obtained. Generally, perform all repairs over a double-J ureteral stent.36,52 Some authors advocate urinary diversion by nephrostomy tube, in addition to stenting, in cases of renal pelvic or proximal ureteral injuries.53,54 The recently described use of now commercially available fibrin sealant offers a promising adjunct for reinforcing ureteral anastomoses.55,56**

**Distal ureteral injuries: The optimal management of ureteral injuries to the distal one-third of the ureter consists of ureteroneocystostomy using a nonrefluxing Politano-Leadbetter submucosal bladder reimplantation.57 After débridement to viable tissue and spatulation, the proximal segment of ureter is brought through the posterior bladder wall, superior and medial to the original hiatus and tunneled submucosally using a 3:1 ratio (tunnel length: ureteral diameter) with fine absorbable suture to avoid reflux. The repair is stented and closed in two layers with a Malecot suprapubic tube and Foley catheter left in place. Care is taken to avoid kinking or unnecessary dissection of the ureter to prevent reflux, obstruction, or extravasation of the repair.1,10,12**

**Involvement of the entire lower one-third of the ureter can be managed by ureteral reimplantation, along with a psoas hitch of the bladder.58 Mobilization of the bladder fundus from the peritoneal reflection and ligation of the contralateral superior vesicle pedicle followed by making an oblique anterior cystotomy perpendicular to the injured ureter allow mobilization of the bladder dome toward the psoas minor tendon, where it is anchored using three interrupted sutures, taking care to avoid involving the genitofemoral nerve. In congenital absence of the psoas minor tendon, the bladder can be fixed to the psoas major muscle belly. Ureteral reimplantation can then be performed medial to the hitch over a ureteral stent. A suprapubic tube is then placed, and closure of the bladder wall in two layers perpendicular to the cystotomy can then be performed.1,10,12**

**An anterior bladder wall flap, or Boari flap, is the best management for injury of the entire lower two-thirds of the ureter, in combination with a psoas hitch.59,60 After adequate mobilization of the bladder, a full-thickness anterior wall U-incision is made. The flap width should be three to four times the ureteral diameter and should be made wider at the base to ensure adequate blood supply and to reduce constriction and loss of bladder capacity. To remain free of tension, the flap should also be at least 3 cm longer than the ureteral deficit. The psoas hitch is made, and the ureter is reimplanted into the flap submucosally, followed by tubularization and closure of the flap. The bladder is closed in two layers with absorbable sutures. Although a Boari flap can bridge up to 15 cm of ureteral damage in this manner, an additional 3 to 4 cm may be obtained through a reverse nephropexy, in which the kidney is dissected off Gerota’s fascia and displaced downwardly and affixed to the retroperitoneal muscles.10,12**

**Upper and midureteral injuries: Primary closure may be possible in repair of partial ureteral transections from stab wounds or blunt trauma but should never be used in reconstructing gunshot wounds. Thermal damage from the missile requires adequate débridement, both proximally and distally to prevent delayed tissue necrosis, and a ureteroureterostomy is required.10,12 Primary repair requires mobilization of proximal and distal ureteral segments for a tension-free anastomosis, using interrupted 4-0 or 5-0 absorbable sutures over a ureteral stent, which should be maintained for 6 weeks.10**

**Any partial or complete laceration to the middle or upper one-third of the ureter, including gunshot wounds, is best repaired by primary ureteroureterostomy (Figure 41-5). Carefully inspect the ureteral ends for discoloration or friability and carry back débridement until**
healthy tissue and free bleeding are obtained. After spatulation of each end of the ureter on opposite sides, a watertight anastomosis free of tension can be performed over a ureteral stent using interrupted 4-0 or 5-0 absorbable sutures. If repair of associated abdominal injuries is planned, a segment of greater omentum dissected from the greater curvature of the stomach should be wrapped around the anastomosis to protect the repair.

Ureteral lacerations can often be managed conservatively with endoscopic stent placement. If laparotomy has already been performed, lacerations can often be repaired by primary closure. UPJ avulsions always require immediate open repair.1

In cases of delayed diagnosis, reoperation for a failed repair, or when delayed repair is indicated secondary to the unstable condition of the multiply injured trauma patient, several other operative techniques are available for ureteral reconstruction in these unique situations.

Injuries that comprise the distal half of the ureter in the setting of poor bladder capacity, extensive pelvic scarring, or pelvic vascular injuries precluding bladder reimplantation may necessitate a transureteroureterostomy. After exposure of both ureters, a 1.5 to 2 cm medial longitudinal ureterostomy is created on the recipient ureter, and the injured ureter is débrided. It is brought through the mesentery above the inferior mesenteric artery and spatulated for an end-to-side anastomosis over a stent placed from the renal pelvis of the injured side across and down to the bladder. A transureteropyelostomy can be used for more extensive injuries involving the distal two-thirds of the ureter. Relative contraindications include prior history of upper-tract transitional cell carcinoma, bilateral renal disease, recurrent urolithiasis, genitourinary tuberculosis, pelvic irradiation, retroperitoneal fibrosis, and chronic pyelonephritis. Use these techniques selectively because they can compromise the function of the normal ureter or pelvis.1,12

Severe injuries to the UPJ and proximal ureter can be managed by ureterocalicostomy, which requires resection of the lower renal pole on the side of the lesion to expose the infundibulum of the inferior calyx.61 The ureter is widely spatulated and a direct end-to-end ureterocalycal anastomosis is performed over a stent. The high rate of anastomotic stricture and extensive renal dissection makes this procedure a last-resort choice for repair.62

A segment of ileum can be used as a ureteral substitute for complete ureteral avulsion.63 The bowel preparation required for ileal interposition precludes its use in the emergent setting; use this maneuver only in a patient whose renal function is relatively intact (serum Cr < 2.5 mg/dL). The ileal neoureter is fashioned from a 20 to 25 cm portion of ileum taken 15 cm proximal to the ileocecal junction. An end-to-end pyeloileal anastomosis is created, with the ileal segment placed in an isoperistaltic direction and implanted into the bladder without tunneling. The common developments of bacteriuria and vesicoureteral reflux have not been associated with a decline of renal function.64,65 Possible complications include hyperchloremic metabolic acidosis, obstruction, prolonged mucus formation, stones, recurrent infections, and ischemic ileal necrosis.12

Complete ureteral avulsions in the setting of either a solitary kidney or compromised renal function can be treated with transplantation of the kidney on the injured side to the iliac fossa with vascular anastomoses of renal and iliac vessels and drainage by a pyelovesicoscopy. Successful long-term preservation of renal function has been demonstrated.12,66,67

If diagnosis is made after 10 to 14 days, use temporary urinary diversion either through percutaneous nephrostomy tube placement or endoscopic ureteral stenting, followed by delayed repair. Associated inflammation will often preclude open repair because the healing tissues are adherent, friable, and difficult to dissect.68 Manage urinoma or abscess formation by percutaneous proximal urinary diversion and antegrade or endoscop-
ic stent placement. Then defer repair and permit adequate time for associated injuries to heal and the acute periureteral inflammatory response to resolve (approximately 3 months). In addition, obtain full ureteral imaging with antegrade and/or retrograde ureteral imaging before undertaking delayed repair.12

A missed ureteral injury often causes no symptoms until urinary extravasation leads to urinoma formation, abdominal pain and swelling, persistent ileus, vomiting, fever, and infection. A rise in serum urea nitrogen level may be evident owing to peritoneal absorption of urine.68,69 Urinomas appear as enhancing confined or free-fluid collections on CT, with or without a fibrous capsule and hydrenephrosis70 (Figure 41-6). Urinoma is best managed by percutaneous drain placement, urinary diversion, and ureteral stenting.71–74 A percutaneous nephrostomy tube allows for proximal urinary diversion and antegrade ureteral stent placement, both facilitating ureteral re-epithelialization and preventing stricture formation.72 If a trial of prolonged drainage and stenting fails to provide ureteral healing and urinoma resolution, surgery is required because the extravasated urine can lead to retroperitoneal fibrosis and ureteral obstruction.74,75 Fistula formation, most commonly ureterocutaneous or ureterovaginal, is another notable consequence of undiagnosed ureteral injury secondary to delayed necrosis or stricture.76 Treatment involves an initial trial of antegrade or retrograde ureteral stenting for at least 4 to 6 weeks, after which time, surgical repair through ureteral reimplantation is required.74

All ureteral repairs should be stented for 4 to 6 weeks. In addition, to prevent urinoma formation, use a retroperitoneal Penrose drain for at least 48 hours or until leakage ceases. The passive drain is preferred over suction drains, which can prolong urinary leakage from the suture line. If there is prolonged or large retroperitoneal drainage, the creatinine level of the fluid can determine if there is urinary leakage. If consistent with urine, the drain should be left in place and removed when the creatinine level is equal to the serum level. Use a transurethral Foley catheter and/or a suprapubic Malecot tube to drain the bladder. Once the urine is clear, remove the Foley catheter; the suprapubic tube is typically removed 7 to 14 days after repair.1

The ureteral stent is generally removed after 4 to 6 weeks by flexible cystourethroscopy, after which time IVU should be performed to assess ureteral function and to avoid missing late complications. We recommend a repeat evaluation at 3 and 6 months to ensure adequate healing and detect stricture or hydrenephrosis.1,12 Short ureteral strictures (< 2 cm) that are detected within 6 weeks can be effectively managed noninvasively with balloon dilation and stenting for 6 weeks. Delayed detection or extremely long strictures necessitate open repair and possible ureteral substitution.74,77–79

Figure 41-6 Radiographic findings of delayed urinoma formation (A). CT, large urinoma anterior to right kidney secondary to delayed ureteral necrosis after gunshot wound. The patient presented 1 week after injury with prolonged ileus, fever, and abdominal distention. Radiographic findings of delayed urinoma formation (B). Retrograde pyelogram, contrast extravasation at site of partial ureteral transection near bullet. Percutaneous drain is seen in urinoma collection. Stent placement led to immediate dramatic improvement.
References

52. Parker JM. Re-emphasizing the importance of urinary tract diversion and splinting in injuries of the upper third of the ureter. J Urol 1971;106:368–70.
Iatrogenic ureteral injuries occur most commonly during abdominal hysterectomies, followed by rectal surgery, vascular surgery, and genitourinary endoscopy. Gynecologic surgeries account for approximately two-thirds of the injuries, whereas colorectal surgery causes about 15% of injuries. Injuries secondary to urologic endoscopy, specifically ureteroscopy, have been increasing owing to more frequent instrumentation with the ureteroscope. These injuries have diminished somewhat with the use of ureteral access sheaths. Gynecologic surgery, specifically radical pelvic surgery, increases the risk of ureteral injury secondary to the loss of blood supply to the distal ureter during the division of the uterine arteries. Frequently, these manifest as fistulas. Gynecologic surgeries, other than hysterectomy wherein such injuries may occur, include incontinence surgery, repair of pelvic prolapse, including repair of large cystoceles, and uterine prolapse surgery such as sacrospinous fixation. In a significant number of cases, sutures used for the reconstruction of the vault and closure of the vaginal cuff can cause kinking of the ureter, resulting in partial obstruction.

**A** In males, 50% of ureteral injuries occur during vascular surgery.

Often, the ureter is involved in the inflammatory process of an abdominal aortic aneurysm. Inflammatory processes that involve iliac aneurysms may encompass the ureter, thus increasing the risk of injury during surgery because of the anatomy distortion. This risk increases significantly with redo surgeries where the amount of fibrosis can be significant.

Resection of retroperitoneal disease processes such as rectal cancer and retroperitoneal tumors (ie, sarcomas and diseases of the pancreas) may cause anatomic displacement and result in accidental injury of the ureter.

**B** To prevent ureteral injuries, the surgeon should attempt to identify the ureter during pelvic surgery. The ureters are intimately involved with pelvic vasculature, specifically over the pelvic brim, and frequently bleeding that occurs in this area during these procedures may require aggressive ligation of the bleeding structures leading to inadvertent injury to the ureter. Clearly, good surgical technique and a good knowledge of the course of the ureter in the retroperitoneum and the deep pelvis, its identification, and preservation during pelvic or retroperitoneal surgery are the best way to avoid iatrogenic ureteral injuries. During clinical evaluation of the presurgical patient, the question of retroperitoneal fibrosis or other conditions that may indicate a potential problem for the identification of the ureter intraoperatively may require preoperative stenting with a ureteral catheter or a JJ stent, allowing the surgeon to better identify the structure intraoperatively.

**C** Iatrogenic ureteral injuries are best managed at the time of injury during surgery. Most intraoperative ureteral injuries, however, are unrecognized. In fact, a literature review shows that up to 65% of intraoperative iatrogenic injuries to the ureter may go unrecognized. The most common types of injury include ligation, angulation, or kinking by resection or suturing of surrounding structures, inadvertent division, partial laceration, devascularization secondary to periureteral dissection, and instrument crush injury. After recognizing iatrogenic ureteral injury involving ligation, removal of the suture that has ligated the structure may be adequate. If a question arises about the viability of the segment that has been ligated, a stent may be placed either in a retrograde or in an antegrade fashion, and then lacerations are repaired and, if amenable, possibly wrapped in omentum or in retroperitoneal fat. Sharp division may require sharp dissection and freshening of the edges and reanastomosis of the ureter. Laceration may also require complete division of the ureter with spatulated anastomosis to ensure a limited risk of stricture formation. A ureteral neocystostomy may be required for injuries to the ureter in the deep pelvis because of ischemia in this area seen with ureteral injuries. This may need reconstruction in the form of a psoas hitch or a Boari flap if ureteral length is inadequate. In the most difficult cases with a significant loss of ureter, the surgeon may need to perform a percutaneous ureterostomy for temporary diversion with later reconstruction, either by reanastomosis to the distal portion of the ureter versus an ileal interposition or other techniques, including transureteral ureterostomy.

**D** The most devastating outcome of a ureteral injury is the formation of ureteral fistulas. These may present as fistulas to the vagina or to the rectum. These are difficult to repair because fistulas require repair with tissues that may have poor blood supply and therefore a higher chance of recurrence. If possible, conservative management of ureteral fistulas is the best approach. If ureteral continuity is renoted, stent placement may allow for adequate healing of the defect and of the ureter with other tissue healing in and ensuring patency and functionality of the ureter. If this simple method does not work, a formal repair in the form of excision of the fistula segment and reanastomosis to the bladder.
may be required. The surgeon should perform this after the inflammation from the original surgery has had enough time to subside, which is 6 weeks in most cases.

### Additional Readings


Bladder injury is a result of either blunt or penetrating trauma to the lower abdomen. Although blunt trauma to the abdomen accounts for approximately 80% of bladder injuries, penetrating bladder injuries are usually associated with other more severe abdominal and vascular injuries, making rapid diagnosis and treatment imperative.1–4 Bladder injuries can be classified as contusions and intraperitoneal or extraperitoneal ruptures. Classification of bladder injury is important because management depends on accurate injury identification.

Contusions are usually not clinically important. Intraperitoneal ruptures are most commonly found at the dome where the bladder is weakest, least supported, and covered by peritoneum. Abdominal trauma to the distended bladder is the usual cause of an intraperitoneal rupture. Extraperitoneal rupture is about twice as common as intraperitoneal rupture and is more commonly associated with pelvic fractures. About 90 to 100% of extraperitoneal bladder ruptures are associated with pelvic fractures. Overall, patients who sustain bladder ruptures have about a 20% mortality rate, primarily owing to the extent of associated injuries, and as with the managing of all traumatic injuries, a team approach is imperative.

Patients who sustain a traumatic bladder rupture usually present with diffuse lower abdominal pain and tenderness on examination and may be unable to void.5,6 Gross hematuria is present in most cases. In those with intraperitoneal ruptures or with a delayed presentation, signs of peritoneal irritation on examination may be present. In many cases, the pain owing to associated pelvic fractures makes the abdominal examination difficult to interpret.

On examination, it is important to evaluate for other associated injuries. Blood at the urethral meatus or a perineal hematoma, along with a high-riding prostate on rectal examination, is suggestive of urethral trauma and should be assessed with a retrograde urethrogram prior to attempted catheter placement. Vaginal bleeding may be a sign of vaginal injury, thus requiring the clinician to assess by performing a complete speculum examination, for which the patient may need anesthesia. Blood on rectal examination may be due to rectal injury and should be fully assessed with anoscopy or sigmoidoscopy as indicated.

Once a urethral injury has been excluded with a retrograde urethrogram, then either a cystogram or computed tomographic (CT) cystogram can be performed to diagnose a bladder rupture.7–10 Perform a cystogram with a water-soluble contrast material, and prior to instillation, obtain a plain film of the abdomen and pelvis. At least 300 cc of contrast is instilled under gravity through the Foley catheter or through a suprapubic tube if a urethral catheter cannot be placed owing to urethral injury. After instillation, anteroposterior, lateral, oblique, and postevacuation films are performed. If possible, perform all views to evaluate for small areas of contrast extravasation, which can be located posterior to the contrast-filled bladder on the anteroposterior film.

A CT cystogram can be performed at the same time CT scanning is being done for evaluation of associated injuries. As with a standard cystogram, instill 300 cc of contrast prior to scanning. Simple Foley clamping is not a reliable method for evaluating bladder rupture when performing a CT cystogram.

With intraperitoneal rupture, extravasated contrast material outlines the intestinal loops and can be seen in the paracolic gutters, even up to the diaphragm (Figure 43-1). With extraperitoneal rupture, extravasated contrast material is limited to the pelvis in what is sometimes termed a “starburst pattern” (Figure 43-2).
Patient with SUSPECTED BLADDER INJURY

A. History
   Physical examination
   Urinalysis

B. Cystography or CT cystogram
   No leakage → Observe
   Leakage →

C. Intraperitoneal rupture
   Antibiotics
   Surgical closure

D. Extraperitoneal rupture
   Antibiotics
   Catheter drainage
   Bladder neck laceration
   Exploratory laparotomy
   Sepsis
   Sever hematuria
   Surgical closure

No leakage → Remove catheter
Leakage
All intraperitoneal bladder ruptures require open surgical repair with closure of the bladder and peritoneum. This is accomplished through a midline abdominal incision that allows for evaluation and repair of associated injuries, if indicated. As mentioned, intraperitoneal ruptures occur at the dome and are typically large. Complete a thorough evaluation for other bladder trauma, including extraperitoneal rupture, which may require extending the intraperitoneal laceration. Close all extraperitoneal injuries intravesically using chromic catgut. Then close the intraperitoneal rupture in two or three layers after débridement of devitalized tissue.

Drain the bladder with a urethral catheter and a large suprapubic catheter brought through a separate incision if the repair is in question, if there is excessive bleeding, or if a urethral injury is present. Otherwise, a large urethral catheter usually provides adequate drainage. Leave a drain in the perivesical space, away from the bladder-closure site and brought out through a separate stab incision. Maintain the patient on broad-spectrum antibiotics starting preoperatively. Remove the urethral catheter 7 to 10 days postoperatively, after a repeat cystogram demonstrates that the bladder has healed with no evidence of contrast extravasation. If no urethral injury is present, remove the suprapubic tube once normal voiding has resumed.

Most extraperitoneal bladder ruptures can be managed successfully with catheter drainage alone. Monitor patients closely and keep on broad-spectrum antibiotics, with a repeat cystogram performed 7 to 10 days after catheter drainage. Indications for surgical repair would include persistent urinary extravasation, severe bleeding/hematuria, or sepsis.

If there is any indication of a possible bladder neck laceration or exploratory laparotomy is being performed for associated injuries, then surgical repair is indicated. This is accomplished by opening the bladder at the dome and repairing the injury intravesically using chromic catgut. Avoid attempting extravesical repair because this is usually limited by pelvic hematoma and could result in excessive bleeding or sepsis.

References
Urethral trauma is almost always secondary to severe injuries that require inspection of the pelvic bone, the suprapubic area, and the external genitalia. When disruption of the lower urinary tract occurs, subsequent drainage and extravasation from the urethra reflect the site of injury above or below the urogenital diaphragm. In the male, when the urethral injury is distal to the urogenital diaphragm, extravasation can occur into the penis, scrotum, anterior thighs, and occasionally into the suprapubic area. When disruption occurs proximal to the urogenital diaphragm, collection of blood and urine occurs periviscerally and is confined, largely, to the true pelvis.

The male urethra is classified into the anterior and posterior segments. The posterior urethra comprises the prostatic and membranous segments and the anterior urethra, consisting of the bulbous and pendulous segments. Injuries to the urinary tract occur in about 10% of all patients who present after blunt, penetrating injury. The posterior urethra is usually damaged as a result of severe, blunt trauma and pelvic-ring fracture. The damage has been estimated to occur in 3 to 25% of all patients with pelvic fracture. When posterior urethral injury occurs, 65% are classified as complete and 35% as partial tears. Anterior urethral injuries are less common and occur as a result of crush injuries, as we have seen in straddle-type trauma or direct penetrating injuries to the penis and urethra. Urethral injuries are rare in female trauma victims. The relative mobility of the female urethra and its lack of attachment to the pubis are the primary reason for the rarity of this injury. Female urethral injury usually occurs as a direct laceration and is diagnosed on physical examination.

Patients who are suspected as having urethral injuries usually have multiple organ injuries, and management must be coordinated with other specialists. First, correct life-threatening injuries before addressing urethral injuries.

A Suspect all patients with pelvic fractures to have a urethral injury. Gross hematuria or blood at the urethral meatus is the most common finding in patients with urethral trauma. If the male urethra tears, the bulbocavernous muscle contracts, and blood is forced out of the urethral meatus. An inability to urinate may be seen in patients with urethral injury; however, more common causes in acute trauma victims include an empty bladder or simply an inability to void on command because of pain or shock from the fractured pelvis. Perineal or genital swelling, resulting from extravasation of blood or urine, may be present. The classic perineal butterfly hematoma is diagnostic of urethral disruption and may not be present in patients examined shortly after injury. Rectal examination is imperative and may reveal a nonpalpable prostate, a pelvic hematoma, and, more importantly, an associated rectal laceration. Abdominal tenderness suggests intraperitoneal extravasation of urine or concomitant intra-abdominal visceral injury and warrants further diagnostic evaluation, such as computed tomography (CT) of the abdomen and pelvis. All female patients must have a vaginal examination. In the absence of a vaginal laceration, urethral injury is unlikely.

B All male patients who present with pelvic fractures associated with gross hematuria, blood at the urethral meatus, perineal swelling, nonpalpable prostate, or an inability to urinate undergo retrograde urethrography. Ideally, a retrograde urethrogram is performed with the patient in the oblique position with the penis stretched perpendicular to the femur. In the trauma setting, however, it is not always possible to position the patient obliquely. Obtain a urethrogram that is adequate to rule out urethral disruption with the patient lying flat by placing the penis on stretch, perpendicular to the lower extremity. Water-soluble contrast (30 to 40 mL) is instilled into the urethra with gentle pressure, and a film is obtained, while the last 10 cc is injected. Use a Brodney clamp bulb syringe or tip of a 12 to 16 French Foley catheter with the balloon inflated in the fossa navicularis to perform this study. If contrast is seen to flow into the bladder without evidence of extravasation, place a Foley catheter and perform a cystogram to rule out a bladder perforation. Partial urethral disruption is diagnosed in the context of extravasation with partial filling of the bladder (Figure 44-1). Extravasation of contrast without filling of the bladder is diagnostic of a complete urethral disruption (Figure 44-2).

C If urinary extravasation is identified, the site of extravasation is determined (ie, posterior urethra or anterior urethra).

D Anterior urethral injuries account for only about 10% of all urethral injuries. They usually occur as a result of blunt trauma to the perineum, causing a crushing effect on the perineal tissues and urethra. Penetrating injuries owing to gun shots or knife wounds may also involve the anterior urethra. Blunt injuries are often ignored by the patient as being insignificant until years later when obstructive urinary flow develops as a result of a urethral stricture.
Patient with SUSPECTED URETHRAL DISRUPTION

A. CT abdomen and pelvis

B. Retrograde urethrogram

C. Normal
   - Intact urethra
     - Indwelling catheter
     - Cystogram

C. Extravasation
   - Urethral disruption

D. Anterior urethral injury
   - Indwelling catheter

E. Blunt
   - Indwelling catheter

F. Penetrating
   - Exploration/repair

G. Posterior urethral injury

H. Partial disruption
   - Primary realignment
     - Indwelling catheter
   - Suprapubic tube

I. Complete disruption
   - Suprapubic tube
   - Delayed repair
Blunt injuries to the anterior urethra seldom result in complete disruption and can usually be managed by catheter drainage. Retrograde urethrogram is performed 7 to 10 days after the injury and before the catheter is removed.

Penetrating injuries involving the anterior urethra usually require exploration and débridement. If the loss of tissue is not extensive, primary urethral anastomosis is the preferred method of treatment. Defects less than 2 cm can be repaired primarily by anastomosis over the catheter. The anastomosis must be tension free, spatulated, and watertight. Manage longer defects by suprapubic tube urinary diversion and delayed urethral reconstruction.

The optimum management of posterior urethral injuries remains controversial, with opinion divided between those who favor immediate urethral realignment over a catheter and those who favor suprapubic urinary diversion, with delayed treatment of the expected urethral stricture. The goal of either treatment is to minimize complications associated with the initial treatment, while minimizing the long-term consequences of pelvic fracture and urethral injury. Patients with posterior urethral disruption should never undergo primary urethroplasty.

Extravasation of contrast with partial filling of the bladder is diagnostic of a partial urethral disruption. These patients may be managed by either primary catheter placement or suprapubic tube placement with treatment of the ensuing urethral stricture should it occur. At our level I trauma center, we treat all patients who present with a partial disruption with a Foley catheter placement. If we are unable to place the catheter, we perform flexible cystoscopy. A guidewire is advanced into the bladder and a catheter is advanced into the bladder over the guidewire. The catheter is left indwelling until the urethra has completely healed (usually 2 to 6 weeks). We perform a retrograde urethrogram alongside the catheter to confirm the absence of extravasation prior to catheter removal. Patients are then observed, and if voiding dysfunction occurs, a stricture should be suspected. If urethral stricture occurs, incision of the stricture will usually prove to be therapeutic. In our experience, no patient with a partial tear has been converted to a complete disruption after attempted catheter placement, and no patient with partial urethral disruption has required formal urethroplasty. Those who favor suprapubic tube placement believe that the traumatized urethra is managed best by avoiding any manipulation.

We diagnose complete urethral disruption by extravasation of contrast without filling of the bladder. Treating posterior urethral disruption is controversial. Complete urethral disruption is best managed by primary urethral realignment. The timing of the realignment depends on the condition of the patient and the presence or absence of other associated injuries. If the patient is clinically stable and no other injuries that require surgical exploration...
exist, we perform urethral realignment. A single attempt at placing the Foley catheter is performed. On rare occasions, the catheter may be placed into the bladder, and a cystogram will confirm the proper position. Then the catheter is left indwelling until the urethra is completely healed (usually 4 to 6 weeks). If the catheter cannot be placed, the patient is taken to the operating room, where the bladder is explored through a lower midline incision.

There are several techniques to realign the urethra. Common to all techniques is to avoid the pelvic hematoma and provide minimal manipulation of the traumatized prostate. In addition, avoid traction on the catheter. The technique currently used involves placing a catheter in a retrograde manner into the urethral defect. The surgeon advances a flexible cystoscope through the bladder neck until the catheter is visualized and advances the cystoscope while following the catheter through the urethra and out of the urethral meatus. Next, the surgeon advances a guidewire into the bladder and a 22 French Council catheter is advanced into the urethra over the wire. A suprapubic tube is not left, and no drains are placed. The patient is maintained on broad-spectrum antibiotics until the urethra has healed. This technique is the least invasive, is easy to perform, does not disturb the pelvic hematoma, and requires instruments familiar to all urologists.

If the patient is too unstable to undergo urethral realignment, a punch suprapubic tube is placed and realignment is carried out when the patient’s condition allows (usually 2 to 10 days). When performing delayed urethral realignment, flexible cystoscopy may successfully negotiate the disrupted urethra and allow the placement of a guidewire over which a Foley catheter may then be placed. The catheter is left until the urethra is completely healed; then we routinely recommend a regimen of intermittent self-catheterization. In our experience, the expected stricture usually stabilizes after 3 months of self-dilation. To date, no patient in our experience has required open urethroplasty for the treatment of recurrent stricture disease. Many urologists believe that a suprapubic tube is the best treatment for patients with complete urethral disruption. If the suprapubic tube is placed, it is best left for 3 to 6 months, which allows resolution of the hematoma; afterward, an open urethral reconstruction is performed.

References
Management of Testicular Trauma
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Trauma to the testicle results from blunt or penetrating injury.1 The insult is most commonly unilateral.2–4 Trauma to the testicle can result in scrotal edema, hematocoele, hydrocele, torsion, fracture, and rupture.5 Causes include assaults, sports injuries, motor vehicle collisions, self-mutilation, and gunshot wounds.1,2,6–8 The history usually reveals the acute onset of signs and symptoms just after injury. Patients commonly complain of severe pain, sometimes accompanied by nausea and emesis.

A Penetrating trauma to the scrotum warrants physical examination and ultrasonography to eliminate the possibility of testicular injury. Any patient with positive or equivocal findings should undergo surgical exploration. Injuries to the urethra, penis, femoral vessels, perineum, or thigh can be associated with up to 80% of penetrating injuries.9

B Examination of the patient with blunt trauma may reveal scrotal ecchymosis, hematocoele, and testicular pain. Physical findings of testicular rupture are nonspecific, although they can occur in up to 50% of cases of severe blunt trauma.10 The tunica albuginea surrounding the testicle can withstand a force of 50 kg.11,12 Blunt trauma of lesser force can result in intratesticular bleeding. A hematocoele develops when the force is great enough to cause a break in the tunica albuginea, causing the seminiferous tubules to be extruded.3 A scrotal hematoma develops if the rupture extends to the junction with the tunica vaginalis.2

C Pain and extent of scrotal edema often make clinical examination difficult.5 If the testis is not palpable and the suspicion of rupture is low, ultrasound imaging are often useful in the evaluation of the patient with testicular trauma. However, its sensitivity and specificity are debated in the literature.4,13–18 Parenchymal heterogeneity on ultrasound imaging may indicate intratesticular hematoma.17 Ultrasound finding of a fracture is a hypoechoic stripe in a testicle with otherwise normal architecture and blood flow.5,19 Features of testicular rupture are an irregular outline caused by separations in the tunica albuginea and heterogeneous texture secondary to ischemia and hemorrhage.5,20–22 Doppler imaging may show decreased or no blood flow.5 Sonography can also reveal incidental findings such as tumors. Developments are being made using magnetic resonance imaging (MRI) to prognosticate future testicular function based on intratesticular hemorrhage.23

D Injuries not associated with intratesticular hematoma or rupture, such as small hematocoeles, epididymal hematomas, or contusions, can be managed with ice, elevation, and analgesics. The testis must be palpable and the tunica intact. Expansion of the hematocoele during observation should warrant surgical intervention. Risks of nonoperative management include infection, atrophy, and necrosis.3

E The aim of surgical treatment is tissue salvage. Early exploration of the grossly abnormal scrotum is recommended.2–4 A dislocated testicle, large hematocoele, or gross rupture of testicular contents recommends immediate surgical intervention. Make a transverse scrotal incision and remove any hematoma. Inspect the testicle, epididymis, and spermatic cord. Definitive treatment is débridement of devitalized tissue and closure of the tunica albuginea with absorbable suture in a running, locked fashion. Removal of testicular tissue may be required if a significant portion of the tunica is lost.8 Extensive injury or infarction24 may warrant orchiectomy, and preoperative discussion of the risk with the patient should occur. In cases of bilateral injury, conservative débridement helps to preserve testicular tissue.20 The wound should be copiously irrigated and a Penrose drain put in place.7,8 The dartos muscle and skin are each approximated with chromic sutures. Fluffed gauze and a scrotal support should be applied postoperatively. Antibiotics are given preoperatively and continued for 7 days.8

The effect of testicular trauma on fertility is unknown.26 Spermatozoa and their antigens are isolated from the immune system by tight junctions of Sertoli cells and a predominance of suppressor T cells in the testes, vas deferens, and prostate.27,28 It has been theorized that a breach in the blood-testis barrier can result in an immune response, resulting in antisperm antibodies that could potentially affect the function of the contralateral testicle.29–32 Kukadia and colleagues found long-term evidence of abnormal semen parameters and testicular atrophy after trauma in eight patients who underwent immediate surgical exploration, although all patients had normal hormonal status and only one patient had detectable levels of antisperm antibodies.33 Several studies have shown that testicular salvage may be achieved in 80 to 90% of ruptures if surgical intervention occurs within 72 hours of trauma.2–4,19 Therefore, the mainstays of treatment should be prompt history and physical examination, with or without ultrasonographic imaging, and early surgical exploration when intratesticular hemorrhage or testicular rupture cannot be ruled out.
References

The ability of the scrotum to expand owing to its viscoelastic properties allows for even large scrotal skin defects to be closed primarily. The excellent blood supply of the perineal area, second only to the face, is the main reason even dirty wounds, after thorough scrubbing with minimal débridement, permit a conservative approach to these lesions with expectations of an eventual good result.

The American Association for the Surgery of Trauma (AAST) has developed an Organ Injury Scaling Committee, which created injury severity scores for individual organs to facilitate clinical investigation and outcomes research. A Scrotum Injury Scale has been published and is in wide use in trauma centers (Table 46-1). This scale will be used in the accompanying flow chart as indicated.

A Blunt trauma to the scrotum without skin damage may contuse the scrotal wall, requiring ice packs only for therapy, if the scrotal contents are normal. Because of their mobility, usually the testes and adnexa are not damaged. If physical examination is difficult, which is most often attributable to a scrotal hematoma or pain, the clinician should perform scrotal ultrasonography. The proper treatment of testicular trauma is discussed in the preceding chapter.

B The AAST classification requires a classification scheme of five grades for all organs. Owing to the qualities of the scrotum, handle all lacerations with primary closure, using absorbable suture material and ice packs if seen in the first few hours after injury. If the wound is contaminated, first perform vigorous scrubbing with either soap or an iodine solution. Severely contused wound edges can appear devascularized because of ecchymosis to the tissues. Débridement should be very conservative. Excise obvious dead tissue only. It is better to allow questionable areas to demarcate in a few days and débride small amounts multiple times than to have too little tissue left to close the wound. After the first day, discontinue ice packs and begin warm soaks for 15 minutes, three times daily.

C Scrotal skin has an amazing ability to stretch and cover quite large defects. Occasionally, small gaps are left unclosed and warm soaks begun. When the bases of these areas are clean, secondary closure can generally be accomplished. When the integrity of the tunica vaginalis has been lost, examine the entire contents of the scrotum, and correct defects prior to closure. All of the prior comments pertaining to contaminated wounds and débridement apply.

D If most of the scrotal wall has been lost and the wound contaminated, after scrubbing, use wet-to-dry dressings over the next few days to help débride devitalized tissue and to get the testicles and adnexa in condition for eventual covering. Some surgeons prefer to place the exposed testicles in thigh pouches as temporary coverage in preparation for eventual repair. Avoid employing this technique until all evidence of contamination and/or infection is controlled. Rarely, major avulsion wounds are clean and do not require this type of treatment prior to scrotal reconstruction.

E The most popular and best cosmetic way to reconstruct the scrotum is to use split-thickness skin grafts, although thigh flaps (especially if the testicles had previously been placed in thigh pouches) or a gracilis myocutaneous flap can be used. The testicles are sutured together in the midline and covered with split-thickness skin grafts, usually harvested from the anterior thigh. The grafts are usually meshed to increase the surface area, which later gives the neoscutrum the appearance of rugae. Absorbable sutures are used for the entire procedure, as well as an immobilizing dressing.

Table 46-1  AAST Scrotum Injury Scale

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Contusion</td>
</tr>
<tr>
<td>II</td>
<td>Laceration &lt; 25% of scrotal diameter</td>
</tr>
<tr>
<td>III</td>
<td>Laceration ≥ 25% of scrotal diameter or stellate</td>
</tr>
<tr>
<td>IV</td>
<td>Avulsion &lt; 50%</td>
</tr>
<tr>
<td>V</td>
<td>Avulsion ≥ 50</td>
</tr>
</tbody>
</table>

References

Patient with SCROTAL INJURY

Skin intact?

**Yes**

**Contents intact?**

**Yes**

Local care

**No**

Scrotal US

**Unsure**

**No**

**Avulsion**

< 50%?

**Yes**

Laceration

**No**

**Avulsion**

≥ 25% or stella?

**Yes**

**Tunica vaginalis and contents intact?**

**No**

Exploration and Primary closure

**Yes**

Primary closure

**Contents intact**

**No**

**Débridement and wet-to-dry dressing**

**Wound clean?**

**Yes**

**Reconstruction**

1. Split-thickness skin grafts
   or
2. Thigh flaps
   or
3. Gracilis flaps

**No**
SECTION 6

GENITOURINARY TUMORS
A The classic triad for renal cell carcinoma (hematuria, flank pain, and flank mass) is now rarely seen. Most renal masses are now discovered as incidental findings during computed tomography (CT) scan or ultrasonography. Flank pain, rarely seen without hematuria, often reflects clot colic. Because a flank mass must be large to be palpated, renal cell carcinoma is detected in this way in fewer than 25% of patients.

B The initial pathway in diagnosis involves distinguishing cystic from solid lesions. Cystic lesions are evaluated by ultrasonography, and if found to be simple cysts, the work-up is complete. More complex cysts require CT evaluation. Bosniak I, or simple cysts with regular margins and without enhancement or septations, do not need further characterization. Bosniak II and III lesions, with progressively more septations, loculations, and calcifications, need follow-up CT for characterization and will often need serial studies to rule out malignant change. Bosniak IV lesions have enhancing solid components and irregular margins on CT and are treated as malignancies.

C The most thorough evaluation of the renal mass is a CT scan with thin sections, studied without contrast followed by intravenous contrast. Valuable information is gained by comparing the Hounsfield units of the different phases. Almost all renal masses with less than 10 Hounsfield units difference on the different phases are benign. The combination of ultrasonography and CT has almost obviated the need for angiography.

D Judicious use of partial nephrectomy for small masses has increased in the past decade. In many cases, significant parenchyma may be preserved while still maintaining clear tumor margins. Some controversy exists over the increased number of nephrectomies for small, incidentally discovered renal masses, with some advocating serially repeating CT scans. The natural history of these masses is still not known. However, renal cell carcinoma has an unpredictable course, with relatively ineffective treatment once metastatic. For this reason, it is usually recommended to operate on these masses using nephron-sparing surgery in appropriate situations. Currently, this includes patients having tumors in a solitary kidney or those with compromised kidney function, as well as isolated tumors less than 4 cm.

E Larger masses requiring nephrectomy may have inadequate work-up with CT alone when suspicion of renal vein or vena caval involvement exists. Generally, venography is rarely indicated, and magnetic resonance imaging (MRI) should be used to evaluate possible tumor thrombus extent. Some additional information about tumor invasion and stage may be gained as well. If on CT scan the mass seems to have a homogeneous density with a very narrow, stellate central lucency, an oncocytoma rather than renal cell carcinoma may be present. Oncocytomas are epithelial tumors composed exclusively of cells with eosinophilic cytoplasm, called oncocytes, arranged in a lobular or alveolar pattern. These masses usually appear homogeneous on CT and MRI. Biopsy is not warranted as specificity is low; renal cell carcinomas may have regions of oncocytes. However, in the future, molecular analysis may allow better preoperative diagnosis of oncocytomas. Preoperative suspicion of oncocytoma often provides an impetus for attempting partial nephrectomy.

F Distinguishing the origin of central masses that involve the collecting system can be difficult using conventional CT. Intravenous pyelogram (IVP) may be helpful in outlining the relationship between the mass and the collecting system. Alternatively, three-dimensional CT or MRI reconstruction is increasingly being used for this purpose.

Additional Readings
Patient with RENAL MASS

Symptomatic renal mass

A History
Physical examination

Incidental discovery
on CT or sonography

B Cystic mass

Nonsuspicious
Follow-up sonogram if increased
Hounsfield units consistent with
hyperdense cyst

Increased density,
internal echoes
or wall irregularity

C CT with and without contrast

Solid mass or highly suspicious cyst
with contrast enhancement > 10 Hounsfield units

< 4 cm mass consistent
with renal cell carcinoma

E > 4 cm mass

F Central mass

D Partial vs total
nephrectomy

If suspicious
of thrombus

IVP vs 3D
reconstruction

MRI

Radical nephrectomy
Wilms’ tumor is one of the most studied neoplasms in history. Its study has allowed great insights into a better understanding of molecular biology and cancer, development of cancer, and the behavior of tumors. The current treatment of Wilms’ tumor has stemmed from early clinical trials and cooperative studies. These trials have led to a multimodal approach to Wilms’ tumor, which includes surgery, chemotherapy, and radiation therapy, resulting in expected survival rates that currently approach 90%.\textsuperscript{1,2} The study and treatment of Wilms’ tumor represent one of modern medicine’s great achievements.

The annual incidence of Wilms’ tumor in North America is approximately 7 per million children, resulting in approximately 450 to 500 cases per year. The peak incidence is seen in children between the ages of 3 and 4 years, with 90% of cases diagnosed before age 7. Wilms’ tumor occurs equally in males and females, with 5% of cases occurring bilaterally.\textsuperscript{1}

Specific congenital anomalies have long been associated with Wilms’ tumor. The National Wilms’ Tumor Study Group I (NWTSG) demonstrated a higher incidence of genitourinary anomalies including renal anomalies (fusion, duplication, and ectopia) and general anomalies such as hypospadias and cryptorchidism. This observation has subsequently been linked to the \textit{WT1} (Wilms’ tumor oncogene), which is responsible for nephrogenesis, genital development, and Wilms’ tumor.\textsuperscript{3} Children with an unusual congenital anomaly of the eye, the loss of the iris (aniridia), have a higher incidence of Wilms’ tumor. Patients with sporadic aniridia may have a 33% chance of developing Wilms’ tumor.\textsuperscript{4,5} In addition, aniridia associated with genital anomalies and mental retardation constitutes the WAGR syndrome. Hemihypertrophy has also been shown to be associated with Wilms’ tumor. These patients have a 3 to 5% increased risk of developing Wilms’ tumor and an increased likelihood of developing adrenocortical carcinoma and hepatoblastoma.\textsuperscript{1,6} Other syndromes commonly associated with Wilms’ tumor include the Beckwith-Wiedemann syndrome (BWS) and Denys-Drash syndrome. BWS includes visceromegaly, omphalocele, mental retardation, macroglossia, and hemihypertrophy. Denys-Drash patients have Wilms’ tumor along with ambiguous genitalia and renal mesangial sclerosis, often resulting in end-stage renal disease.\textsuperscript{4,5}

Wilms’ tumor is classified as hereditary or nonhereditary based on the two-hit mutational model proposed by Knudson and Strong.\textsuperscript{7} Hereditary cases are bilateral, occur in younger individuals, and are associated with other anomalies or syndromes. The two most common chromosomal loci involved in the development of Wilms’ tumor are the loss of 11p13, which includes the tumor suppressor gene \textit{WT1}, often seen with the WAGR syndrome, and loss of 11p15 (\textit{WT2}), most commonly associated with BWS. In addition, approximately 20% of Wilms’ tumor specimens have demonstrated the loss of the long arm of chromosome 16 (16q), which may correlate with a poorer prognosis, independent of stage or histology. Mutation of the tumor suppressor gene \textit{p53}, located on chromosome 17p13, is typically seen in adult-onset Wilms’ tumors. Finally, genetic alterations have also been isolated to chromosomes 7p and 1p.\textsuperscript{8,9}

\textbf{A} Children with Wilms’ tumor typically appear well, and the most common physical finding is a palpable abdominal mass.\textsuperscript{10} Approximately one-third of patients present with abdominal pain, which, when acute in onset, may reflect hemorrhage into the tumor. These patients may develop fever, rapidly enlarging abdominal mass, or hypotension. Gross hematuria is unusual; however, up to 25% of patients may exhibit microscopic hematuria.\textsuperscript{1} Other signs include congestive heart failure, varicocele, or hepatomegaly, all of which can suggest intravascular extension of the tumor.\textsuperscript{11,12} Hypertension, secondary to renin secreted from the tumor, may also be present.

\textbf{B} Radiologic imaging is essential in Wilms’ tumor patients and is usually confirmatory. The goals of imaging are to localize the source of the mass, identify associated genitourinary anomalies, confirm the presence of a functioning contralateral kidney, and exclude extension of the tumor into the inferior vena cava (IVC).\textsuperscript{13} Ultrasonography accomplishes the first two goals and assesses IVC involvement. If a caval thrombus is suspected, cavography or magnetic resonance imaging scan should be obtained to delineate the extent.\textsuperscript{1} Computed tomography (CT) scan of the abdomen can document a contralateral functioning kidney and can detect bilateral tumors (Figure 48-1).\textsuperscript{14} Finally, perform a chest radiograph or chest CT to rule out pulmonary metastases. Routine urinalysis, complete blood count, and basic blood chemistries complete the preoperative work-up.
Patient with SUSPECTED WILMS' TUMOR

**History**
- Physical examination

**Ultrasonography**
- CT abdomen/pelvis/chest
- Complete blood count, metabolic profile, urinalysis
- Chest radiograph

**Unilateral**
- Solitary kidney
- Renal insufficiency

**Bilateral**
- Nephrectomy, lymph node sampling
- If unresectable, biopsy

**Consider partial nephrectomy**
- Possible biopsy and preoperative chemotherapy

**Biopsy both kidney masses**
- Preoperative chemotherapy

**Stage Histology**
- Favorable histology
- Unfavorable histology

**Stage I–II**
- I with anaplasia

**Stage III–IV**
- Focal anaplasia
- II–IV

**Diffuse anaplasia**
- II–IV

**1,800 cGy abdomen**

**AMD, VCR, DOX**
- (24 weeks)

**AMD, VCR, DOX, CPM, VP-16**
- (24 weeks)

**Abdominal and lung radiotherapy**

**A**

**B**

**C**

**D**

**AMD, VCR**
- (18 weeks)
C Accurate staging of Wilms’ tumor is critical to establish the appropriate chemotherapeutic and radiotherapeutic intervention. In the absence of distant metastases and/or bilateral involvement, accurate staging of Wilms’ tumor requires surgical exploration. The current staging system of the NWTSG is shown in Table 48-1. Four year survival rates per stage are I, 95%; II, 91.1%; III, 90.9%; IV, 80.9%; and V, 70%. The most current significant predictor of survival, however, is the histology of the tumor. Eventually, better understanding and studies of the molecular characteristics of the tumor will help to elucidate predictors of the tumor and subsequent behavior. Today, however, histology remains the most important predictor of the tumor’s behavior. Histology is classified as favorable or unfavorable (anaplastic). Anaplastic changes, present in 5% of Wilms’ tumors, include markedly enlarged, hyperchromatic nuclei and increased mitotic figures. The presence and distribution of anaplasia correlate with a poor prognosis characterized by an increased resistance of the tumor to therapy. The only exception to this rule is stage I focal anaplastic tumors, which have identical survival rates to those nonanaplastic tumors of the same stage.

D The initial treatment of most patients with Wilms’ tumor is a radical nephrectomy. Employ a transperitoneal approach to explore the contralateral kidney, if present, in its entirety prior to nephrectomy of the involved kidney. If the contralateral kidney is disease free, a radical nephrectomy is performed with selective lymph node sampling for accurate staging. Formal lymph node dissection has no impact on outcome and is not recommended. The presence of bilateral tumors significantly changes the treatment plan. Perform open or percutaneous biopsy of both kidneys to obtain histologic information. Then treat the patient according to NWTSG protocol, planning further exploration after the initial course of therapy with the aim to preserve kidney tissue. Then reassess with an abdominal CT to determine if resection is feasible. Consider partial nephrectomy as long as surgical margins are not compromised.

Partial nephrectomy for unilateral tumors is controversial. NWTSG recommends nephron-sparing surgery in the setting of bilateral disease, renal insufficiency, and solitary kidney. The surgical complication rate is approximately 12.7% and includes bowel obstruction, vascular injury, infection, and hemorrhage.

Preoperative chemotherapy is reserved for patients with bilatera disease, massive disease, IVC extension, and inoperable tumor at surgical exploration. Currently, patients are treated according to the NWTS-V, shown in Table 48-2.

The most common sites of metastasis are the lungs and lymph nodes. Follow up with periodic chest radiography, abdominal CT scan, or ultrasonography. Treat

Table 48-1 Staging System NWTSG*

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Tumor limited to kidney and completely excised. The renal capsule is intact and the tumor was not ruptured prior to removal. There is no residual tumor. The vessels of the renal sinus are not involved.</td>
</tr>
<tr>
<td>II</td>
<td>Tumor extends beyond the kidney but is completely excised. There is regional extension of the tumor (ie, penetration of the renal capsule, extensive invasion of the renal sinus). The tumor may have been biopsied or there may be local spillage of tumor confined to the flank. Extrarenal vessels may contain tumor thrombus or be infiltrated by tumor.</td>
</tr>
<tr>
<td>III</td>
<td>Residual nonhematogenous tumor confined to the abdomen: lymph node involvement, diffuse peritoneal spillage either before or during surgery, peritoneal implants, tumor beyond the surgical margin either grossly or microscopically, or tumor not completely removed.</td>
</tr>
<tr>
<td>IV</td>
<td>Hematogenous metastases (lung, liver, bone, brain, etc) or lymph node metastases outside the abdominopelvic region are present.</td>
</tr>
<tr>
<td>V</td>
<td>Bilateral renal involvement at diagnosis.</td>
</tr>
</tbody>
</table>

*NWTSG-IV.

Table 48-2 NWTS-V Treatment Protocol

<table>
<thead>
<tr>
<th>Stage</th>
<th>Radiotherapy</th>
<th>Chemotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>I, II FH or I with anaplasia</td>
<td>None</td>
<td>P/I AMD + VCR (18 weeks)</td>
</tr>
<tr>
<td>III–IV focal anaplasia</td>
<td>1,080 cGy</td>
<td>P/I AMD + VCR + DOX (24 weeks)</td>
</tr>
<tr>
<td>II–IV diffuse anaplasia</td>
<td>Yes*</td>
<td>AMD, DOX, VCR, CPM, VP-16 (24 weeks)</td>
</tr>
</tbody>
</table>

*Abdominal irradiation based on local tumor stage and 1,200 cGy to both lungs.
recurrences aggressively with chemotherapy and selected surgery and radiotherapy. The clinician must be aware of the complications, both long and short term, of radiotherapy, chemotherapy, and surgery to counsel the patient accordingly.

References

Angiomyolipoma, a benign tumor composed of fat, smooth muscle, and abnormal blood vessels, occurs mainly in women, and in 80% of cases, it occurs on the right side. Patients with tuberous sclerosis have an 80% lifetime incidence of developing angiomyolipoma, although only 40% of patients with this lesion have the syndrome. Angiomyolipomas are usually diagnosed between the third and fifth decades. Although benign in nature, they can hemorrhage acutely and may present as severe abdominal or flank pain. Many angiomyolipomas are detected incidentally on sonography or computed tomography (CT). Ultrasonography will identify a hyperdense area within the mass, suggesting the presence of fat.

Cystic masses are characterized by sonography, using the Bosniak classification system. Bosniak I, or simple cysts with regular margins and without enhancement or septations, do not need further characterization. Bosniak II and III lesions, with progressively more septations, loculations, and calcifications, require a follow-up CT for characterization and will often need serial studies to rule out malignant change. Bosniak IV lesions have enhancing solid components and irregular margins on CT and are treated as malignancies.

The best characterization of renal masses is by CT scan, without contrast and then with contrast. Enhancing lesions that differ more than 20 Hounsfield units between the two are suspicious for carcinoma, whereas nonenhancing lesions that differ < 10 Hounsfield units are usually benign, provided that the CT cuts are thin enough to identify the entire lesion. The technique allows for comparison of identical regions.

Fat within the mass suggests angiomyolipoma; renal cell carcinoma does not contain fat. Fat content on CT scan will reveal negative Hounsfield units, typically < 20. Care must be taken to ascertain that the fat is within the mass and not perirenal fat or inflammatory reaction. Renal cell carcinoma has not been described within an angiomyolipoma; thus, finding fat within a renal mass permits clinicians to make the nonoperative definitive diagnosis of angiomyolipoma. MRI with fat suppression differentiates indeterminate lesions.

Renal angiomyolipoma may be followed up by serial imaging if the mass is less than 4 cm or for slightly larger lesions if they are stable and asymptomatic. Several series have shown that smaller lesions are much less likely to hemorrhage or to cause symptoms. Angiomyolipomas > 4 cm are more likely to grow and require more frequent imaging. Generally, all angiomyolipomas > 8 cm require intervention because of hemorrhagic risk. Nephron-sparing surgery or selective arterial embolization is generally attempted whenever possible. When a lesion is acutely hemorrhaging, consider embolization as the first-line therapy.

**References**

Patient with ANGIOMYOLIPOMA

Patient with flank or abdominal pain
Renal mass seen on CT/sonogram incidentally

A History
Physical examination

B Cystic mass
Sonogram (if not already performed)

Bosniak I
Bosniak II/III
Bosniak IV (see text for differentiation)

C Follow sonographically

Not suspicious

D CT scan done without and with contrast

Suspicious for renal cell carcinoma

Angiomyolipoma

Indeterminate lesion

F MRI with fat suppression

E Partial or radical nephrectomy

G Serial imaging

H Selective arterial embolization (if bleeding)
Primary retroperitoneal tumors refer to benign and malignant tumors of mesenchymal origin that arise in the retroperitoneal space. Most retroperitoneal tumors are malignant (70 to 80%) but overall represent only 0.2% of all malignancies. Although no etiologic factors have been identified, prior radiation exposure, exposure to asbestos and herbicides, and trauma may be contributing factors. The most common retroperitoneal tumors in descending order are liposarcomas, leiomyosarcomas, fibrosarcomas, and neurogenic sarcomas. Many pleomorphic variants of the above tumors are being reclassified as malignant fibrous histiocytomas. Other malignant tumors include rhabdomyosarcomas, malignant hemangiopericytomas, malignant schwannomas, and synovial sarcomas. Benign tumors include lipomas, pelvic lipomatosis, myelolipomas, retroperitoneal xanthogranulomas, leiomyomas, and ganglioneuromas. Retroperitoneal sarcomas account for 10 to 15% of all soft tissue sarcomas. In addition to a primary retroperitoneal tumor, the differential diagnosis of a mass in the retroperitoneum includes hematoma, abscess, cyst, or a tumor of a retroperitoneal organ (eg, kidney or pancreas).

A Retroperitoneal tumors characteristically present with insidious abdominal enlargement and weight loss. Of patients, 20% initially present with metastatic disease. The most common presenting feature is vague pain, located most often in the abdomen (followed by pain in the back and lower extremities). Fever may be present, secondary to central tumor necrosis. A palpable abdominal mass is the most consistent physical finding that is found in approximately 75% of patients. The tumor may impinge on the gastrointestinal tract and cause loss of appetite, early satiety, nausea, vomiting, obstipation, or diarrhea. Vascular and lymphatic compression may lead to claudication and lower extremity edema. Urinary frequency, dysuria, flank pain, and hydrenephrosis can result directly from tumor encroachment on genitourinary structures. Finally, compression of various neurologic structures can result in sciatica or motor and sensory changes.

The staging of retroperitoneal tumors follows the American Joint Committee on Cancer Grade, Tumor, Node, Metastases (TNM) classification of soft tissue sarcomas. This system incorporates tumor grading (G) into the traditional TNM system with G1, G2, and G3 corresponding to well-differentiated, moderately well-differentiated, and poorly differentiated grades, respectively. Primary tumor size (T) is designated as either T1, ≤ 5 cm in greatest diameter, or as T2, > 5 cm in greatest diameter. Tumors are further staged by regional lymph node metastases (N0 vs N1) and then by distant metastases (M0 vs M1). Increasing tumor stage from I to III corresponds to worsening tumor grade from G1 to G3. Stage IV disease corresponds to local or distant metastasis.

B Computed tomography (CT) scans provide the most reliable means of imaging primary retroperitoneal tumors. Delineate vascular involvement with either magnetic resonance imaging (MRI) or angiography. Barium contrast studies are indicated if gastrointestinal symptoms are present or if the initial CT scan suggests gastrointestinal involvement. Finally, excretory urography is almost invariably required to evaluate the contralateral kidney because ipsilateral nephrectomy is required in 25 to 30% of patients for complete surgical resection of the retroperitoneal tumor with negative margins. Three-dimensional CT scans may obviate the need for these other modalities as this technology becomes more readily available to medical centers nationwide.

C Sarcoma is a surgical disease; therefore, the only treatment capable of cure is complete surgical excision. The most important variable for disease-free survival is a negative surgical margin, followed by low tumor grade. According to most investigators, complete resection is possible in 40 to 60% of cases. This usually requires en bloc resection of the tumor with two concepts in mind. First, retroperitoneal tumors generate a “pseudocapsule” as they grow because their large size compresses surrounding tissues. The primary tumor sheds cells that infiltrate along fascioaponeurotic planes beyond the limits of the pseudocapsule. The surgeon therefore must make the excision well outside the tumor pseudocapsule to ensure complete excision. Second, adjacent organs and structures may need to be excised to achieve complete resection. As a result, bowel preparation is done preoperatively; bowel resection may be required in up to 20% of cases. Ureretal stent placement has also been advocated. In decreasing frequency, the adjacent organs sacrificed during complete resection are the kidney (32 to 46%), colon (25%), adrenal gland (18%), pancreas (15%), and spleen (10%). Right-sided masses may require caval resection, whereas left-sided masses may need aortic resection with grafting. Other structures, such as the lumbar arteries, inferior mesenteric artery, and sympathetic chain, can be sacrificed ipsilaterally if the collateral pathways from the contralateral side are not injured.
Primary Retroperitoneal Tumors

Patient with SUSPECTED PRIMARY RETROPERITONEAL TUMOR

Signs and Symptoms:
- Insidious abdominal enlargement and weight loss
- Vague abdominal pain (or in back or lower extremities)
- Palpable abdominal mass
- Gastrointestinal symptoms: nausea, vomiting, obstipation, diarrhea, loss of appetite, early satiety
- Genitourinary symptoms: dysuria, urgency, urinary retention, flank pain
- Neurovascular symptoms: claudication, lower extremity edema, sciatica, motor/sensory changes

A

B

Medical evaluation

Normal

Abdominal CT scan

Other pathology

Other work-up

Retroperitoneal mass

Excretory urography

Other imaging

Gastrointestinal symptoms present

Vascular involvement

Gastrointestinal barium studies

MRI or angiography

Complete resection

Surgical excision of mass

Follow with CT scans

Adjuvant IORT

Incomplete resection

Adjuvant Repeat surgical excision if recurrence

Metastases

Signs and Symptoms:
- Insidious abdominal enlargement and weight loss
- Vague abdominal pain (or in back or lower extremities)
- Palpable abdominal mass
- Gastrointestinal symptoms: nausea, vomiting, obstipation, diarrhea, loss of appetite, early satiety
- Genitourinary symptoms: dysuria, urgency, urinary retention, flank pain
- Neurovascular symptoms: claudication, lower extremity edema, sciatica, motor/sensory changes
Access retroperitoneal tumors through transperitoneal or thoracoabdominal surgical approaches. The transperitoneal approach consists of either an extended midline incision or a chevron incision. These approaches allow optimum access to the vascular structures in the midline and are preferred for tumors of the midabdomen or pelvis. Other surgeons, however, favor a thoracoabdominal or modified thoracoabdominal incision, especially for tumors of the upper quadrants and the flanks. These approaches allow easier access to the retroperitoneum. Access sarcomas of the lower abdomen using an abdominouinguinal incision. Debulking or partial resection is still beneficial and can improve overall quality of life. Avoid open biopsy of retroperitoneal tumors because it can lead to peritoneal implantation and sarcomatosis. CT-guided biopsy is appropriate when lymphoma or metastatic disease is suspected.

Survival is most influenced by the ability to achieve complete en bloc surgical resection of the primary retroperitoneal tumor. Current studies show complete resection rates of 40 to 60% with 5-year survival > 60% in these patients. Heslin and colleagues reported 5- and 10-year survival rates of 63% and 46%, respectively. Median survival in patients who underwent complete versus incomplete resection was 70.3 months versus 24.4 months. In addition to complete en bloc resection, survival also depends on tumor grade. Storm and Mahvi analyzed survival as a function of tumor grade and found a marked difference in survival between low-grade and high-grade tumors at 2 years (83% vs 54%), 5 years (74% vs 24%), and 10 years (41% vs 11%). Debulking is advocated when complete resection is impossible. Several small series, however, favor subtotal resection over debulking; it may prolong disease-free survival.

Although retroperitoneal sarcomas are sensitive to radiation therapy, the toxicity caused to intra-abdominal organs; namely, the small intestines, hampers the ability to deliver adequate doses for treatment. Therefore, the current role of adjuvant radiation therapy has been limited to the use of intraoperative radiation therapy (IORT), with postoperative low-dose, external-beam radiotherapy to minimize resulting small-bowel toxicity. We advocate IORT in those patients undergoing surgery who may have an incomplete surgical resection or positive margins of resection. Currently, no randomized studies support the use of adjuvant chemotherapy in primary retroperitoneal tumors, except for studies that showed success with treatment of embryonal rhabdomyosarcoma in the pediatric population. However, use doxorubicin for advanced metastatic retroperitoneal sarcoma. When compared with other chemotherapeutic agents, doxorubicin achieved the same overall response, with the lowest rate of toxicity. In this 1995 study, patients achieved a remission of 44 to 48 weeks and a median survival of 51 to 55 weeks.

Nevertheless, recommendations vary about whether patients should be followed with CT scans every 3 months for the first 1 to 2 years after having undergone complete or incomplete surgical resection of a primary retroperitoneal tumor. After this initial period, obtain CT scans yearly. Local recurrence rates are approximately 25% after resection of a primary tumor and 41% after prior resection of a local recurrence. Nearly all local and distant recurrences usually present within 5 years of follow-up. After surgical resection of local disease, the pattern of recurrence among patients with recurrences is as follows: metastases at multiple sites in 47%, isolated local recurrences in 30%, isolated lung recurrences in 17%, and recurrence at other sites in 6%. Treat an isolated pulmonary metastasis with pulmonary resection only in the absence of extrapulmonary disease as the 3-year survival rate can be as high as 30 to 40%. Repeat surgical excision is indicated in most patients with recurrence. A 1994 study by Wang and colleagues demonstrates increased survival for those patients who underwent complete resection on their second operation. In this study, 30 patients underwent reoperation at a mean interval of 23 months. Patients who successfully underwent complete resection on reoperation had a median survival of 33 months versus 14 months for those patients without complete secondary resection.

### Additional Readings


In 2002, bladder cancer will be diagnosed in 54,500 people in the United States; 12,600 will die from the disease.¹ Men have nearly three times the incidence of bladder cancer compared with women. Several factors increase the risk of bladder cancer. These include smoking, chronic bladder infections, prior treatment with cytoxan chemotherapy, chronic exposure to bladder stones, repeated chemical exposure to aniline dyes, 2-naphthylamine, xenylamine, and benzidine. Unfortunately, there is no reliable screening test for bladder cancer, although patients felt to be at high risk may undergo urine sampling for microhematuria or abnormal cytology. Smoking cessation should be advised in all tobacco users as a preventive measure.

A Transitional cell carcinoma (TCCA) is the most common histologic variant of bladder cancer, accounting for 90% of tumors. The most common symptoms at presentation are hematuria (gross or microscopic) and/or irritative voiding (urgency, frequency, and dysuria).

B History and physical examination are important in the evaluation of bladder cancer. Specifically, one should question the patient about voiding pattern, evidence of hematuria, constitutional symptoms and prior history of tobacco use, chemical exposure, chronic bladder infections, or stone disease. Physical examination should rule out adenopathy, bone tenderness, or a pelvic or rectal mass. Urine cytology, cystoscopy, and upper tract imaging (intravenous pyelography or computed tomography [CT] or magnetic resonance urography) provide further evidence of tumor location; abnormalities in any of these studies should prompt cystoscopy under anesthesia with retrograde pyelograms, bladder biopsies, and/or tumor resection. The management of upper tract abnormalities is discussed in Chapter 47, “Renal Cell Carcinoma/Oncocytoma,” and Chapter 54, “Cancer of the Renal Pelvis and Ureter.”

C Transurethral resection of bladder tumor (TURBT) should include an examination under anesthesia and sampling of the bladder muscular wall to fully assess depth of invasion. It may also be appropriate to biopsy multiple areas of mucosa to identify multifocal carcinoma in situ (CIS). Examination under anesthesia is an integral part of the evaluation of bladder cancer; the presence of induration or a mass denotes extravesical tumor extension and may alter the patient’s treatment plan. The cystoscopic summary should include three components: (1) precise description and illustration of tumor location, (2) notation of the completeness of resection, and (3) assessment of clinical stage. In the occasional case of an extensive but clearly well-differentiated papillary tumor, staged endoscopic resections may be necessary to completely remove the tumor.

D Restaging TURBT within 2 to 6 weeks is recommended in the patient with incomplete, undersampled, or uncertain resection. This is especially important in the patient with Tis, Ta, or T1 disease, as well as the patient with suspected T2 disease who is being considered for a bladder preservation treatment strategy. Up to 29% of patients thought to have superficial or early-stage disease may be upstaged, and 22% of individuals believed to have muscle-invasive disease may be downstaged, ultimately altering treatment in 33% of patients.²

E The pathologist plays a pivotal role in management decisions in bladder cancer. Clinical history indicating the appearance of the tumor or previous therapy is often very helpful in distinguishing reactive changes, treatment effect, and CIS. Invasion into the lamina propria and certainly into the muscular wall demonstrates increased potential for distant metastases; muscle invasion is rarely treated completely with TURBT and requires additional therapy for adequate local control. The classification of tumor grading has been revised several times in the past. The most recent consensus was developed to clarify and distinguish histologic features of urothelial neoplasms.³

F Clinical staging is completed with CT or magnetic resonance imaging (MRI) to assess intra-abdominal nodal and visceral sites of metastasis. The upper tracts should be evaluated with intravenous pyelogram or retrograde pyelography. Chest radiography provides initial evaluation of the thorax and mediastinum. A bone scan should be obtained if the patient complains of bone pain, has known locally advanced or metastatic disease, or an unexplained elevation in the serum alkaline phosphatase level. Pathologic staging for adenocarcinoma of the bladder has been outlined by the American Joint Committee on Cancer (Table 51-1).⁴

G Recurrence rates of superficial or early-invasive TCCA are fairly high, ranging from 50 to 70%. Adjuvant treatment strategies have thus been adopted after TURBT to reduce these rates. Intravesical chemotherapy used in conjunction with TURBT can reduce the risk of recurrence by 44 to 73% in patients with primary Ta and T1 tumors and by 38 to 65% in patients with recurrent Ta, T1, and Tis tumors when compared with TURBT alone.⁵,⁶ Intravesical immunotherapy using bacillus
Patient with SUSPECTED TRANSITIONAL CELL CARCINOMA OF THE BLADDER

A Hematuria or irritable voiding

B History
   Physical examination
   Upper tract imaging
   Urine cytology
   Cystoscopy

C Complete TURBT

D Restaging TURBT

E Pathologic evaluation

F Clinical staging

G Intravesical chemotherapy

H Radical cystectomy and urinary diversion

J Bladder preservation

K Neoadjuvant chemotherapy

L Surveillance
Table 51-1  TNM Staging System (2002)

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary tumor (T)</td>
<td>Primary tumor cannot be assessed</td>
</tr>
<tr>
<td>TX</td>
<td>No evidence of primary tumor</td>
</tr>
<tr>
<td>Ta</td>
<td>Noninvasive papillary carcinoma</td>
</tr>
<tr>
<td>Tis</td>
<td>Carcinoma in situ: “flat tumor”</td>
</tr>
<tr>
<td>T1</td>
<td>Tumor invades subepithelial connective tissue</td>
</tr>
<tr>
<td>T2</td>
<td>Tumor invades muscle</td>
</tr>
<tr>
<td>pT2a</td>
<td>Tumor invades superficial muscle (inner half)</td>
</tr>
<tr>
<td>pT2b</td>
<td>Tumor invades deep muscle (outer half)</td>
</tr>
<tr>
<td>T3</td>
<td>Tumor invades perivesical tissue</td>
</tr>
<tr>
<td>pT3a</td>
<td>Macroscopically</td>
</tr>
<tr>
<td>pT3b</td>
<td>Microscopically (extravesical mass)</td>
</tr>
<tr>
<td>T4</td>
<td>Tumor invades neighboring organs or body wall</td>
</tr>
<tr>
<td>T4a</td>
<td>Tumor invades prostate, uterus, vagina</td>
</tr>
<tr>
<td>T4b</td>
<td>Tumor invades pelvic wall, abdominal wall</td>
</tr>
</tbody>
</table>

Regional lymph nodes (N)

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>N0</td>
<td>No regional lymph node metastasis</td>
</tr>
<tr>
<td>N1</td>
<td>Metastasis in a single lymph node, 2 cm or less in greatest dimension</td>
</tr>
<tr>
<td>N2</td>
<td>Metastasis in a single lymph node, more than 2 cm but not more than 5 cm in greatest dimension; or multiple lymph nodes, none more than 5 cm in greatest dimension</td>
</tr>
<tr>
<td>N3</td>
<td>Metastasis in a lymph node, more than 5 cm in greatest dimension</td>
</tr>
</tbody>
</table>

Distant metastasis (M)

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>MX</td>
<td>Distant metastasis cannot be assessed</td>
</tr>
<tr>
<td>M0</td>
<td>No distant metastasis</td>
</tr>
<tr>
<td>M1</td>
<td>Distant metastasis</td>
</tr>
</tbody>
</table>

Calmette-Guérin (BCG) also provides a significant reduction in recurrence that is greater than 50% in this population. Despite improved rates of disease-free survival, standard induction courses of intravesical chemotherapy and immunotherapy do not improve disease-specific survival. However, when an induction course of BCG is followed by a series of maintenance doses consisting of weekly BCG given for 3 weeks at 3, 6, 12, 18, 24, 30, and 36 months after induction, disease-free and overall survival can be prolonged. In patients who fail an initial or maintenance course of intravesical therapy, it may be reasonable to try another agent; however, one must consider the risk of progression and not delay definitive treatment.

Radical cystectomy is the most effective means of cancer control of nonmetastatic high-risk TCCA of the bladder with a 10-year disease-free survival rate of 66%. The broad indication for cystectomy is a superficial, early-stage, or invasive tumor that is refractory to or unlikely to be controlled by transurethral resection and intravesical therapy. Early cystectomy may have a profound impact on survival in view of the 30 to 40% rate of clinical understaging. Effective local control in the pelvis is achieved in 93% of cases with cystectomy. Indications for partial cystectomy are limited and generally apply to isolated tumors or those within diverticulum. Classic teaching suggests that patients with CIS should not be candidates, although the use of intravesical BCG to treat CIS may have broadened this application. Alternatives to cystectomy include observation, systemic chemotherapy, radiation therapy, or a combination of chemotherapy and radiation. These modalities may be required in patients who are poor surgical risks, who refuse surgery, or who are elderly.

Urinary diversion can be accomplished using incontinent or continent abdominal stoma or orthotopic continent reconstruction. Over the last 5 years, the paradigm for choosing a urinary diversion has changed substantially. Contemporary series now suggest that an orthotopic neobladder should be the standard method of urinary diversion as opposed to the ileal conduit. The evolution of patient selection and surgical technique has led to improved outcomes for orthotopic diversion. An orthotopic neobladder provides a safe and functionally beneficial method of urinary diversion and is the preferred method in both men and women, although, under certain conditions, there are still patients who are better served with an ileal conduit. Motivated patients are considered for orthotopic neobladder diversion if they have a preoperative serum creatinine < 2.0 mg/mL, normal preoperative bowel function, a negative urethral margin based on intraoperative frozen section at the time of cystectomy, and an intact sphincter after complete tumor resection.

Bladder preservation may be feasible in selected patients. Radiotherapy is preceded by aggressive TURBT and offers an improved rate of survival when performed in conjunction with chemotherapy. Up to 42% 5-year disease-specific survival can be achieved in patients with preserved bladders, with the best overall survival outcome in younger patients with lower-stage tumors without lymphovascular or nodal involvement. Superficial or early-stage recurrence can be managed with TURBT with or without intravesical chemotherapy, but one must seriously consider salvage cystectomy.

Systemic chemotherapy for bladder cancer has improved appreciably with the development of more tolerable regimens that have similar efficacy to traditional agents. Historically, the M-VAC (methotrexate, vinblastine, Adriamycin [doxorubicin], and cisplatin) regimen was most effective and viewed as the standard of chemotherapeutic care. However, toxicity was known to be a limiting factor in delivering full-dose therapy. More recently, platinum-based strategies have been investigated in combination with the taxanes and gemcitabine as doublets or triplets. One strategy,
gemcitabine and cisplatin, has a similar efficacy to M-VAC but results in much less toxicity. Overall, multiple chemotherapy combinations exist, with most providing 20 to 35% complete responses and a median survival of 12 to 14 months. When used as a neoadjuvant to radical cystectomy, evidence suggests that M-VAC and other similar regimens may have a survival advantage when compared with radical cystectomy alone in patients with muscle-invasive disease, but this remains controversial. Neoadjuvant approaches make use of local disease as a marker and may downstage tumors prior to cystectomy, but primary therapy is potentially delayed and patients may progress while on treatment. The use of adjuvant chemotherapy following cystectomy is appealing for patients with locally advanced or node-positive disease, but the survival benefit offered is unclear. With this strategy, early removal of the primary tumor is permitted and treatment is based on pathologic staging. Unfortunately, studies with adequate patient numbers have not been accomplished, and many questions remain unanswered.

**References**

Carcinoma of the Prostate is the most frequent solid malignancy in American men and is the second leading cause of death from malignancy in that population. In the past, many patients presented with advanced disease; however, with early detection based on digital rectal examination and prostate-specific antigen (PSA), more and more patients are detected with confined disease that is amenable to curative therapy.

A Patients with carcinoma of the prostate typically present with an elevation in PSA. Most patients are asymptomatic or have minimal bladder outlet obstructive symptoms, which are likely secondary to benign prostatic hyperplasia. In patients with advanced disease, particularly bony metastases, many will present with bone pain. Fortunately, these patients are seen infrequently in the era of PSA.

B Physical examination is an essential component of the evaluation of all patients with possible prostatic disease. With malignancy, the gland may be irregular, and a hard area may be present; on the other hand, when detecting earlier tumors, based on an elevation of PSA, the gland is palpably benign in most instances. Ultrasonography is used frequently today to assess the size of the prostate but also is important in assisting in biopsy.

C PSA has proven essential in detecting early carcinoma of the prostate. The American Cancer Society recommends that all men over age 50 years have a yearly digital rectal examination and a PSA determination; however, if a patient has a predilection for carcinoma of the prostate based on family history or race, we recommend that these studies begin at age 40 years. If abnormalities are noted, further evaluation including prostate biopsy is usually carried out.

D Prostate biopsy is typically performed under ultrasound guidance. Although initially directed at the peripheral zone in a sextant manner, current evidence indicates that a greater number of biopsies should be performed, and, in most instances, 8 to 12 are obtained during a biopsy session. When cores are assessed—providing information not only on whether the patient does or does not have prostate cancer—valuable information with respect to the grade and volume of disease provide significant prognostic information.

E Approximately 10% of patients undergoing simple prostatectomy for seemingly benign disease are found to have carcinoma. If only a small amount of tissue is present, clinicians prefer repeat biopsy or resection to assess for the presence of residual disease. If residual or extensive disease is noted at the time of the initial surgery, evaluate to detect the presence of more extensive disease. Appropriate treatment based on these findings and the patient’s age and physical status is indicated.

F In patients with confirmed carcinoma of the prostate, further evaluation is indicated. Not all patients require a bone scan, but it is generally indicated for those with an initial PSA > 10 or in the presence of bilateral or high-grade (Gleason 7 or above) disease on biopsy. Similar controversy relates to lymph node dissection, which, in the past, had been routinely performed prior to definitive therapy. Studies indicate that the positivity of lymph node dissection is often below 15%, and with the use of information based on tumor volume—grade and PSA—often these can be used to predict who should and who should not have a lymph node dissection.

G Debate continues about the timing for initiating endocrine therapy in patients with defined metastatic disease. Proponents of early treatment argue that disease progression is delayed; conversely, those favoring observation and delayed treatment argue that symptoms should be treated when they occur, and one must consider the side effects and cost of endocrine therapy. Luteinizing hormone–releasing hormone antagonists and agonists and/or antiandrogens are well accepted today, but debate continues about the value of total androgen blockade versus the use of luteinizing hormone–releasing hormone alone.

H Chemotherapy is usually reserved for patients with either hormonally unresponsive disease or recurrent disease following an initially satisfactory response to hormonal therapy. New protocols (eg, vaccines) are being developed, but experience indicates that these approaches, either alone or in combination, will have an increasing role in managing patients who have failed androgen ablative therapy.

I The decision to proceed with either radical prostatectomy, radiation therapy, or observation is often based on the experience and background of the urologist and the health status of the patient. With locally extensive but nonmetastatic disease (Stage T3), some prefer radiation therapy, but others believe that surgical excision should be carried out. Radical prostatectomy is becoming increasingly preferred for localized disease, particular-
Carcinoma of the Prostate

Patient with SUSPECTED CARCINOMA OF THE PROSTATE

A History
B Physical examination
C PSA

Prostatic nodule or induration or elevation of PSA

D Prostate biopsy

Negative
Positive

Prostate biopsy

E Bone scan, lymph node dissection if indicated based on biopsy and PSA

Observation

Androgen blockade or Observation

G Metastatic disease

Androgen blockade or Observation

H Chemotherapy and other treatment protocols

I Radical prostatectomy

Radiation therapy Observation

Confined disease

Radical prostatectomy

J Radical prostatectomy

Radiation therapy Observation

Confined disease

Radical prostatectomy

Radiation therapy Observation

Additional Readings


Hellerstedt BA, Pienta KJ. The current state of hormonal therapy for prostate cancer. CA Cancer J Clin 2002;52:154–79.


Adenocarcinoma of the bladder is uncommon, representing 1 to 2% of all cancers arising in the bladder. The best known entity is adenocarcinoma of urachal origin; however, this, in fact, is probably one of the rarest lesions. These tumors are located at the dome of the bladder and involve the bladder wall beneath the normal epithelium but may also traverse the epithelium. Primary adenocarcinomas arising from the bladder mucosa (often multicentric) and secondary lesions from direct extension or metastases from other pelvic organs are much more common. Urachal cancers tend to occur in younger individuals with a mean age of 51 years, some 10 years younger than those with nonurachal adenocarcinoma or transitional cell carcinoma of the bladder.1

Adenocarcinomas may have a glandular, colloid, or signet-ring pattern. Primary lesions of the bladder arise from glandular metaplasia of transitional epithelium that has often suffered chronic irritation.1 Identification of cystitis glandularis adjacent to an adenocarcinoma generally implies origin within the bladder. Historically, there were no specific histologic features to distinguish primary bladder adenocarcinoma from secondary adenocarcinomas. Recently, an increased effort has been directed at establishing immunohistochemical profiles to accomplish this. Specific immunohistochemical stains that may offer valuable insight into differentiating primary bladder and secondary colon adenocarcinomas include B-catenin (important in colorectal tumorigenesis), cytokeratins 20 and 7 (CK-20, CK-7), thrombomodulin (TM), and carcinoembryonic antigen (CEA).2 Endoscopically, a tumor at the vesical neck, trigone, or prostate can be a primary adenocarcinoma of the bladder invading the prostate or a prostatic carcinoma extending into the base of the bladder. Prostatic acid phosphatase and prostate-specific antigen (PSA) immunohistochemical stains can help in this circumstance. In women, a tumor involving the bladder floor may relate to direct extension of a uterine, cervical, or vaginal tumor. Bimanual examination is necessary and offers great insight into the tumor origin. Use of immunohistochemical markers such as vimentin and OC125 may help to distinguish endometrial and cervical/ovarian cancers, respectively.3

Typical signs and symptoms of localized or regional tumors are similar to those of any carcinoma of the bladder, with irritative voiding, gross or microhematuria, and ureteral or urethral obstruction in cases of bulky tumor volume. Increased mucus within the urine may be an added sign. Risk factors include chronic bladder irritation and obstruction. In children, a history of bladder extrophy offers increased risk; adenocarcinoma is the most common type of bladder cancer associated with that congenital malformation.

A The diagnosis of adenocarcinoma of the bladder rests heavily with the pathologic interpretation. Transurethral resection of the tumor will confirm histology, provide clinical staging, and offer some detail about tumor differentiation. Clinical staging is completed with computed tomography (CT) or magnetic resonance imaging (MRI) to assess intra-abdominal nodal and visceral sites of metastasis. Evaluate the upper tracts with intravenous pyelogram or retrograde pyelography. Chest radiography provides initial evaluation of the thorax and mediastinum. The clinician should obtain a bone scan if the patient complains of bone pain or has known locally advanced or metastatic disease or an unexplained elevation in the serum alkaline phosphatase level. Pathologic staging for adenocarcinoma of the bladder has been outlined by the American Joint Committee on Cancer and is the same for transitional cell carcinoma (see Chapter 51, “Transitional Cell Carcinoma of the Bladder”).4 Because this staging method is difficult to apply to urachal cancers, a separate system was devised in 1984 (Table 53-1).5 A uniform grading system has not been adopted.1

Table 53-1  Staging System for Urachal Carcinoma

<table>
<thead>
<tr>
<th>Stage</th>
<th>Tumor Extent</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Confined to the urachal mucosa</td>
</tr>
<tr>
<td>II</td>
<td>Invasion confined to the urachus</td>
</tr>
<tr>
<td>III</td>
<td>Local extension</td>
</tr>
<tr>
<td>IIIA</td>
<td>Bladder</td>
</tr>
<tr>
<td>IIIB</td>
<td>Abdominal wall</td>
</tr>
<tr>
<td>IIIC</td>
<td>Peritoneum</td>
</tr>
<tr>
<td>IIID</td>
<td>Viscera other than the bladder</td>
</tr>
<tr>
<td>IV</td>
<td>Metastatic spread</td>
</tr>
<tr>
<td>IVA</td>
<td>Regional lymph nodes</td>
</tr>
<tr>
<td>IVB</td>
<td>Distant sites</td>
</tr>
</tbody>
</table>

Adapted from Sheldon CA et al.7
Patient with ADENOCARCINOMA OF THE BLADDER

Biopsy of bladder showing adenocarcinoma

A

Review panel of special stains with pathologist
Prostatic acid phosphates
Prostate-specific antigen
CEA
CK-7/CK-20
Vimentin

CT scan of the abdomen and pelvis
plus
Intravenous pyelogram or retrograde pyelograms
or
CT scan or magnetic resonance urogram

B Metastatic carcinoma

Upper gastrointestinal series
Gastrointestinal endoscopy
Full gynecologic examination
Abdominal/pelvic CT scan

Treat primary tumor
Palliative bladder therapy

C Pelvic cancer with local extension

Proctoscopy
Barium enema
Pelvic examination
Dilatation and curettage

Treat primary tumor
Palliative bladder therapy vs pelvic exenteration

D Primary bladder cancer

Urachal cancer
Other site in bladder

Radical cystectomy

Partial cystectomy
Excision of urachus and umbilicus
or
Radical cystectomy
A diagnosis of adenocarcinoma necessitates consideration of metastatic disease. These lesions are uncommon but are well described. The history frequently reveals a previous adenocarcinoma, generally of the rectum, stomach, endometrium, breast, prostate, or ovary. Other sites of metastases, such as lung, bone, and lymph nodes, are usually evident at the time of clinical staging. Patients should be evaluated for other primary sites before definitive treatment of the bladder is undertaken.

A large pelvic mass can involve the bladder, uterus, ovaries, or lower gastrointestinal tract, and it may be impossible to determine the site of origin, particularly with undifferentiated lesions. Areas of transitional cell carcinoma (invasive or in situ) associated with adenocarcinoma suggest a bladder origin. Consultations with a gynecologic oncologist and colon and rectal surgeon are often needed. Clinical staging may reveal disease localized to the pelvis. In patients with a good performance status, pelvic exenteration may offer palliation, local control, and cure in a subgroup of patients.

Primary adenocarcinoma of the bladder has an overall poor prognosis, with most studies demonstrating a 5-year survival of 20 to 40% irrespective of treatment. The survival rates are influenced by the fact that most patients present at an advanced stage of disease with poorly differentiated lesions. Almost all lesions are invasive into the bladder wall, and transurethral resection alone is rarely adequate. Lymphatic extension into the retroperitoneum is also common. Local control is possible with a partial cystectomy with en bloc excision of the urachal mass and umbilicus for urachal lesions and occasionally for other isolated adenocarcinomas. Rationale for this strategy is provided by long-term disease-free survival in carefully selected patients with low-volume disease. Careful sampling of the mucosa away from the visible lesion is necessary, or relapse rates may be as high as 38 to 50%.

Other cases of urachal carcinoma may require radical cystectomy because of tumor extent. Treatment of urachal cancers offers an overall 44% 2-year survival, 37% 5-year survival, and 17% 10-year survival. Five-year survival rates after partial cystectomy may be >50% when applied to early-stage patients. Radical cystectomy should be done in most nonurachal adenocarcinoma cases if feasible. This treatment strategy provides 5- and 10-year survival rates for nonurachal cancer of 17 to 55% and 10%, respectively. Historically, adjuvant chemotherapy or external radiation therapy has not altered survival significantly.
References


Cancer of the Renal Pelvis and Ureter
Cheryl T. Lee, MD, and James E. Montie, MD

In 2002, transitional cell carcinoma (TCCA) of the upper urinary tract continues to pose challenges for cancer detection and treatment. The disease is relatively uncommon, with approximately 3,000 cases diagnosed in the United States per year, accounting for 5% of urothelial malignancies and 10% of renal tumors.1,2 Like cancers of the lower urinary tract, men have a higher incidence than do women. The urothelium of the upper urinary tract is subject to the same risk factors as the bladder and urethra, namely tobacco use, chronic inflammation (pyelonephritis or certain nephropathies), chronic exposure to upper tract stones, and repeated chemical exposure to aniline dyes, 2-naphthylamine, xenylamine, and benzidine. An added risk is also evident in patients with a history of bladder cancer; 2 to 4% of these patients develop upper tract TCCA.1 Smoking cessation should be advised in all tobacco users as a preventive measure.

The management of upper tract TCCA has been redefined in the past decade because of technologic advances that have revolutionized the evaluation of upper tract filling defects and the diagnosis and treatment of upper tract tumors, particularly smaller, low-stage lesions.

A The most common presenting signs and symptoms of upper tract tumor are hematuria (gross or microscopic), a filling defect on imaging with or without associated hydronephrosis, and back pain. An upper tract filling defect may be tumor, blood clot, renal calculus, a fungus ball, or sloughed papilla. Chapter 8, “Radiolucent Filling Defects,” describes the appropriate diagnostic algorithm.

B History and physical examination continue to be important in the evaluation for upper tract tumor. The patient must be questioned about evidence of hematuria, chronic pyelonephritis, upper tract stone disease, constitutional symptoms, prior history of tobacco use, and chemical exposures. Physical examination should rule out adenopathy or bone tenderness. Urine cytology and upper tract imaging (intravenous pyelography or computed tomography [CT] or magnetic resonance [MR] urography) provide further evidence of tumor location. Repeat imaging may be required to determine whether a filling defect has become dislodged (generally excluding tumor at that site) or whether radiographic characteristics suggesting tumor (goblet sign on intravenous pyelogram [IVP]) exist. When cancer is detected, TCCA is the most common histologic variant.

C Abnormalities in any of the above studies should prompt retrograde pyelography and ureteroscopic evaluation with ureteral washings and biopsy of suspicious areas. The endoscopic evaluation may provide valuable clarification of tumor histology, grade, and potentially stage; however, ureteroscopic biopsy can be hampered by small fragments that leave one relying on their visual inspection. Thus, a ureteroscopic summary is very important and should include (1) precise description and illustration of the tumor appearance, size, and apparent depth of invasion; (2) evidence of tumor location(s); (3) notation of the completeness of biopsy and/or fulguration; and (4) assessment of clinical stage. The bladder must also be evaluated carefully as patients with upper tract tumor have a 30 to 50% risk of developing lower tract disease.3

D When the diagnosis of TCCA is well established, it is critical to consider multiple tumor and patient factors when making a treatment decision. Tumor size, grade, stage, and location all guide treatment strategy, but tumor stage remains the most important prognostic factor for recurrence and disease-specific survival.2 Tumor staging for the renal pelvis and ureter has been outlined by the American Joint Committee on Cancer (Table 54-1).4 Apart from stage, one must also weigh the value of renal preservation against the reality of tumor threat. Traditionally, organ preservation was entertained if a patient had a solitary functioning kidney, multifocal urothelial tumors, or an abnormal or threatened contralateral kidney. This remains standard practice, particularly in view of the significant mortality of dialysis, with a 5-year survival rate of 19% in patients between age 65 and 74 years.5 However, modern endoscopic strategies have allowed a wider application of conservative treatment options.

E Endoscopic treatment of low-grade, noninvasive renal pelvic and ureteral tumors is now possible with improved instrumentation in ureteroscopy and enhanced experience with percutaneous techniques. Retrograde ureteroscopic tumor removal can be accomplished using rigid, semirigid, or flexible instrumentation. The technique used may be dictated by the tumor size, location, and the patient’s anatomy. Rigid systems will be more effective at managing larger tumor, although these instruments are often unable to access upper ureteral lesions. Electrocautery and the holmium and neodymium YAG lasers have all been used successfully for tumor ablation. Small working endoscopic channels with decreased irrigant flow can compromise the visual field, however, and can limit the therapeutic applications. Percutaneous management, a better approach to selected renal pelvic tumors, has the benefit of larger working channels that can accommodate resections and
Patient with CANCER OF THE RENAL PELVIS AND URETER

A. Hematuria or filling defect on imaging
   - Urine cytology
   - Cystoscopy
   - IVP/CT or MR urography

B. Diagnostic
   - Abnormal findings
   - Retrograde pyelography
   - Ureteroscopy with/without washings and biopsy

C. TCCa of the upper tract

D. E F. Clinical Ta/Tis
   - Biopsy/fulguration/resection
     - Low-grade Ta
     - High-grade Ta/Tis
       - BCG
         - Surveillance
           - No disease
           - Treatment failure
             - Surveillance
               - Low-volume
                 - Low-grade Ta
                 - High-volume Ta
                   - High-grade Ta/Tis

G. > Clinical T1
   - Clinical staging
     - T1/T2 with/without T3
     - T3/T4/N+/M+
       - Segmental ureterectomy vs ureterectomy and ileal interposition
         - Chemotherapy
           - Restaging
             - If downstaged
               - Surveillance
                 - No disease
                 - Treatment failure
                   - Nephroureterectomy
Table 54-1 TNM Staging System for the Renal Pelvis and Ureter (2002)

<table>
<thead>
<tr>
<th>Primary tumor (T)</th>
<th>Distant metastasis (M)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TX</td>
<td>M1 Distant metastasis</td>
</tr>
<tr>
<td>T0</td>
<td>M0 No distant metastasis</td>
</tr>
<tr>
<td>Ta</td>
<td>N1 Metastasis in a single lymph node, 2 cm or less in greatest dimension</td>
</tr>
<tr>
<td>Tis</td>
<td>N2 Metastasis in a single lymph node, more than 2 cm but not more than 5 cm in the greatest dimension; or multiple lymph nodes, none more than 5 cm in greatest dimension</td>
</tr>
<tr>
<td>T1</td>
<td>N3 Metastasis in a lymph node, more than 5 cm in greatest dimension</td>
</tr>
<tr>
<td>T2</td>
<td>NX Regional lymph nodes cannot be assessed</td>
</tr>
<tr>
<td>T3</td>
<td>M1 Distant metastasis</td>
</tr>
<tr>
<td>T4</td>
<td>M0 No distant metastasis</td>
</tr>
</tbody>
</table>

*Laterality does not affect the N classification.

---

cautery instruments that urologists are accustomed to, permitting more complete biopsy, fulguration, and staging at a single session. However, percutaneous management has the potential risk of extravasation and spillage of cancer cells outside the kidney when obtaining renal access and dilating the nephrostomy tract.

Tumor recurrence remains the most serious consequence of conservative treatments. With any conservative approach, one must ensure that a salvage therapy is available for failures. When monitored closely, most patients are still candidates for open resection if they fail endoscopic approaches. Recurrence rates of renal pelvic and ureteral tumors treated with ureteroscopy are 33 to 35% and 31 to 32%, respectively. Tumor grade and size do impact recurrence, with a rate of 26% for grade I, 44% for grade II, and 25% for lesions < 1.5 cm compared with 50% for tumors > 1.5 cm.1,6 Using a percutaneous approach, an overall 22 to 44% recurrence rate has been observed, which also correlates with tumor grade.6 Percutaneous treatment of low-grade disease is particularly justified with a recurrence rate of 0 to 27% and no associated progression or metastasis.6 A reasonable initial approach to the small (< 1.5 cm) low-grade ureteral or renal pelvic tumor would be ureteroscopic ablation. Multiple or large low-grade renal pelvic tumors in the patient who is a poor candidate for nephroureterectomy would likely benefit from initial percutaneous management.

---

**C** Carcinoma in situ (CIS) presents a much greater treatment challenge than low-grade superficial disease, in part because of its often multifocal nature. This is reflected in the higher recurrence and progression rates of high-grade superficial disease treated endoscopically or percutaneously.6 Adjuvant strategies have been employed to retard endoscopic treatment failure and preserve organ function. Upper tract immunotherapy and chemotherapy have been applied and present some logistical problems relative to delivering adequate drug dosage whether by antegrade or retrograde techniques. There is limited experience with all agents, with only few reports describing the use of bacillus Calmette-Guérin (BCG), thiotepa, and mitomycin C; the efficacy of these agents remains unclear. Adjuvant upper tract BCG may have some benefit, with reports of a decrease in the recurrence rate of grade I tumors from 50% to 14% and in grade II and III tumors from 50 to 23%, although this benefit has not been observed in other studies.1,6 Although BCG delivery can be cumbersome, a recent study of 41 renal units treated in 37 patients with Ta or Tis disease has demonstrated that percutaneous BCG can be delivered without seeding the nephrostomy tract and without undue morbidity; acceptable 3% and 5% rates of BCG inflammation and septicemia were observed, respectively.7 The median recurrence-free and progression-free survival was 21 and 34 months at 42 months of follow-up.

**D** If invasive tumor is suspected at the time of biopsy, the full extent of disease must be assessed. Clinical staging is completed with CT or magnetic resonance imaging (MRI) to assess intra-abdominal nodal and visceral sites of metastasis. Chest radiography provides initial evaluation of the thorax and mediastinum. A bone scan should be obtained if the patient complains of bone pain or has known locally advanced or metastatic disease or an unexplained elevation in the serum alkaline phosphatase level. The authors do not recommend elective endoscopic or percutaneous management of T1 disease in the patient with a normal contralateral kidney in view of the 20 to 55% progression rate of grade II and III tumors.6

**E** Nephroureterectomy with bladder cuff excision continues to be the standard treatment for organ-confined invasive upper tract TCCA, particularly in the mid- to upper ureter and renal pelvis. Other conservative open approaches include partial nephrectomy, pyelotomy with tumor excision, distal or segmental ureterectomy, and ureterotomy with tumor excision, all considered in the presence of a solitary kidney, diminished renal function, or bilateral disease. The temptation of segmental ureterectomy for midureteral lesions should be avoided in the patient without renal compromise in view of the 30% recurrence rate within the ureter distal to the initial lesion.8 The major concern after conservative procedures is tumor spillage and local recurrence, which can approach 62% for open renal pelvic procedures and 15% for ureteral procedures.5 Excision of the entire ureter with a small cuff of bladder...
The success of systemic chemotherapy for upper tract disease has paralleled those agents used for bladder cancer. Cisplatin-based regimens have demonstrated activity against metastatic upper tract urothelial cancer with combined complete and partial response rates of 54%, slightly less than rates seen for TCCA of the bladder.

The proximal margin of the ureter must be examined intraoperatively. Using this approach in the patient with high-grade and invasive disease must be done with caution as a significant number of these patients will die of recurrent disease. Staging ipsilateral pelvic lymphadenectomy is generally performed in association with distal ureterectomy. Regional hilar lymphadenectomy does not generally improve survival and is not a standard part of nephroureterectomy; however, resection of grossly enlarged nodes discovered at exploration is encouraged to confirm staging and prompt adjuvant chemotherapeutic treatment.

Recurrence after primary open surgery occurs in 27% of patients at a median of 12 months. As is expected, advancing stage correlates with worse 5-year disease-free survival (DFS), with Ta/CIS having 73%, T1 76%, T2 59%, T3 40% and T4 0%; T4 patients have a 30% 2-year DFS. Stage has a similar impact on disease-specific survival (DSS), with 5-year rates of 100% for Ta/CIS, 92% for T1, 73% for T2, 41% for T3, and 0% for T4. Median DSS for T4 patients is 6 months.

Advances in video imaging and fiberoptic technology have allowed the standard management of upper tract tumors to shift from open surgery to minimally invasive surgery. Increasing experience over the past decade suggests several benefits of laparoscopic nephroureterectomy over traditional open nephroureterectomy. Laparoscopic nephroureterectomy has been shown to offer less time to recovery with shorter hospital stay and shorter requirement of pain medication while having rates of recurrence, local control, and disease-specific survival comparable to those for open nephroureterectomy. Thus, in many instances, the laparoscopic approach is the treatment of choice.

The most responsive metastatic sites are lung and lymph nodes. Unfortunately, long-term responses are uncommon, and the estimated median duration of survival is 14 months. A selected group of patients may be clinically downstaged and become eligible for radical surgical intervention. Adjuvant postoperative radiotherapy has little impact on survival and is not used routinely.

As in the bladder, periodic surveillance is critical after treatment of upper tract TCCA. Any patient treated endoscopically or percutaneously must be prepared to commit to rigorous surveillance with periodic ureteroscopy as well as periodic imaging (IVP or CT or MR urography). Flexible ureteroscopy is recommended every 3 months for the first year and every 6 months thereafter. Ureteroscopy is more sensitive in detecting recurrence than is imaging and should be the primary surveillance tool. This will allow for the early detection of recurrent disease and the application of salvage therapies. After nephroureterectomy, abdominal imaging such as CT urography is optimal at surveying the contralateral kidney and ureter as well as the ipsilateral renal bed. Studies should be obtained at least annually, depending on tumor stage. Chest radiographs should be obtained biannually. A bone scan is obtained in the individual with bone pain or unexplained fracture. The lower urinary tract should be screened with flexible cystoscopy and urine cytology every 3 months for the first 2 years, every 6 months for the next 3 years, and then annually if no recurrence is observed.

References
Rhabdomyosarcoma (RMS) involves the genitourinary system in 20% of cases. There is a bimodal age distribution with peaks in children < 2 years of age and then again in teenagers. Pathologically, embryonal RMS represents the most common histologic variant, with bladder demonstrating the botryoid subtype and prostate demonstrating the solid form. The survival rate in lower urinary tract RMS (bladder and prostate) is not as good as that of other genitourinary sites (vagina, uterus, paratestis).1–3

A Consider RMS of the lower urinary tract in children with symptoms of voiding dysfunction and urinary tract obstruction, such as frequency, stranguria, and urinary retention with or without hematuria and/or passage of tissue. A mass is often palpable clinically representing tumor and/or the distended bladder.

B Perform appropriate imaging. Magnetic resonance imaging (MRI) and computed tomography (CT) scanning provide excellent detail of the abdomen and pelvis. Filling defects may be evident in bladder RMS, and elevation of the bladder neck may be noted in prostatic lesions. It is often difficult, however, to delineate the tissue of origin. Obstruction may lead to hydronephrosis. CT scanning has the advantage of depicting the retroperitoneal lymph nodes, and concurrent evaluation of the lungs can also be performed in lieu of a chest radiograph. A bone scan is usually performed as well, after the diagnosis has been ascertained.4

C Diagnosis is confirmed by cystoscopy and by obtaining multiple representative biopsies during examination under anesthesia. Bone marrow aspiration and/or biopsy along with placement of a long-term indwelling line for chemotherapy are done at the same time. Based on endoscopy, biopsy, and examination under anesthesia, the tumor, grader, node, metastasis (TGNM) system is now used to establish the disease stage (Table 55-1).5

D Initial therapy has become less aggressive surgically with hopes of organ preservation (bladder). Variations of the VAC/VA-based chemotherapy protocol have become the mainstay of therapy (vincristine, dactinomycin, cyclophosphamide). High-risk and recurrent-disease patients may require additional chemotherapy regimens, including platinum, etoposide, melphalan, and/or ifosfamide. Partial cystectomy may be considered initially for bladder dome involvement or disease localized to the supratrigonal area but more often is performed after chemotherapy. Radiation therapy is not initially instituted except for high-risk or extensive disease.6

Table 55-1 Intergroup Rhabdomyosarcoma TGNM Staging System

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Favorable site; nonmetastatic</td>
</tr>
<tr>
<td>2</td>
<td>Unfavorable, small; nonmetastatic with negative nodes</td>
</tr>
<tr>
<td>3</td>
<td>Unfavorable, big or positive nodes; nonmetastatic</td>
</tr>
<tr>
<td>4</td>
<td>Any site with metastases</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>TGNM System</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumor (T)</td>
<td>T&lt;sub&gt;site&lt;/sub&gt;-Confined to site of origin</td>
</tr>
<tr>
<td></td>
<td>T&lt;sub&gt;site&lt;/sub&gt;—Fixation to surrounding tissues ≤ 5 cm</td>
</tr>
<tr>
<td></td>
<td>T&lt;sub&gt;site&lt;/sub&gt;—Fixation to surrounding tissues &gt; 5 cm</td>
</tr>
<tr>
<td>Histology (G)</td>
<td>G&lt;sub&gt;1&lt;/sub&gt;-Favorable histology (botryoid, embryonal, spindle cell)</td>
</tr>
<tr>
<td></td>
<td>G&lt;sub&gt;2&lt;/sub&gt;-Unfavorable histology (alveolar, undifferentiated)</td>
</tr>
<tr>
<td>Regional lymph nodes (N)</td>
<td>N&lt;sub&gt;0&lt;/sub&gt;-Regional nodes not clinically involved</td>
</tr>
<tr>
<td></td>
<td>N&lt;sub&gt;1&lt;/sub&gt;-Regional nodes clinically involved</td>
</tr>
<tr>
<td>Metastases (M)</td>
<td>M&lt;sub&gt;0&lt;/sub&gt;-No distant metastases</td>
</tr>
<tr>
<td></td>
<td>M&lt;sub&gt;1&lt;/sub&gt;-Metastases present</td>
</tr>
</tbody>
</table>

E Poor response to chemotherapy may necessitate partial bladder resection or total cystectomy. Isolated prostatic RMS often will lead to prostatectomy and even cystoprostatectomy. Local recurrences rarely lead to total exenteration. Radiation therapy may be employed earlier in the course of therapy in poorer prognostic sites, such as the prostate and infratrigonal areas.7–9

F Good response radiologically is confirmed on second-look (and often multiple-look) surgeries and biopsies. The isolated finding of maturing rhabdomyoblasts on biopsy does not suggest ongoing disease or the need for more aggressive therapy.10

References
Patient with RHABDOMYOSARCOMA OF THE LOWER URINARY TRACT

A. History and physical examination
   Symptoms of urinary tract obstruction or voiding dysfunction

B. Imaging: CT/MRI
   Pelvis/abdomen
   CT (radiography) chest

C. Examination under anesthesia (EUA)
   Endoscopy with biopsy

D. Institute chemotherapy (with/without radiation therapy)

E. Radical surgery
   Rescue chemotherapy with/without radiation therapy (controversial)

F. Multiple second looks with biopsy and imaging

Benign prostatic hyperplasia (BPH) is a common disorder that affects most men over age 60 years. Although not all patients have symptoms of bladder outlet obstruction secondary to the disorder, histologic changes of prostatic enlargement are evident in the overwhelming majority of men. The cause of the disorder is unknown but is believed to relate to a hormonal imbalance that occurs in the aging man. Patients usually present with symptoms of bladder outlet obstruction—weakness of the urinary stream and hesitancy or irritable symptoms, including nocturia, frequency, and urgency. Recurrent urinary tract infections can also be secondary to the presence of residual urine and poor bladder emptying.

A The symptoms associated with BPH are, in many respects, similar to the symptoms of patients presenting with carcinoma of the prostate. The two disorders are often associated, thus making it impossible to differentiate between them based on manner of presentation or symptoms alone.

B The physical examination is essential in evaluating these patients, but it should be emphasized that the degree of symptoms does not seem to necessarily relate to the actual size of the prostate. Patients with severe symptoms and findings of bladder outlet obstruction may have small glands; other patients with large glands are able to compensate well. The prostate gland should be symmetric and smooth, and the median sulcus and lateral margins should be distinct. To help in assessing the patient, the International Prostate Symptoms Score (IPSS) tends to provide quantitative data on subjective symptoms. Patients’ responses to these questions often provide a valuable tool that helps guide further therapy.

C If a patient has a prostatic nodule or an elevation in prostate-specific antigen (PSA) at the time of evaluation, perform a prostate biopsy. If a biopsy is positive, evaluate the patient further for extent of carcinoma of the prostate. Evaluate and assess those with negative biopsies in a similar manner, as symptomatic patients who present with obstructive or irritative symptoms.

D Although urinalysis should be performed during the assessment of patients who present with bladder outlet obstructive symptoms to determine the presence of hematuria and infection, imaging of the upper tract is not as necessary. Clinicians recommend serum creatinine levels to ensure that renal impairment does not occur. The debate remains about whether there is a need for routine, postvoid residual urine determination. Imaging studies that had been performed in the past, as well as cystoscopic examination, are unnecessary when evaluating patients unless the patient experiences some other related problems, such as gross hematuria.

E Patients have several options following an initial evaluation. Observation alone can be carried out. If the patient is having minimal to mild symptoms and understands the availability of treatment, observation is a reasonable option. Notably, in a group of patients observed, one-third may worsen, one-third may improve, and one-third may note some improvement in their symptomatology with time.

F Various medical therapies are available to patients with benign prostatic hyperplasia, but they primarily fall into two categories: endocrine therapy and alpha-blockade. Endocrine therapy interferes with the conversion of testosterone to dihydrotestosterone, and with treatment, approximately 30% of gland volume will be reduced over a 6-day period, with continued improvement in urinary symptoms. If treatment is withdrawn, gland growth will occur.

Alpha-blockade, which benefits symptomatic patients, often tends to be more dramatic, with a shorter onset of action than endocrine therapy. Approximately 60 to 70% of patients have a positive response; however, side effects such as dry mouth and hypotension may occur.

G Many interventional therapies exist. Transurethral resection of the prostate (TURP) is the oldest, but various other surgical procedures have been introduced. These include transurethral incision of prostate (TUIMP), microwave therapy, laser prostatectomy, high-intensity focus ultrasonography (HIFU), and heated water. Many of these techniques continue to evolve, and experiences continue to increase, thus determining not only the short-term responses but their durability as well.

Additional Readings
Patient with SUSPECTED BENIGN PROSTATIC HYPERPLASIA

A History
B Physical examination
   IPSS Symptom Score
C Prostate nodule or induration or elevated PSA
   Prostate biopsy
   Positive
   Negative
   Evaluation and therapy
   Follow periodically
D Diffuse enlargement
   Benign prostatic hyperplasia
   Urinalysis, Serum creatinine
E Observation
F Medical therapy
   Alpha-blockers
   Hormonal agents
G Intervention
   TURP
   TUIP
   Transurethral microwave therapy
   Transurethral needle ablation
   LASER
   HIFU
   Heated water

**Benign Prostatic Hyperplasia**


A Approximately 50% of patients with urethral cancer have a history of previous sexually transmitted disease, urethral stricture, and urinary obstructive and irritative symptoms. Approximately 40% of patients describe the sensation of a mass in the perineum, about 30% percent have fistula formation, and 25% have periurethral abscess. These represent the later stages of urethral cancer. Symptoms appear to vary with the site of origin of the particular tumor. Those arising in the urethral meatus and fossa navicularis produce local discomfort, painless hematuria, a burning or itching sensation, urinary frequency, and a pink or yellowish discharge that occurs either spontaneously or following coitus. Often, tumors arising in the pendulous urethra are associated with a decreased force of stream. When the proximal or bulbomembranous urethra is involved, the patient usually describes obstructive and irritative symptoms. Because these tumors have often progressed by the time they are diagnosed, a palpable induration may be present on rectal examination.

B Aspirated cytologies may establish the diagnosis of malignancy. The sine qua non for diagnosis, however, is adequate biopsy. The surface of a particular lesion may disclose only inflammation or scar tissue; thus, repeated and deep biopsy is often necessary to establish or confirm the diagnosis of urethral cancer.

C Magnetic resonance imaging (MRI) has been shown to be more effective than computed tomography (CT) in determining depth of invasion of urethral and penile cancers. The tunica albuginea has low signal intensity and can be distinguished from the spongiosum. MRI and CT both detect lymphadenopathy.

D Although radiation alone has few reports of success in superficial tumors of the distal urethra, several recent case reports combining 5-fluorouracil, mitomycin, and external beam radiation to the primary site and to both inguinal and deep pelvic nodes before surgery have shown disease-free survival at 5 years. However, there have been no randomized trials that compare chemoradiation alone against surgery and adjuvant therapy.

E Distal lesions that have not extended may require partial penectomy for adequate local excision. More proximal lesions may need radical penectomy with perineal urethrostomy for adequate local excision. In the absence of clinically detectable lymph node metastases, the prognosis for a 5-year survival of distal lesions is at least 50%. Conversely, posterior urethral cancers have a 10 to 26% 5-year survival, which reflects the progression of these cancers before detection and resultant inadequate efficacy of treatment.

F, G The lymphatic drainage of the penis consists of a cutaneous pathway in which the lymphatics drain into the superficial inguinal and subinguinal nodes, and a deep pathway in which the glans, corpus cavernosum, and corpus spongiosum drain into the deep inguinal nodes and then into the external iliac nodes. Lymphatic drainage of the penile urethra generally accompanies that of the glans penis. Drainage of the bulb, membranous, and prostatic urethra occurs along the dorsal vein of the penis to the external iliac nodes, along the pudendal artery to the obturator and internal iliac nodes, and ultimately to the presacral nodes. Urethral cancer differs from cancer of the penis in that clinically enlarged inguinal nodes generally imply metastatic disease rather than simple benign inflammation. Generally, when the presence of palpable lymph nodes has led to a therapeutic lymph node dissection, more diffuse regional extension of disease is encountered, with resultant bleak prognosis.

Additional Readings
Patient with URETHRAL DISCHARGE, HEMORRHAGIC SPOTTING, SYMPTOMS OF OBSTRUCTION

A History
Physical examination

Retrograde urethrography

Stricture

B Cystoscopy/biopsy

C Imaging (MRI)

D (Experimental) Chemoradiation, rebiopsy, reimage

E Tumor in glandular penis

F Tumor in pendulous urethra

G Tumor in proximal or bulbar urethra

Transurethral resection superficial lesion

Partial penectomy/inguinal lymphadenectomy

En bloc dissection of perineum, bilateral deep groin nodes

Partial/radical penectomy, perineal urethrostomy, inguinal lymphadenectomy
A The diagnosis of urethral cancer in the female is based primarily on a high index of suspicion in any patient who complains of persistent dysuria, perineal pain, or dyspareunia, especially in the context of negative urine culture, prior frequent instrumentation, or urethral diverticulum. Urethral bleeding is present in 60 to 75% of patients with urethral carcinoma, dysuria in about 33%, and urinary frequency and perineal pain in 25%. Urinary frequency, palpable mass, and new onset of incontinence are seen in only about 5% of these patients. Urethral carcinoma shows a 4:1 predilection for women over men.

B Although squamous cell carcinoma is the most common urethral neoplasm in females (70%), adenocarcinoma (13%) is the most common form of cancer that forms in a urethral diverticulum. This may reflect the common association of a urethral diverticulum with the periurethral glands and chronic irritation at this site. Transitional cell carcinoma contributes to another 15% of female urethral carcinoma.

C In early stages, urethral cancers in the female may resemble urethral caruncles. However, carcinoma more commonly involves the dorsal portion of the urethra, whereas a urethral caruncle more often involves the ventral portion, which is not a preneoplastic lesion.

D In later stages, urethral cancers may spread along the urethra or to the labia and vulva. Lymphatic spread may also occur—the lymphatics from the distal urethra drain into the inguinal nodes. Palpable inguinal nodes usually suggest metastatic carcinoma. Magnetic resonance imaging (MRI) of the pelvis may show whether or not tissue extension and/or nodal spread have occurred.

E Extensive ulceration and tissue necrosis, with fistulization and extension along and through tissue planes, may accompany proximal urethral cancers. These tumors may drain into pelvic lymph nodes, specifically, the external iliac, obturator, and presacral nodes.

F Up to two-thirds of the distal urethra in the female may be removed without seriously compromising urinary continence. The surgeon may consider partial vulvectomy in attempting to obtain clear surgical margins. In all but the earliest tumors, prognosis for tumors in the proximal urethra is generally poor. Despite surgery, 5-year survival rates range between 10 and 20%, in comparison with distal urethral cancer survival rates, which range from 40 to 50%. Radiation alone, whether by external beam or by radium implants, has not demonstrated a survival advantage over surgery. Moreover, the radiation doses necessary for control of advanced tumors cause great morbidity. The perivulvar tissue may not tolerate the high dose of radiation required for effective treatment. A number of case reports of chemoradiation, as an adjunct to or instead of surgery, have been reported in the last few years, combining 5-fluorouracil and mitomycin. The chemotherapy acts as a radiosensitizer and may interfere with cellular repair processes after a sublethal dose of radiation. However, there have been an insufficient number of cases or long-term follow-up to recommend this treatment at this time in place of traditional surgical extirpation.

Additional Readings
Patient with DYSURIA/HEMORRHAGIC SPOTTING (No hematuria)

A. History, physical examination

Cystoscopy
Retrograde cystourethrogram

Mass and/or diverticulum

Aspiration cytology
Transurethral biopsy
MRI of pelvis

B

Tumor in distal two-thirds of urethra

D. Transurethral resection of “early lesion”

Excision of distal urethra with partial vulvectomy (in “late” lesions to obtain clear margins) with or without chemoradiation

E. Cystourethrectomy
Partial or total pelvic exenteration
Experimental: chemoradiation

F

Tumor in proximal urethra

C

Experimental: chemoradiation
Carcinoma of the penis is a rare disease (1/1 × 10^5 Americans), which infrequently, if ever, afflicts men who are circumcised at birth. The histology is squamous cell, and the tissue of origin is the penile skin, in general, and the prepuce, in particular. Etiology relates to the neoplastic properties of smegma and the association of human papillomavirus with verrucous (Buschke-Löwenstein) penile carcinoma. Delayed presentation is not uncommon with the mean delay in diagnosis of 8 months. The most common site of tumor development is the glans penis, followed by the prepuce, and, most rarely, the penile shaft. Penile cancer grows locally with a propensity for corporal or urethral invasion. Lymphatics from the prepuce drain via the dorsal lymphatics that decussate at the base of the penis and drain to the superficial and deep inguinal lymphatics. The lymphatics of the glans, corpora, and urethra drain to the deep inguinal and external iliac nodes.

Treatment and prognosis are based on the depth of invasion assessed on biopsy. Table 59-1 illustrates the tumor, node, metastasis (TNM) staging of penile carcinoma. Depth of invasion, vascular invasion, grade, and p53 status appear most predictive of progression. Superficial lesions confined to the epithelium carcinoma in situ (CIS) can be managed with circumcision and topical 5-fluorouracil, imiquimod (5%) creams, or neodymium:YAG or CO₂ laser therapy. Invasive lesions have traditionally been managed by partial or total penectomy; however, penile sparing alternatives, including radiotherapy and Mohs’ surgery, have been advocated. No conclusive evidence exists to support one treatment over another.

Table 59-1  TNM Staging of Penile Carcinoma

<table>
<thead>
<tr>
<th>Primary Tumor (T)</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Tx</td>
<td>Primary tumor cannot be assessed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T0</td>
<td>No evidence of primary tumor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tis</td>
<td>Carcinoma in situ</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ta</td>
<td>Noninvasive verrucous carcinoma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T1</td>
<td>Tumor invades subepithelial connective tissue</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T2</td>
<td>Tumor invades corpus spongiosum/cavernosum</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T3</td>
<td>Tumor invades urethra/prostate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T4</td>
<td>Tumor invades other adjacent structures</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Regional Lymph Nodes (N)</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Nx</td>
<td>Nodes cannot be assessed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>N0</td>
<td>No metastases</td>
<td></td>
<td></td>
</tr>
<tr>
<td>N1</td>
<td>Metastasis in a single superficial inguinal node</td>
<td></td>
<td></td>
</tr>
<tr>
<td>N2</td>
<td>Metastases in multiple/bilateral superficial nodes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>N3</td>
<td>Metastases in deep inguinal or pelvic nodes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>N4</td>
<td>Fixed inguinal lymph nodes</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Distant Metastases (M)</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Mx</td>
<td>Distant metastasis cannot be assessed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>M0</td>
<td>No distant metastasis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>M1</td>
<td>Distant metastasis</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Patient with CARCINOMA OF THE PENIS

A

Surgery
Circumcision, partial or total penectomy

Lymph nodes not palpable

Tumor well differentiated, < T2

Observe
Examine every 2 months for 2 years, then every 6 months

Tumor moderately/poorly differentiated, ≥ T2

Bilateral superficial lymph node dissection (LND)
Nodes deep to fascia lata

Lymph nodes negative
Lymph nodes positive

Observe
Examine every 2 months for 2 years, then every 6 months

Deep LND:
nodes deep to fascia lata
Pelvic LND:
external iliac and obturator nodes
SECTION 6 Genitourinary Tumors

B The presence of palpable inguinal lymph nodes that fail to resolve after 4 weeks of antimicrobial therapy remains an indication for ilioinguinal lymphadenectomy (Algorithm 2). In patients with palpably normal inguinal nodes, inguinal lymph node metastasis is predicted by tumor stage (≥T2), vascular invasion, and percentage of poorly differentiated cancer (>50%). Bilateral superficial lymphadenectomy is warranted in this circumstance. Prophylactic inguinal lymphadenectomy does not appear justified in compliant patients with ≤T1 stage, without vascular invasion and <50% poorly differentiated cancer (Algorithm 2). When metastases are detected clinically in one groin, contralateral metastases will be present in 60% of cases, owing to crossover of lymphatics at the base of the penis. If metastatic disease is found in the ipsilateral groin dissection, perform contralateral lymph node dissection. Sentinel lymph node (superficial epigastric group) dissection for penile cancer is associated with a significant false-negative rate (>25%) and thus generally not recommended.

C Inguinal lymphadenectomy can be curative in patients with small-volume inguinal metastases and those with more significant adenopathy that responds to combination chemotherapy. Major complications occur in one-third of the patients undergoing inguinal dissections. Necrosis of the skin flap (8 to 62%), lower extremity lymphedema (23 to 50%), wound infection (10 to 17%), seroma formation (6 to 16%), and death (1 to 2%) are most common. Minimize skin flap necrosis by transposing the head of the sartorius muscle to cover the defect left over the femoral vessels.

D The technique of inguinal lymphadenectomy is most frequently performed with an oblique incision below and parallel to the inguinal crease because it maintains both the integrity of the inguinal ligament and of the cutaneous blood supply. Most surgeons attempt to preserve the saphenous vein to minimize lower extremity edema. The surgeon seeks the lymphatic tissue superomedial to the saphenous vein. By definition, lymph nodes superficial to the fascia lata are defined as superficial, and lymph nodes deep to the fascia lata are defined as deep.

E Fixed inguinal lymph nodes (stage N4) are unresectable and indicate incurable disease not amenable to surgical therapy. Clinicians have used palliative radiation therapy in this setting. Chemotherapy is, in general, ineffective. Most series report experience with cisplatinum-based therapies with objective response rates of 66%, rendering about one-third resectable. Alternatively, the vincristine, bleomycin, and methotrexate (VBM) regimen has been used with similar results.

Additional Readings
A solid testicular mass identified by physical or radiologic examination is always concerning and requires a thorough evaluation. This finding should be considered cancer until proven otherwise. Testicular tumors are rare and account for about 1 to 2% of all malignancies in men. They are, however, the most common tumors in males between age 15 and 34 years. In the United States, the estimated number of new testis cancer cases in 2002 was 7,500, with 400 estimated deaths. The exact cause of testicular cancer remains unknown. It has been hypothesized that testicular atrophy is a common pathway wherein several etiologic factors may be involved in testis tumor development. Infection, trauma, heat, toxins, and cryptorchidism can all lead to testicular atrophy. There is a familial tendency toward testicular tumors. Several studies have demonstrated a relative risk of 1.96 to 4.3 to the father and a relative risk of 9.8 to 12.3 to the brother of an individual with the disease.

**A** Evaluation begins with a complete urologic history and a physical examination. The classic presentation of testicular cancer is painless swelling or enlargement of the testis. However, in 1987, Kennedy and colleagues reported initial symptoms of 5,172 patients with testicular cancer; these symptoms included a swollen or enlarged testis (58%), mass in the testis (27%), painful testis (33%), tender breasts (3%), and a history of trauma (4%). Acute trauma has not been proven as a causative factor; however, it may initiate awareness of a mass. On examination, an enlarged testis or nodule on the testis is generally noted. Examination may be more difficult in a patient with a tender testis or large hydrocele. Ultrasonography may be performed to add to the evaluation and has been shown to be highly reliable in differentiating between intratesticular and extratesticular lesions.

**B** Once a testicular mass is discovered, obtain tumor markers prior to surgery. Serum tumor markers, human chorionic gonadotropin (hCG), α-fetaprotein (AFP), and lactate dehydrogenase (LDH), are well established in managing testicular germ cell tumors and aid in diagnosis, in prognosis, in monitoring treatment, and in predicting relapse. The absence of elevated serum tumor markers in a patient with a testicular mass does not rule out cancer. hCG is secreted by syncytiotrophoblastic cells present in certain germ cell tumors: embryonal carcinoma, teratoma, choriocarcinoma, and less than 20% of seminomas. The serum half-life of hCG is 16 to 24 hours. AFP is synthesized by yolk sac components or germ cell tumors. An elevated AFP is diagnostic of nonseminomatous disease. It is never produced by pure seminoma or by choriocarcinoma. Levels of AFP peak at 12 to 14 weeks gestation and begin to fall after week 16 to undetectable levels after the first year of life. The serum half-life of AFP is 4.5 days. LDH is an enzyme expressed by multiple cell types that include erythrocytes and cells in the liver, kidney, and muscles. LDH as a tumor marker has limited sensitivity but, nonetheless, has been found to be an independent prognostic variable in several large multivariate analyses of testicular germ cell tumors. Serum tumor markers are followed after radical orchietomy and should fall proportionate to their respective half-lives. A disproportionate fall or increase indicates residual disease. However, patients without elevations in serum markers may still have disease. Tumor markers are helping to define prognostic groups and therapeutic regimens.
Patient with SOLID TESTICULAR MASS

A History, physical examination

B Serum markers (hCG, AFP, LDH)

C Biopsy or radical orchiectomy

D Assess stage

E Seminoma (normal AFP)

F Nonseminomatous germ cell tumor

Germ Cell Tumor

Non-Germ Cell Tumor

Stage-dependent treatment

Stage-dependent treatment
C To obtain a diagnosis, the surgeon performs a radical orchiectomy with control of the spermatic cord through an inguinal incision. In select patients, diagnosis can be made by testicular biopsy. Transscrotal orchiectomy or testicular biopsy is contraindicated because of potential contamination of the scrotal lymphatics. Testicular cancers are divided into two large groups, comprising germ cell tumors and non–germ cell tumors.

D Clinicians base treatment decisions on evaluation of the removed surgical specimen, on the clinical extent of disease, and on the values of tumor markers. These factors are all considered in the TNM pathologic staging system. The orchiectomy specimen provides the following information about the mass (T): cancer type, size, and the extent of testicular, epididymal, and spermatic cord or scrotal involvement, as well as determining the presence or absence of vascular-lymphatic invasion. Determine nodal (N) and metastatic (M) involvement by studying the most likely areas for spread. Obtain computed tomography (CT) scans to evaluate the abdomen and pelvic regions. Evaluate the chest by radiography and obtain a CT scan when the radiograph is suspicious or when the abdominal CT scan is positive. CT scan is a reliable method of determining retroperitoneal lymph node involvement and size. The limitation of CT scan, however, is that it will under- or overstage the disease approximately 25% of the time. Clinical staging essentially consists of stage A or I, confined to the testis; stage B or II, retroperitoneal nodal involvement; stage C or III, metastases to visceral organs or involvement above the diaphragm.

E Seminoma accounts for nearly 48% of germ cell tumors, which usually present during the fourth and fifth decades. Initial metastasis is to the periaortic lymph nodes near the renal hilum for left-sided lesions and to the precaval lymph nodes between the aortic bifurcation and renal pedicle with frequent crossover to the periaortic nodes for right-sided lesions. Spread may also occur hematogenously to the lung, liver, brain, bone, kidney, adrenal gland, gastrointestinal tract, or spleen. Treat seminomas with a nonseminomatous component as non–seminomatous tumors. Seminomas are very radiosensitive; as a result, radiation is a key part of early-stage treatment. For stage I disease, treatment consists of radical orchiectomy and infradiaphragmatic radiation therapy. While still under investigation, clinical stage I can be treated with orchiectomy, followed by surveillance. Stage II disease, without bulky nodes (> 5 cm), should be treated with orchiectomy and radiation. Treat stage II bulky disease and stage III disease with orchiectomy and chemotherapy. Close follow-up is the rule.

F Generally, nonseminomatous germ cell tumors are more locally aggressive and have a high metastatic potential. Patterns of lymphatic and hematogenous spread are similar to seminomatous germ cell tumors; however, choriocarcinoma demonstrates the most aggressive natural history, with early hematogenous spread. Non–seminomatous germ cell tumors are treated with surgery and/or platinum-based chemotherapy, depending on the stage of disease. Stage I disease is treated with radical orchiectomy, followed by chemotherapy if tumor markers do not normalize. If markers normalize, options include surveillance or nerve-sparing retroperitoneal lymph node dissection (RPLND) because 30% of patients will relapse without additional treatment. The presence of lymphatic, vascular, scrotal, or spermatic cord invasion increases the likelihood of retroperitoneal lymph node involvement, and RPLND may be preferred in these circumstances. In addition, absence of yolk sac elements or presence of embryonal carcinoma may predict relapse. For stage II disease with few and small nodes, treat with radical orchiectomy and RPLND, followed by chemotherapy if RPLND demonstrates cancer. Treat those with more extensive stage II disease or stage III disease with radical orchiectomy and chemotherapy. After completing chemotherapy, if tumor markers have normalized, resect residual radiographic abnormalities.

References


Testis tumors are quite rare in children, accounting for 1 to 2% of pediatric solid tumors. Historically, management was based on experience with adults, but pediatric testis tumors are pathologically and clinically distinct from their adult counterparts. Nearly 90% of adult testis tumors are seminomas, embryonal carcinomas, or nonseminomatosus mixed germ cell tumors, which account for fewer than 10% of tumors in children. Conversely, the two most common prepubertal tumors—yolk sac and teratoma—account for fewer than 1% each of adult tumors. Gonadal stromal tumors are relatively common in children but quite rare in adults. These differences in histologic subtype result in significant differences in natural history, with metastases occurring in 61% of adult patients but only 9% of children. Therefore, the algorithm for managing testicular tumors in children is different from that for adults. The seminal histologic changes appear to occur at puberty; therefore, tumors occurring in postpubertal adolescent males are best managed under adult algorithms.

A Most children with a testis tumor will present with a testicular mass. Extratesticular masses occurring in the scrotum of boys are rarely malignant, usually representing epididymal cysts, varicoceles, hernias, or hydroceles of the cord. Most testicular tumors are painless, hard masses, although rarely they may present with pain related to acute hemorrhage. On physical examination, a mass that cannot be separated from the testis is assumed to be a testis tumor until proven otherwise. Ultrasonography is very helpful in making this distinction when the physical examination is unclear. Rarely, testis tumors may present with a reactive hydrocele. Because hydroceles are very common and testis tumors very rare, the vast majority of boys with a hydrocele will not have a tumor. But if the hydrocele is large and firm enough to preclude palpation of the testis, a sonogram should be obtained.

B Most testis tumors in children are primary testis tumors. The distribution of primary testis tumors registered in the Prepubertal Testis Tumor Registry of the Urologic Section of the American Academy of Pediatrics is displayed in Table 61-1. Tumors may be of germ cell or stromal origin (the exception being gonadoblastomas, which contain elements of both). Yolk sac tumors are always treated as potentially malignant, and teratomas and epidermoid cysts are universally benign in prepubertal patients. Gonadal stromal tumors have generally behaved in a benign fashion in children except for some undifferentiated stromal tumors and occasional Sertoli cell tumors in children over 5 years old.

### Table 61-1 Relative Frequency of Tumor Types Registered in the Prepubertal Testis Tumor Registry of the Urologic Section of the American Academy of Pediatrics

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>Number</th>
<th>Percent</th>
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<tbody>
<tr>
<td>Yolk sac tumor</td>
<td>244</td>
<td>62</td>
</tr>
<tr>
<td>Teratoma/epidermoid cyst</td>
<td>105</td>
<td>26</td>
</tr>
<tr>
<td>Stromal tumors*</td>
<td>42</td>
<td>11</td>
</tr>
<tr>
<td>Gonadoblastoma</td>
<td>4</td>
<td>1</td>
</tr>
</tbody>
</table>

Adapted from Ross et al.1

*Stromal tumors include juvenile granulosa cell, Leydig cell, Sertoli cell, and undifferentiated stromal tumors.

C Ultrasonography can help distinguish intratesticular from extratesticular scrotal masses. It can also determine whether the entire testis is replaced with tumor or if there is some normal testicle that may be salvaged if the tumor is benign. Serum α-fetoprotein (AFP) is elevated in 90% of children with yolk sac tumors. AFP is very specific for yolk sac tumor but may be physiologically elevated in normal infants (including those with benign tumors). Generally speaking, a child over 1 year of age with a testicular mass and an elevated AFP can be assumed to have a yolk sac tumor. Infants with an elevated AFP may have benign tumors, though AFP levels are rarely > 100 ng/mL in normal children over 6 months of age. The ultrasonographic characteristics of various testis tumors have been described. However, the findings are not specific enough to alter management, which is based on the AFP level and whether salvageable testis is present.

D Tumors that are likely benign based on AFP level and that appear to have salvageable normal testis on ultrasonography should be managed initially with an excisional biopsy. An inguinal exploration is performed with early control of the spermatic cord (by rubber-shod clamp or soft tourniquet). The testis is delivered within the tunica vaginalis and draped off. The tunica vaginalis is opened and the testis examined. If still feasible, the tumor is excised with a margin of normal testicular parenchyma and a frozen section evaluation obtained. If a teratoma is diagnosed and the child is near pubertal age, the surrounding parenchyma should be examined for its pubertal status. If the tubules are immature, the tumor may be treated as benign. However, if the tubules show evidence of maturation, the tumor should be treated as potentially malignant because some adult teratomas behave in a malignant fashion. If a benign histology is confirmed, the testis is closed with
Patient with PREPUBERTAL TESTICULAR TUMORS

A. Presentation

B. Primary testis tumor

C. Ultrasonography and AFP

Likely benign

D. Excisional biopsy with frozen section

Replace testis in scrotum

Likely malignant

E. Inguinal orchiectomy

Pathology

F. Metastatic evaluation

G. Treatment/follow-up

H. Treatment
SECTION 6 Genitourinary Tumors

absorbable suture and returned to the scrotum. If the biopsy reveals a malignant tumor (usually yolk sac) or potentially malignant tumor (such as an undifferentiated stromal tumor or a Sertoli cell tumor in an older child), then an inguinal orchiectomy should be performed.

E If the tumor is felt to be malignant or if it replaces the testis, precluding testis-sparing surgery, then an inguinal orchiectomy is performed. An inguinal exploration is performed with early clamping of the spermatic cord. The testis is then delivered into the inguinal canal with the tunica vaginalis intact. The cord is ligated and divided at the internal ring, using at least one permanent suture for identification in the event that a retroperitoneal lymph node dissection should become necessary. The entire specimen is sent to pathology intact and the inguinal incision is closed.

F Pediatric testis tumors have a metastatic pattern similar to that of adult tumors. The primary sites for metastases are the retroperitoneal lymph nodes and the lungs. However, metastases occur less commonly (80% of pediatric yolk sac tumors are Stage I), and, when they do occur, only a minority have metastases limited to the retroperitoneum. The metastatic evaluation usually includes a computed tomographic (CT) scan of the abdomen and pelvis and a chest radiograph. The only tumor marker that is elevated in yolk sac tumor is AFP. AFP levels should be obtained immediately postoperatively if not done preoperatively. A follow-up level is obtained approximately 1 week later. In the absence of metastases, this level should be less than half of the initial level (because the half-life of AFP is approximately 5 days).

G As with adult germ cell tumors, the selection of adjuvant therapy for yolk sac tumor depends on the stage of the tumor. Patients with Stage I tumors (no evidence of metastases and normalization of AFP postoperatively) are generally observed closely without adjuvant therapy because most recent series have shown no advantage to chemotherapy for these patients.1,3–7 Patients are evaluated 1 month after orchiectomy with a CT of the abdomen and pelvis, chest radiography, and a serum AFP. For 2 years, the serum AFP and chest radiograph are repeated every 4 to 6 weeks and the CT scan every 2 to 3 months. Recurrent disease is usually treated with chemotherapy, even if it appears to be limited to the retroperitoneum. If the patient remains free of disease for 2 years, then he is almost certainly cured, and minimal follow-up is required beyond that point.3 The recurrence rate for patients with Stage I tumor managed by observation is approximately 20%, and virtually all of these patients can be salvaged with chemotherapy.

Patients with radiographic evidence of metastases and/or persistent elevation of AFP require adjuvant therapy. With the widespread use of AFP to detect occult metastases and improvements in multiagent chemotherapy, the reliance on retroperitoneal lymph node dissection (RPLND) to diagnose and treat metastatic disease in children has waned. In theory, RPLND is less beneficial for children than for adults because yolk sac tumors in children have a predilection for hematogenous spread, with only a minority of metastases being limited to the retroperitoneum.8 The operative morbidity of RPLND in children is significant, including wound complications, bowel obstruction, chylous ascites, and anejaculation as adults because of injury to the sympathetic nerves.9 Chemotherapy is very effective in treating metastatic yolk sac tumor. The most commonly used regimens include cisplatin in combination with other agents such as etoposide and bleomycin. Because children with metastatic disease often have multiple sites of spread, chemotherapy is particularly appropriate for these patients.

Patients with metastatic disease or failure of the AFP to normalize are generally treated with chemotherapy. Remember that a “normal” AFP in small children may be quite high. Consider performing a modified RPLND in the presence of minimal retroperitoneal disease and a normal AFP. An RPLND should also be considered when retroperitoneal disease is not responding to chemotherapy or for a persistent mass following chemotherapy when the AFP level has normalized. Chemotherapy with second-line agents should be used for patients failing to respond to standard agents. Surgical excision and radiation should also be considered for those with limited sites of metastatic disease who fail to respond to chemotherapy.

H Secondary tumors of the testis are extremely rare, and treatment depends on the primary tumor. The most common secondary tumor to affect the testis in prepubertal boys is leukemia. Only 2% of boys with acute lymphoblastic/lymphocytic leukemia (ALL) will have overt clinical evidence of testicular involvement at diagnosis.10 This is usually reflected in firm diffuse enlargement of one or both testicles and portends a poorer prognosis. Subclinical (ie, microscopic) involvement of the testes is present in approximately 20% of patients with ALL at the time of diagnosis.11 However, most patients with microscopic testicular involvement achieve a complete remission following modern standard chemotherapy. Conversely, some patients without evidence of testicular involvement at diagnosis will ultimately relapse in the testicles. Therefore, pretreatment testicular biopsy is unnecessary because it does not predict those patients who are prone to have persistent or relapsing disease at that site.

With modern ALL chemotherapy, testicular relapse occurs in fewer than 1% of cases.12 Postchemotherapy biopsy in the absence of physical findings (to rule out occult persistence of tumor in the testes) is therefore no
longer routine. Those few patients with testicular enlargement persisting or occurring after chemotherapy should undergo biopsy to confirm testicular ALL. Most of these patients will be found to have relapsed at other sites as well and require additional intensive systemic chemotherapy to prevent ultimate clinical hematologic relapse.\(^{13}\) Radiation to the testicles is also required. Most patients with testicular relapse following chemotherapy can be salvaged and attain long-term survival. Relapse during chemotherapy portends a more dire outcome.

**References**

Nongerminal cell testicular tumors are rare, accounting for only 5 to 10% of all testicular neoplasms.1 This group is divided into primary and secondary testicular tumors (Table 62-1). The most common presenting symptom is a solid testicular mass that requires exploration. Radical orchiectomy is warranted in most cases, although testis-sparing surgery should be considered for universally benign tumors discovered at exploration. Subsequent therapy with lymph node dissection, radiation, and/or chemotherapy depends on clinical staging and pathology.

A Leydig cell tumors, or interstitial cell tumors, are rare and account for 2 to 3% of all testicular neoplasms.1–2 Although the most common presenting symptom is a testicular mass, these tumors can produce several hormonal substances, including androgens, estrogen, corticosteroids, and progestins and therefore may be associated with a virilizing or a feminizing syndrome. Of adults, 20 to 30% present with gynecomastia, whereas all presenting prepubertal males are virilized.1–3 Histologically, these tumors may appear to be anaplastic; however, their clinical course may be that of a benign tumor. Tumors confined to the testicle with no evidence of spread require no further treatment, other than close observation. Malignant Leydig cell tumors occur only in adults; approximately 10% show evidence of spread, which is the only reliable criterion for malignancy.1–3 These malignant tumors require subsequent treatment with lymph node dissection and/or chemotherapy. In contrast, Leydig cell tumors in prepubertal children have a uniformly benign course, and enucleation has been suggested for their treatment in this population.4,5

B Sertoli cells are the supportive cells of the seminiferous tubules. Sertoli cell tumors are rare, fewer than 100 having been reported in the literature. These usually benign tumors occur in prepubertal children (most under age 1 year). In a recent review of 60 cases, only 4 of the patients were younger than age 20 years.6 Sertoli cell tumors can produce hormones, and a feminizing syndrome is present in one-third of cases. As with Leydig cell tumors, approximately 10% are malignant, based on the presence of metastasis.1,2 Retroperitoneal lymph node dissection is indicated in the uncommon patient with demonstrable metastases.

C The universally benign clinical behavior of an epidermoid cyst makes it amenable to testis-sparing enucleation, if recognized preoperatively or during scrotal exploration.4 However, management with radical orchiectomy is common, owing to uncertainty in diagnosis. Almost all cases are identified in young adults. They are less frequent in prepubertal boys. Ultrasonography may demonstrate a well-circumscribed ovoid lesion with variable echogenicity (“target” or “onion” appearance).

D Although rare, lymphoma is the most common testicular neoplasm diagnosed in men over age 50 years. Moreover, about 40% are bilateral. Differentiation from seminoma is important in terms of treatment and is made possible by noting the presence of malignant cells confined to the interstitium of the testis and the absence of intratubular spread. The systemic disease requires treatment and usually involves chemotherapy.

E Children with acute lymphoblastic leukemia may have leukemia cells that involve the testes. The testicle appears to be a common site of relapse or persistence of leukemic cells, presumably owing to the poor susceptibility of testicular tissue to chemotherapeutic agents. Routine end-of-therapy biopsy of the testes has no clinical value.7 Biopsy is essential to the diagnosis in any known leukemic patient who has testis enlargement. Treat leukemic infiltration of the testicle by testicular radiation, followed by reinstitution of systemic chemotherapy.3,8

F Metastatic disease to the testicle is usually discovered as an incidental finding at time of autopsy. Common tumors that may metastasize to the testis include tumors of the prostate, lung, gastrointestinal tract, kidney, and melanoma, with tumors of the prostate being the most common.2 These tumors may reach the testis by hematogenous, lymphatic, or direct extension or by retrograde extension via the vas deferens. Aim treatment at eradication of the primary tumor.

Table 62-1 Classification of Nongerminal Testicular Tumors

<table>
<thead>
<tr>
<th>I. Primary tumors</th>
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</thead>
<tbody>
<tr>
<td>A. Gonadal stromal tumors</td>
</tr>
<tr>
<td>1. Leydig (interstitial) cell</td>
</tr>
<tr>
<td>2. Sertoli cell</td>
</tr>
<tr>
<td>3. Granulosa cell</td>
</tr>
<tr>
<td>B. Gonadoblastoma</td>
</tr>
<tr>
<td>C. Epidermoid cyst</td>
</tr>
<tr>
<td>D. Mesenchymal tumors (ie, fibroma, leiomyoma, angioma, mesothelioma, etc)</td>
</tr>
<tr>
<td>E. Miscellaneous</td>
</tr>
<tr>
<td>1. Carcinoid</td>
</tr>
<tr>
<td>2. Adenocarcinoma of rete testis</td>
</tr>
<tr>
<td>3. Adrenal rest</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>II. Secondary tumors</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Reticuloendothelial tumors (ie, lymphomas, leukemic infiltration)</td>
</tr>
<tr>
<td>B. Metastases</td>
</tr>
</tbody>
</table>

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References
SECTION 7

URINARY STONE DISEASE
Urinary stone disease affects 10 to 12% of the population at some time during their lives. Calcium oxalate urolithiasis occurs in approximately 65% of these patients, other stone types being seen less frequently (uric acid 5 to 10%, calcium phosphate 5%, magnesium ammonium phosphate and carbonate apatite 15%, and cystine 1%). Mixed stones are often present. To identify all predisposing factors that may relate to the disorder is essential. In 80 to 90% of patients, a predisposing factor can be identified and treatment should be instituted to reduce or eliminate recurrent disease.

A The patient requires a general medical evaluation. If the patient presents with acute colic, a physical examination is mandatory and will often assist in detecting the presence of various abnormalities associated with stone formation. A history of stone episodes, use of medications, history of urinary tract infections, and associated medical disorders may also assist in detecting the factors that cause the disorder. A family history of stone disease helps identify patients who are likely to have recurrent disease.

B Stone analysis is essential. If previously passed or surgically removed stones are available, analyze these, as well as any stones associated with the presenting episode when recovered. Simple chemical analyses are not satisfactory; crystallographic and/or electron diffraction studies are preferable and can be performed in commercial laboratories promptly and at minimal cost.

C An elevated serum calcium level on more than two occasions highly suggests hyperparathyroidism. Associated laboratory studies, including serum phosphorous, chloride, and alkaline phosphatase, assist in the diagnosis. In addition, obtain serum parathormone levels to establish the diagnosis. These patients may also have other metabolic disorders; thus, obtaining a 24-hour urine collection is important after excising the abnormal parathyroid tissue and correcting hypercalcemia.

D One to two 24-hour urine collections are essential to patient evaluation. Obtain the collection while patients are on their regular diet. In addition to volume determination, analyze the specimen for calcium, uric acid, oxalate citrate, and phosphorous and creatinine. In addition, obtain a serum blood urea nitrogen (BUN), creatinine, and electrolytes.

E Hypercalciuria is the most frequent cause of urolithiasis. Some clinicians feel it unnecessary to differentiate between absorptive and renal hypercalciuria and use various treatment regimens. Others attempt the differentiation using calcium fast and load tests and, based on the test results, selectively treat the patient. If this study is done, place the patient on a restricted calcium and sodium diet for 1 week.

F Clinicians occasionally see hyperoxaluria that is secondary to hyperabsorption—owing to small bowel disease with resultant malabsorption syndrome—in patients with regional enteritis and in those who have had small bowel bypass surgery for morbid obesity. Treating hyperoxaluria is difficult and often unsuccessful. Clinicians see marginal increases in oxalate excretion in patients with normal intestinal tracts; these are often attributable to increased ingestion of oxalate-containing products. Apply appropriate dietary restrictions in this group of patients.

G Hyperuricosuria is present in 20% of patients with calcium oxalate urolithiasis. These patients often respond to dietary restriction; the use of medications to limit uric acid excretion may help.

H Hypocitraturia is present in 10% of patients with recurrent calcium oxalate urolithiasis. Citrate supplement, primarily potassium citrate, assists in correcting this condition.

I Renal tubular acidosis is present in a minority of patients with recurrent calcium oxalate/calcium phosphate urolithiasis. Hypercalciuria and hypocitraturia are often associated with this disorder. Appropriate treatment includes increasing fluid intake and alkalinization with oral agents. Potassium citrate is being used increasingly in managing this disorder.
Patient with URINARY CALCULI

A

History
Family history
Physical examination

B

Stone analysis

C

Assess serum calcium

< 10.5 mg/dL
Hyperparathyroidism

> 10.5 mg/dL

D

Assess 24 h urine; serum studies

E

Hypercalciuria
( > 4 mg/kg/24 h)

Calcium fast and load tests

Absorptive hypercalciuria

Appropriate medical management

F

Hyperoxaluria
( > 40 mg/24 h)

Renal hypercalciuria

Appropriate medical management

G

Hyperuricosuria
( > 800 mg/24 h, male)
( > 750 mg/24 h, female)

Appropriate medical management

H

Hypocitraturia
( < 300 mg/h)

Appropriate medical management

I

Citrate
( < 20 mg/24 h)

Renal tubule acidosis

Alkali Fluids
Penicillamine

Appropriate medical management
Additional Readings


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Worster A, Haines T. Does replacing intravenous pyelograph with non-
contrast helical computed tomography benefit patients with sus-
A Most important in the treatment of bladder calculi is the identification and correction of those factors predisposing to the formation of calculi. A thorough history is essential to detect symptoms and other systemic manifestations that may relate to stone formation. A history or the presence of an indwelling Foley catheter for an extended period antedating the diagnosis of bladder stones is important. Physical examination is essential, as well as urine culture, to assess for the presence of urinary tract infections (UTIs).

B Stone formation in children usually occurs in young males living in underdeveloped countries. These stones are often composed of uric acid and urate salts and do not recur following surgical removal. Clinicians believe that the etiology of the stone relates to specific dietary factors early in life. Recurrences are unusual because of early changes in these patterns.

C The presence of an indwelling Foley catheter with associated UTI frequently results in bladder stone formation. Monitoring of UTIs in these patients helps, along with daily irrigation with various solutions. Irrigation of the bladder to wash out debris and small stones that are likely to form throughout the day is probably the most important aspect of treatment.

D When evaluating adults with bladder stones, one must assess for the presence of bladder outlet obstruction. Benign prostatic hyperplasia and urethral stricture in the male are the most common causes; the clinician can usually assess these by urethrogram and cystoscopic examination. Typically, these stones are composed primarily of uric acid and urate salts. Should prostatic hyperplasia of urethral stricture exist, carry out stone removal or fragmentation, in addition to relieving the obstruction, either by open surgical or transurethral approaches. Laser, ultrasonography, and electrohydraulic lithotripsy under cystoscopic observation are effective methods of fragmenting bladder stones. Monitoring of the patients postoperatively to ensure relief of the obstruction is imperative.

E In patients with no obstruction, urodynamic studies are needed to assess for disorders of voiding that may result in incomplete emptying of the bladder with associated UTI and stone formation. If voiding dysfunction is identified, make attempts to correct this disorder after stone removal. This is essential to ensure that recurrent disease does not occur.

Additional Readings
Patient with BLADDER STONE

A History, physical examination → Urine culture

B Child

Stone removal

C Indwelling catheter

Monitor UTI

Irrigation

D Adult

Cystoscopy assessment of residual urine

E No obstruction

Bladder outlet obstruction

Urodynamics

Stone removal

Stone removal

Monitor residual urine

Relief of obstruction
Urinary stone disease is fairly common in industrialized countries, affecting 1 to 5% of the population, including a 20% lifetime risk for a white male. Calcium stones, including calcium oxalate and calcium phosphate, account for 73% of all stones, and calcium oxalate stones have a recurrence rate of 10% at 1 year, 35% at 5 years, and 50% at 10 years without medical treatment.1,2

Stone formation in the urinary tract is a complex process that involves supersaturation of the urine with the involved ions, as well as the chemical interplay of urinary inhibitors, complexing agents, and promoters. Inhibitors are agents in the urine that inhibit crystal formation and are effective at very low concentrations. These include citrate, magnesium, pyrophosphate, nephrocalcin, and glycosaminoglycans.1 Glycosaminoglycans prevent crystal aggregation but are less effective against crystal growth, whereas nephrocalcin is a potent inhibitor of calcium oxalate monohydrate crystal aggregation and growth.1 Complexing agents form soluble complexes with lattice ions, calcium phosphate, and oxalate and decrease free ionic activity, which reduces crystal formation. Citrate is a potent complexer of calcium, with its maximal effect at a pH of 6.5, and magnesium complexes oxalate.1 Promotors encourage crystal formation and aggregation, and there are few pure promotors of urinary stone formation; some inhibitors such as glycosaminoglycans and Tamm-Horsfall protein can act as promotors, depending on the state of crystal aggregation.1

Diagnosis of a calcium stone and clinical assessment of the patient for possible urgent intervention is essential before considering medical management options because medical management is primarily aimed at preventing calcium stone recurrence after existing stones are eliminated with extracorporeal shock wave lithotripsy (ESWL), endoscopic technique, or nephroscopic or open surgery.

A Patients with urolithiasis most commonly present with renal colic and abrupt onset of severe paroxysmal pain on the affected side. The pain usually originates in the flank and may radiate to the ipsilateral groin or scrotum or labia. This is a visceral pain, resulting from ureteral obstruction, and fluctuates with ureteral peristalsis. There is often microscopic or gross hematuria, owing to the abrasive effect of the stone on the urothelium. Patients with stones may also present with infection that is complicated by the ureteral obstruction, resulting in dysuria, fever, leukocytosis, and sepsis. Incidental stones may also be found radiographically during the evaluation of another process.

Evaluating a suspected calcium stone begins with a complete history and physical examination. Past medical history can reveal previous episodes of nephrolithiasis, as well as metabolic and dietary risk factors for stone disease. Hyperparathyroidism, malignancy, previous bowel surgery, and renal tubular acidosis predispose patients to hypercalciuria and/or hyperoxaluria and subsequent calcium stones.2 Family history of stones, bone disease, or gout can also increase the risk of calcium stone disease.3 Strenuous exertion or outdoor activity in warm climates can lead to dehydration, predisposing a person to stone formation. Excess dietary intake of calcium, oxalate, or protein and low fluid consumption can also result in urinary calculi. Chemical composition of previous stones, if known, can give clues to the type of stone at current presentation, along with the underlying etiology of stone formation and recurrence.

Physical examination is often nonspecific for stone disease. Patients usually have palpable costal-vertebral angle tenderness and tenderness in the ipsilateral lower abdomen. Gross examination of the urine may reveal hematuria and possibly stone debris, or even the causative stone.

B To perform an initial laboratory evaluation of an acute patient with stones, include a urinalysis and a urine culture and sensitivity to assess urinary pH and check for the presence of urinary tract infection. In addition, if infection is suspected, obtain a complete blood count to assess for systemic leukocytosis, indicating impending sepsis. For patients with preexisting renal function impairment or a solitary functioning kidney, check serum creatinine to determine if renal function is acutely compromised.

Further laboratory tests that can be performed electively in the ongoing evaluation of a patient with stone formation include serum calcium, phosphate, electrolytes, alkaline phosphatase, and uric acid levels, as well as chemical composition of stone fragments that have passed or were removed.3 Collect a 24-hour urine sample and evaluate the sample for calcium, oxalate, uric acid, citrate, sodium, magnesium, pH, and volume.

Radiographic evaluation is based on the acuity of stone disease and the overall clinical picture of the patient. Nonenhanced spiral computed tomography (CT) is the standard study for emergency evaluation of acute flank pain.4,5 It is quick, does not require bowel
Calcium Oxalate/Calcium Phosphate Calculi

Patient with SUSPECTED CLINICAL STONE DISEASE

A. History
   Physical examination

B. Imaging and urinalysis

C. Suspicion for calcium oxalate/phosphate stone

D. Clinical assessment
   - Sepsis, pain, or urinary tract obstruction
   - Elective stone surgery
   - Emergent urinary tract decompression

E. Stable
   - Stone analysis
   - Diagnose and treat metabolic abnormality
   - Anti-stone therapy

F. Follow-up
A KUB shows the relative position of a calculus to adjacent bony and visible soft tissue structures. The KUB can also be used to determine if a previously seen stone has progressed or passed. Calcium stones are radiodense and can be visualized with a KUB.

Intravenous urogram (IVU) is useful for evaluating the location of the stone in the urinary tract, as well as the severity of obstruction from the calculus. This study provides anatomic and qualitative functional information about the kidneys and can be used to find possible etiologies of stone formation owing to anomalous anatomy and function.

If the patient’s clinical condition is stable, plan ESWL or endoscopic, nephroscopic, or open surgery to remove the calculus. Then further laboratory testing and chemical analysis of the stone can be performed, allowing the clinician to diagnose any metabolic abnormality and to plan an anti-stone treatment regimen if necessary.

Sepsis, associated with urinary tract obstruction, is a urologic emergency that requires prompt decompression of the obstructed system. This can be done by cystoscopic passage of a ureteral stent or by percutaneous placement of a nephrostomy tube. Ureteral stents can cause more irritative symptoms than percutaneous nephrostomy tubes, require more frequent analgesic administration, use more radiograph exposure for insertion, and remain in the kidney longer after stone treatment. A lower quality of life is especially pronounced in males and younger patients with ureteral stents. Ureteral stenting may, however, offer better success of stone clearance after ESWL than a nephrostomy tube. Ureteral stents can cause more irritative symptoms than percutaneous nephrostomy tubes, require more frequent analgesic administration, use more radiograph exposure for insertion, and remain in the kidney longer after stone treatment.

Implementing medical therapy relies on understanding the etiology of calcium stones. Calcium phosphate stones are often found mixed with calcium oxalate stones. Pure calcium phosphate stones are relatively rare—typically seen only with very active stone disease when the pressure for crystallization is high—and most often occur with tubular acidification defects, such as distal renal tubular acidosis. Medical therapy for calcium stones is primarily targeted at calcium oxalate stones and the underlying etiologies for their formation. Causes of calcium oxalate stones include hypercalciuric conditions such as hyperparathyroidism, which causes a resorptive hypercalciemia with hypercalciuria, absorptive hypercalciuria owing to increased vitamin D–dependent intestinal uptake of calcium, and renal hypercalciuria, resulting from a renal wasting of calcium. Low urinary citrate also leads to calcium oxalate stone formation as citrate complexes urinary calcium, reducing the concentration of its free ionic form. Hypocitraturia results in increased proximal tubular reabsorption of citrate and is often seen with metabolic acidosis conditions, specifically, distal renal tubular acidosis and intestinal diseases that cause chronic diarrhea and malabsorption. Hyperoxaluria and hyperuricosuria also lead to calcium oxalate stone formation. Hyperoxaluria leads to oxalate crystal formation that combines with calcium ions in the urine to form calcium oxalate stones. Hyperuricosuria promotes calcium oxalate stones by providing uric acid crystals that form as nuclei for calcium oxalate stone formation.

Treatment options depend on the metabolic abnormality. Treat primary hyperparathyroidism with parathyroidectomy. Other forms of hypercalciuria can be treated with thiazide diuretics. Thiazides have been shown to reduce the stone-forming rate in calcium stone–forming patients. Prescribe potassium citrate for hypocitraturia. In addition to increasing urinary citrate, potassium citrate also alkalinizes urine, leading to increased renal calcium reabsorption, reducing excreted urinary calcium.
dietary purines, but these patients often have to be placed on allopurinol to adequately reduce urinary uric acid levels.

Diet can also play an important role in stone formation. Low fluid consumption leads to supersaturation of urine, increasing the chance of stone precipitation. Hydrate patients who form stones to produce a 24-hour urine volume of > 2 to 3 L daily. High-protein diets increase urinary calcium and uric acid excretion and decrease citrate excretion, and an elevated dietary sodium to potassium ratio increases urinary calcium excretion and decreases citrate excretion. Increased fiber intake has been correlated with a reduced risk of stone formation, most likely because of increased urinary citrate. Carbohydrate and fat consumption do not appear to increase stone formation, although carbohydrate consumption induces elevated calcium excretion. Dietary magnesium and phosphorus consumption do not appear to alter stone formation; however, administration of supplemental orthophosphates decreases urinary calcium excretion. This is likely owing to decreased vitamin D activity and less intestinal absorption of calcium.

Patients with stones have significant reduction in stone formation when we use medical therapy. For this reason, to emphasize the importance of persisting with treatment, periodic follow-up and observation are important. Schedule patients for yearly visits, monitor urine chemistries, and obtain periodic radiographs.

References
Uric acid stones present in various ways. In addition to those indicated, there may be incidental findings on tomographic, ultrasonic, and radionuclide excretion studies.

A Contrast studies almost always lead to establishing the presence of a radiolucent filling defect and are often helpful in monitoring therapy.

B If the index of suspicion of uric acid stone is high and urinary cytology is normal, a therapeutic trial of allopurinol (300 mg orally 4 times daily), alkalinization of the urine (potassium citrate, sodium bicarbonate) to pH 6.5 to 7.0, restriction of dietary purines, and an increase of daily urine volume to 2 L are worthwhile to possibly avoid subsequent invasive procedures. Ensure care is taken with alkalinization to avoid precipitating calcium salts on the surface of a uric acid stone. A coating of calcium salts can prevent a uric acid stone from dissolving. Many uric acid stones in excess of 1 cm in diameter have been dissolved by alkalinization. If the defect disappears, prophylaxis to prevent recurrence is needed. This may range from one or more of the measures already mentioned to that of prostatectomy if the filling defect was a bladder stone.

C Short of chemical analysis of the stone, endoscopy is the most direct means of diagnosing a radiolucent filling defect. The recent advent of ureteroscopy makes endoscopy an extremely important diagnostic measure.

D If a stone is visualized and if its size and position, as well as the patient’s age, favor removal, perform one of the following techniques: (1) extracorporeal shock wave lithotripsy, (2) irrigation with alkali, (3) basketing with the ureteroscope, (4) fragmentation (ultrasound, laser, or electrohydraulic) through the ureteroscope, or (5) percutaneous removal. A therapeutic trial of systemic alkalinization may precede stone manipulation if ureteroscopy establishes the diagnosis. However, if removal does not appear technically difficult, it is usually in the best interest of the patient to remove the stone at the first endoscopy.

E Most patients with uric acid stone formations have a metabolic renal defect that results in forming persistently acidic urine at pH 5.5 or below. In most, uric acid excretion is normal. Preventive therapy is directed at correcting this problem, and oral administration of an alkali (potassium citrate, sodium bicarbonate) is usually sufficient. If hyperuricosuria is present, allopurinol is administered because dietary purine restriction often does not help. Similarly, uric acid stones form in patients with ileostomies, owing to the presence of a highly acidic, highly concentrated urine. Patients with malignancies (eg, leukemia, lymphoma) who are administered chemotherapeutic agents are also at risk because of the high rate of cell breakdown, purine release, and increased uric acid excretion. Again, alkalinization is very important in this group of patients.

Additional Readings
Patient with URIC ACID CALCULI

Hematuria
Flank pain
Suprapubic pain
Colic

History
Physical examination

A Urinalysis, urine culture
Contrast-enhanced radiography

Treat any infection
Relieve any high-grade obstruction

Radiolucent filling defect

Urinary cytology

Normal

Abnormal

Defect persists

B Therapeutic dissolution
Trial for 1 month

Defect disappears

C Cystoscopy and ureteroscopy (see Chapter 8, “Radiolucent Filling Defects”)

Tumor

Biopsy

D Stone
Remove stone if reasonable and feasible

Subsequent action depends on pathology

Stone sent for analysis if possible

E Prophylaxis

Benign process

Observe

E Prophylaxis
Cystine stones are relatively uncommon and account for approximately 1% of the entire stone-forming population. Cystinuria, an autosomal, recessive, inherited disorder, affects amino acid transport of the epithelial cells of the renal tubule and gastrointestinal tract. Cystine, lysine, arginine, and ornithine are present in increased amounts in the urine, and if it were not for the low solubility of cystine, the disorder would be of no clinical import. About 1 in 20,000 individuals in the general population are affected with this disorder, and although patients with cystine stones form a minority of all patients with urinary stones, cystinuria remains a dilemma to the clinician because of management problems and the frequency of recurrent disease.

A It is important to obtain a full stone history. Interestingly, a clinician can elicit a family history of urolithiasis in approximately 50% of patients. The average age at the time of initial stone formation is generally lower than in patients with calcium oxalate stones, and the diagnosis of homozygous cystinuria often lags several years behind the onset of stone formation. Stone analysis is essential and therefore should be performed on all stones retrieved, either by spontaneous passage or surgical removal. An appropriate analysis often establishes a correct diagnosis. Obtain urine cultures to exclude the presence of associated urinary tract infection. At times, patients who seemingly have infection stone disease can have underlying cystinuria.

B It is imperative to assess the entire urinary tract. Congenital disorders can exist in this patient population, and multiple stones can be present throughout the kidneys and/or ureters. If renal obstruction is present, this must be relieved. Undertake attempts at dissolution in patients who are free of obstruction.

C When an obstructed system exists, usually because of a ureteral stone, this must be relieved. Ureteral catheters can be placed, but percutaneous nephrostomy placement benefits more often.

D Following appropriate relief of the obstruction, the clinician can then undertake stone dissolution by using several techniques. In the obstructed system, direct irrigation with alkaline solutions, such as sodium bicarbonate with acetylcysteine, has been effective. Sodium bicarbonate maintenance has also been used in oral preparation, but sodium potassium citrate and potassium citrate alone appear to be better agents for obtaining sustained alkalinization of the urine. Urinary alkalinization must achieve a pH of at least 7.5 for effectiveness. Use of D-penicillamine or α-mercaptopyrpylglutamic acid is also effective in dissolving already-formed stones and in maintaining patients in order to prevent new stone formation. If stone dissolution is unsuccessful, fragmentation or surgical removal by various techniques is usually indicated. Experience has demonstrated that these stones are relatively resistant to fragmentation by extracorporeal shock wave lithotripsy. Dissolution often fails because other components (ie, magnesium ammonium phosphate or calcium oxalate) have often absorbed onto the previously formed cystine stones.

E Prophylaxis with alkalinization and high-level intake is most important. Use of disulfide-binding agents helps, but, owing to potential toxicity, monitor patients closely. Follow-up with radiographs and urinalysis to monitor response to therapy.

Additional Readings


Cystine Stones

Patient with CYSTINE STONES

A  History
    Physical examination

  Stone analysis
    Urine culture
    24-Hour urine for cystine

B  Assessment of urinary tract

Renal or ureteral obstruction
  C  Relieve obstruction
     Stone dissolution or fragmentation removal

No obstruction
  D  Dissolution of stone(s)
     Fragmentation or removal if dissolution unsuccessful

E  Prophylaxis
Infection stones account for approximately 15 to 20% of all urinary calculi. They occur most frequently in women (the ratio of affected females to males is 2:1) and, when located in the kidneys, usually assume a staghorn configuration. Infection stones also occur with increased frequency in patients who have external urinary diversions or indwelling urethral catheters that have been used on a long-term basis. Although all infection stones are associated with infection of the urinary tract with urea-splitting organisms, approximately one-half originate from an underlying, readily identifiable anatomic or metabolic defect.

A. A thorough history is essential when evaluating patients with infection stone disease. A history of infection is important as it relates to stone formation. Assess the voiding pattern of patients and make an attempt to detect the presence of associated disorders (ie, diabetes mellitus), which may result in a neurogenic bladder and voiding dysfunction. The presence of a urinary diversion or an indwelling Foley catheter may be important in inducing stone formation. Finally, one must assess the patient for congenital anomalies and/or a history of urinary tract obstruction that may relate to the association of urinary tract infection and stone formation. Urine cultures are essential in evaluating these patients; it is imperative to identify all organisms and obtain sensitivities. Radiologic studies are essential to assess the anatomy of the urinary tract.

B. Stone removal is usually necessary, provided that the patient’s medical status permits. This can be carried out by means of an open surgical procedure, but clinicians employ percutaneous techniques more often. Many believe that this approach should be the central one. They have used extracorporeal shockwave lithotripsy in treating infection stones, but if a significant proportion of matrix material exists, fragmentation is difficult. Postlithotripsy irrigation with 10% hemiacidrin may be required. Urinary tract infections can be suppressed while the stone is present, but the infection will usually recur once antibiotics are discontinued.

C. Stone analysis is essential. Approximately 50% of patients with infection stone disease have an underlying metabolic disorder; it is often useful to identify the presence of components in the stone other than magnesium ammonium phosphate and carbonate apatite.

D. Metabolic evaluation is essential to exclude the presence of underlying metabolic disorders. Experience indicates that, with clearing the urinary obstruction and infection, calcium excretion rises, and, at times, clinicians identify hypercalciuria in patients who have a low preoperative urinary calcium excretion.

E. If metabolic disease is present, correcting the underlying disorder is essential. Monitor these patients to detect recurrent urinary tract infection.

F. In patients who have no metabolic disorders other than urinary tract infection, managing the infection is essential. Monitor closely patients with normal anatomic and physiologic urinary tracts for recurrence of infection and, when identified, treat the infection promptly. For patients who have intractable urinary tract infections (eg, ileal conduit diversion), using the urease inhibitors helps in decreasing the incidence of stone recurrence.

**Additional Readings**

Patient with INFECTION STONES

A History

B Stone Removal

C Stone analysis

D Metabolic evaluation of the patient

E Metabolic disease

Correction of underlying disorder

Medical management based on specific stone type

F Observation

No metabolic disease identified

Urine culture and sensitivity Radiologic studies
A Patient presenting with renal calculi may be either symptomatic or asymptomatic. A stone obstructing the ureteropelvic junction typically causes severe flank pain with or without nausea and vomiting. If there is concomitant infection, the patient may present with fever or clinical manifestations of sepsis. In this instance, the patient should undergo immediate urinary diversion, via either antegrade or retrograde stenting, and be started on appropriate antibiotic therapy. Patients whose pain cannot be controlled with oral analgesics or who present with anuria (likely owing to a stone in a solitary kidney) must be hospitalized and undergo prompt, if not immediate, intervention. Incidentally found renal calculi (on radiographic imaging done for an unrelated complaint) are usually asymptomatic and nonobstructing.

If infection is evident, obtain a urine culture and begin appropriate antibiotic therapy. Hematuria is frequently seen in association with urolithiasis but is not necessary for the diagnosis. A pH of 8 suggests an infection stone, whereas a pH in the range of 5.5 to 6 may be secondary to a uric acid stone. On microscopic examination, cystine crystals have a classic hexagonal shape.

Plain film of the abdomen, intravenous pyelogram, retrograde pyelogram, ultrasonography, computed tomography (CT), radionuclide studies, and magnetic resonance imaging (MRI) can all be utilized in the work-up of a patient presenting with renal colic. Physician preference usually directs the modality chosen. Patients presenting to the emergency department will often undergo spiral CT because of its speed, sensitivity, and specificity.1

Determination of the size and number of stones present is paramount as this is usually the most important factor guiding further therapy.2

B Patients presenting with a urinary pH < 6 or a history of cystine or uric acid stones should undergo a trial of dissolution therapy.

C The majority of patients with stone burden < 1 cm in total diameter may be managed successfully with extracorporeal shock wave lithotripsy (ESWL) regardless of stone composition or location.3–6 The need for indwelling ureteral stenting post-ESWL is generally accepted for larger stones, allowing fragments to pass without causing significant obstruction.7–9 ESWL is also used to treat most stones between 1 and 2 cm, although stone composition and location (lower pole) can significantly decrease stone-free outcomes.10,11 Percutaneous nephrolithotomy (PCNL) and ureterorenoscopy (URS) both have good results in treating hard or lower pole stones 1 to 2 cm in size.12,13 Anatomic lower pole configurations have been speculated to be factors in poor outcome, specifically the infundibular width, length, and angle in relation to the renal pelvis and ureter.12,14,15 The recommended primary treatment of lower pole stones > 1 cm is PCNL.12,16 Stones that fail ESWL owing to composition (eg, cystine, calcium oxalate monohydrate, and calcium phosphate dihydrate stones) should undergo PCNL with or without subsequent ESWL.10,11,17,18

D The 1988 National Institutes of Health (NIH) Consensus Conference recommended that stones larger than 2 cm should be initially treated with PCNL followed by ESWL if necessary.19 Advancement in the technology of URS has popularized its use in this patient population.20–24 However, it has been recommended that PCNL should remain the primary treatment unless special indications dictate the need for URS.24

E Bulky staghorn calculi or any stone associated with an anatomic abnormality requires more extensive intervention. Historically, these were treated only with open surgical removal with correction of the anatomic abnormality.25,26 More recently, the recommendation has been expanded to PCNL with or without ESWL or open surgery.14,27–37 According to one survey, the majority of responding urologists perform PCNL for the initial treatment of staghorn calculi.

F ESWL is not recommended in the case of distal obstruction. Patients with associated ureteropelvic junction (UPJ) obstruction may be treated with either combined open/laparoscopic pyeloplasty and pyelolithotomy or combined PCNL and antegrade endopyelotomy.36

Calyceal diverticula and contained stones may be treated with open repair of the diverticula and stone extraction or PCNL and endoscopic correction of the offending infundibulum.36,38 Ureteroscopic treatment may also be possible if the diverticulum is of a mid- or upper pole calyx and the stone burden is small.39,40 When endoscopic approaches fail and the stone is contained within a large anterior diverticulum with little overlying parenchyma, laparoscopic diverticulectomy may be performed.41–43 ESWL is generally performed only when the neck of the infundibulum is large.44–48
Patient with SUSPECTED RENAL CALCULI

A
History
Physical examination
Urinalysis
Imaging

B
Suspected cystine or uric acid stone
Trial of dissolution therapy

C
< 2 cm
ESWL

D
> 2 cm
PCNL with/without ESWL vs URS

E
Bulky staghorn

F
Special cases
ESWL vs PCNL vs URS vs open surgery

G
Stone analysis
Medical therapy

PCNL vs URS

Open surgery vs PCNL with/without ESWL

Unfavorable anatomy or > 1 cm
Solitary kidney
Bleeding diathesis
Morbid obesity

Favorable anatomy or < 1 cm

< 2 cm

> 2 cm

Location

Upper/midpole calyx
Renal pelvis

Lower pole calyx

PCNL vs URS

Open surgery

PCNL vs URS
Nephrolithiasis associated with a horseshoe kidney can be treated by prone ESWL if the stone burden is small and the collecting system has relatively normal anatomy.49 Although the option of URS in selected cases has been entertained, PCNL is the treatment of choice for large stones or in kidneys with poor drainage (eg, UPJ obstruction).50-52

In patients with a small stone in a solitary kidney, ESWL with ureteral stenting may be considered first-line therapy.53 ESWL failures or larger stones can be treated with URS. PCNL is reserved only for staghorn calculi or previous treatment failures.54

Patients with renal ectopia, specifically within the pelvis, and stones should be initially treated with prone ESWL.58 If ESWL fails or is deemed inappropriate, open, laparoscopic, or URS approaches can be considered.56,57

Body mass index has been shown to be a significant factor in the outcome of ESWL.58 Morbidly obese patients often exceed the safety limits of the lithotripsy gantry or table. Also, the increased distance to the stone and difficulty visualizing the stone during ESWL render this a less than satisfactory mode of therapy. PCNL is also a technologically difficult procedure in such patients, requiring special, longer instruments.59 URS is often the preferred treatment of obese patients with nephrolithiasis as it can be done without special instruments or new techniques.56,60

Severe scoliosis and musculoskeletal contractures can restrict the ability to accurately focus renal stones for effective ESWL. PCNL and URS can both be considered for treatment.

Bleeding diatheses in patients with stones must be corrected prior to treatment with ESWL or PCNL.61 If the coagulopathy cannot be corrected, URS with holmium laser lithotripsy is recommended.62

G The reported recurrence rate of first-time stones is 50%.63 Therefore, it is recommended that patients undergo evaluation for a treatable cause of stone disease, which is found in up to 97% of patients.64 A detailed history assessing diet and fluid intake, previous urinary tract infections, activity, medical conditions, prior surgeries, and familial urinary disease should be taken. A metabolic stone work-up is performed to identify factors that may predispose the patient to stone formation. Appropriate medical therapy can then be instituted.

The goal of treatment of renal calculi is to eliminate stone burden with minimal morbidity. Prompt patient evaluation with history, physical examination, and adequate radiographic imaging is paramount in preventing further suffering and renal injury. A multitude of potential algorithms is available to the urologist. Careful consideration of the stone burden, composition, and location, as well as the patient’s informed preferences and comorbidities, should guide the treatment of renal stone disease.

References


Ureteral stones originate in the kidney and become obstructed during passage through the ureter. Most stones that enter the ureter are small enough to pass; however, some stones are too large to pass and lodge in the ureter. The ureteropelvic junction, the ureterovesical junction, and the crossing of the ureter over the iliac vessels are the narrowest parts of the ureteral lumen and are the locations of most impacted ureteral stones. Diagnosis of a ureteral stone and clinical assessment of the patient for possible urgent intervention is essential before observing the patient for spontaneous stone passage or treating the stone with extracorporeal shock wave lithotripsy (ESWL), endoscopic technique, or nephroscopic or open surgery.

**A** Patients with urolithiasis most commonly present with renal colic, abrupt onset of severe paroxysmal pain on the affected side. The pain usually originates in the flank or lower abdomen and may radiate to the ipsilateral groin and scrotum or labia. This is a visceral pain, resulting from ureteral obstruction, and fluctuates with ureteral peristalsis. The obstructed ureter produces prostaglandins, which stimulate ureteral peristalsis to aid in stone passage. There is often microscopic or gross hematuria owing to the abrasive effect of the stone on the urothelium. Patients with stones may also present with infection that is complicated by the ureteral obstruction, resulting in dysuria, fever, leukocytosis, and sepsis. Incidental stones may also be found radiographically during the evaluation of another process.

Evaluation of a suspected ureteral stone begins with a complete history and physical examination. Past medical history can reveal previous episodes of nephrolithiasis as well as metabolic and dietary risk factors for stone disease. Bone disease, gout, or family history of stone disease can also increase the risk of stone disease. Strenuous exertion or outdoor activity in warm climates can lead to dehydration, predisposing a person to stone formation. Excess dietary intake of calcium, oxalate, or protein and low fluid consumption can also result in urinary calculi. Chemical composition of previous stones, if known, can give clues to the type of stone at current presentation as well as the underlying etiology of stone formation and recurrence.

Physical examination is often nonspecific for stone disease. Patients usually have palpable costal-vertebral angle tenderness as well as tenderness in the ipsilateral lower abdomen. Gross examination of the urine may reveal hematuria and possibly stone debris, or even the causative stone.

Urinalysis frequently shows hematuria, including red and white blood cells. Stone crystals may also be seen on microscopic evaluation. The presence of a large number of leukocytes, bacteria, or nitrites may indicate a concurrent urinary tract infection, which may warrant immediate decompression of the upper urinary tract obstruction. If infection is suspected, a complete blood count should also be obtained to assess for systemic leukocytosis indicative of impending sepsis. Patients with preexisting renal function impairment or a solitary functioning kidney should have a serum creatinine checked to determine if renal function is acutely compromised.

**B** Radiographic evaluation is based on the acuity of stone disease and the overall clinical picture of the patient. Nonenhanced spiral computed tomography (CT) is the standard study for emergency evaluation of acute flank pain. It is quick, does not require bowel preparation or intravenous contrast exposure, has high sensitivity and specificity for calculi, and can reveal nonurologic etiologies of pain simulating renal colic from ureteral calculi.

A KUB shows the relative position of a calculus to adjacent bony and visible soft tissue structures. The KUB can also be used to determine if a previously seen stone has progressed or passed.

Intravenous urogram (IVU) is useful for evaluating the location of the stone in the urinary tract, as well as the severity of obstruction from the calculus. This study provides anatomic and qualitative functional information about the kidneys and can be used to find possible etiologies of stone formation owing to anomalous anatomy and function.

**C** After the preliminary diagnostic evaluation, including basic laboratory studies and imaging, the patient can be assessed for the need of urgent or elective management. Urgent surgical intervention is indicated for sepsis, persistent pain, and urinary tract obstruction as would occur with bilateral obstructive calculi, or an obstructive calculus in a solitary functioning renal system.

If the patient’s clinical condition is stable and the pain is tolerable with oral analgesic medication, the ureteral stone can be observed for spontaneous passage. Rates of spontaneous stone passage depend on stone size and the location of the stone in the ureter. Coll and colleagues reported the following spontaneous passage...
Patient with SUSPECTED URETERAL CALCULI

A. History
   Physical examination

B. Imaging

Ureteral stone
   - Sepsis, pain, or urinary tract obstruction
     - Urgent urinary tract decompression
   - Stable
     - Observation
       - Lack of stone progression
         - Spontaneous stone passage
       - Elective stone surgery

No stone
   - Reassess diagnosis

C. Observation

D. Urgent urinary tract decompression

E. Elective stone surgery

F. Stone analysis
   - Medical therapy and follow-up
rates in relation to diameter of the stones: 1 mm, 87%; 2 to 4 mm, 76%; 5 to 7 mm, 60%; 7 to 9 mm, 48%; and for stones larger than 9 mm, 25%.6 Passage rate for stones located in the proximal, mid-, and distal ureter, and ureterovesical junction are 48%, 60%, 75%, and 79%, respectively.6

**D** Urgent intervention is indicated for urosepsis, severe ureteral obstruction, uncontrollable pain, persistent gross hematuria, lack of stone progression, and patients employed in a profession where an episode of renal colic could be dangerous.

Sepsis associated with urinary tract obstruction is a urologic emergency that requires prompt decompression of the obstructed system. This can be done by cystoscopic passage of a ureteral stent or by percutaneous placement of a nephrostomy tube. Ureteral stents can cause more irritative symptoms than percutaneous nephrostomy tubes, require more frequent analgesic administration, use more x-ray exposure for insertion, and remain in place longer after stone treatment.7 A lower quality of life with ureteral stents is especially pronounced in males and younger patients.7 Ureteral stenting may, however, offer better success of stone clearance after ESWL than nephrostomy tube placement.8 Additionally, intravenous antibiotics should be employed to clear the infection. Once the sepsis has resolved and the urine is confirmed sterile by culture, elective stone treatment and removal can be performed.

**E** ESWL, endoscopic, or open surgery can be planned to remove the calculus if observation fails to result in spontaneous passage. Indications for intervention with ureteral calculi include intolerable or intractable symptoms, infection, obstruction, and a stone that is unlikely to pass spontaneously.2 Ureteroscopy with intracorporeal lithotripsy is more commonly used for distal ureteral calculi. This modality is also more effective for treating proximal ureteral stones than ESWL; however, ESWL is useful for proximal stones < 10 mm owing to lower morbidity and anesthesia requirement than with ureteroscopy.9 Open stone surgery is rarely indicated for ureteral stones but may be considered for patients with multiple ureteral stones, failed endoscopic treatment or ESWL, concurrent abdominal surgery, or abnormal anatomy that prevents ureteroscopy.5

**F** After recovery from either spontaneous passage or stone removal, a metabolic work-up identifies factors predisposing to stone formation. Stone analysis should be performed and appropriate therapy instituted.

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**References**

SECTION 8
THE URETER
A The findings of bilateral dilation of the upper urinary tracts, in association with a markedly distended bladder that does not empty completely on real-time ultrasonography suggests prune-belly syndrome (PBS). These anatomic abnormalities may be seen as early as 15 weeks of gestation. In utero intervention, with placement of a vesicoamniotic shunt to decompress the urinary tract and alleviate oligohydramnios, may prevent pulmonary hypoplasia, although renal function may not be affected (Figure 71-1).

B The typical features of PBS allow for an obvious postnatal diagnosis (Figure 71-2A, 71-2B). The constellation of findings that include a deficiency in abdominal musculature of the lower abdomen, bilateral nonpalpable testes, and an abnormal urinary tract, characterized by tortuous, dilated ureters, by an enlarged bladder, and by a dilated prostatic urethra, are typical of Eagle-Barrett syndrome or the triad syndrome. The incidence of PBS is estimated to equal that of extrophy of a bladder (1 of 40,000 live births). It represents a spectrum of disease, with the severe end associated with profound oligohydramnios, leading to pulmonary hypoplasia and renal dysplasia. Others may have significant urinary tract pathology but renal function that is relatively normal. In the absence of chronic or recurrent urinary tract infections, these patients can thrive in stable coexistence with their uropathy. Evaluating a newborn found with PBS would include a renal and bladder sonogram to provide a baseline assessment of the upper urinary tracts, as well as the bladder and its associated emptying. A voiding cystourethrogram study may document evidence of vesicoureteral reflux, a larger than normal bladder capacity with an open bladder neck, and dilated prostatic urethra, which narrows in the membranous area. A urachal diverticulum may be present at the bladder dome. Valvular obstruction, in conjunction with PBS, is rare. The presence of megalourethra is seen more frequently in PBS than in other conditions. This can include the megalourethra of either fusiform or scaphoid types.

C PBS patients who have normal renal function may benefit from early abdominoplasty, using either the Monfort or the Randolph technique (Figure 71-3). Both of these techniques adequately reconstitute the patient’s waistline and can be combined with bilateral orchiopexies. In addition to the cosmetic benefits and exposure for genitourinary reconstruction, abdominoplasty seems to improve voiding efficiency. Major urinary tract reconstruction can be undertaken at the same time. This approach allows for excellent exposure of the gonadal vessels and, when performed early, can be done without division of the spermatic vessels. Alternatively, consider a Fowler-Stephens technique where the spermatic vessels are divided and the blood supply is then based on the deferential vessels. Testicular biopsies of PBS patients have demonstrated the presence of germ cells and Ad spermatogonia. Isolated reports now exist about the use of assisted reproductive techniques that allow for sperm retrieval.

D For those patients who have impaired renal function, the emphasis is on ensuring that there is no evidence of
obstruction and on preventing urinary tract infections that can cause further detriment to compromised kidneys. Using diuretic renography can help assess the differential function and washout from the kidneys. To prove that there is appropriate washout from the dilated ureters, however, can be somewhat more problematic. High diversion would be rarely indicated, but cutaneous pyelostomies may be performed if the systems are redundant and stagnant. End cutaneous ureterostomy can be performed if a single ureter is obstructed. Complete lower urinary tract reconstruction, including ureteral tapering and reimplantation along with reduction cystoplasty, can improve ureteral peristalsis and can reduce the postvoid residual.\textsuperscript{14}

**E** Urethral abnormalities that require early attention may also be present. To facilitate bladder drainage, urethral atresia will warrant an early postnatal vesicostomy. With stabilization of renal function and the absence of urinary tract infections, patients can be maintained in this fashion for several years. Often antibiotic prophylaxis will be necessary to minimize the chance of urinary tract infections, owing to the stasis in the ureters. Then embark upon judicious use of urethral dilation. Even with minimal patency to the urethra, place a guidewire initially under endoscopic guidance and then advance a small ureteral catheter through the urethra and out through the vesicostomy. Over a period of many weeks, progressive dilation of the urethra can be accomplished.

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**Figure 71-2** Typical appearance of infant with prune-belly syndrome (PBS) (A). Close-up view of patent urachus seen in patient with urethral atresia and PBS (B).

**Figure 71-3** Appearance of patient (see Figure 71-2A) who underwent Monfort abdominoplasty and bilateral orchidopexies at 3 months of age. He required vesicostomy as newborn secondary to urethral atresia.
Prune-Belly Syndrome

with patience,\textsuperscript{15} This has resulted in normalization of the urethral caliber and in subsequent vesicostomy closure. In the face of a dilated proximal urethra, a urethrotomy of the membranous urethra has been performed, which can facilitate bladder emptying.\textsuperscript{16,17} This procedure is meant to reduce the normal urethral outlet resistance and to provide for balanced voiding. By using these principles, the surgeon can repair a megalourethra in much the same way as hypospadias surgery.

\section*{References}

Megauereter refers to a ureter that is too wide. Numerous disorders can cause ureteral dilatation (typically > 7 mm); these are listed in Table 72-1. A methodical evaluation can provide the correct diagnosis in most cases.

Primary obstructed megaureter and nonobstructed megaureter probably represent opposite extremes of a spectrum of the same anomaly. The primary obstructed megaureter results from abnormal development of the distal ureter, with collagenous tissue replacing the muscle layer. There is disruption of normal ureteral peristalsis, and the proximal ureter widens. Usually a ureteral catheter will pass through the distal segment without difficulty, but in some cases there is a true stricture. On sonogram, the ureter can be quite wide, and there is a variable degree of hydronephrosis. On intravenous urogram, the distal ureter is more dilated in its distal segment and tapers abruptly at or above the ureterovesical junction. The lesion may be unilateral or bilateral. Dilatation of the upper collecting system and calyceal blunting are suggestive of obstruction, but this needs to be confirmed with diuretic renography.

Megauereter predisposes to urinary tract infection (UTI), stones, and flank pain because of urinary stasis.

In most cases, diuretic renography and sequential sonographic studies can reliably differentiate obstructed from nonobstructed megaureters. Most megaureters diminish in size over time, with resolution or significant reduction of hydronephrosis in as many as 85%. Obstructed megaureters require surgical treatment, with excision of the narrowed segment, ureteral tapering, and reimplantation of the ureter. The results of surgical reconstruction are usually good, but the prognosis depends on preexisting renal function and whether complications develop.

A Megauereters are usually discovered through screening ultrasonography of the kidneys and bladder because of a prenatal diagnosis of hydronephrosis or postnatal UTI, hematuria, or abdominal pain. A careful history, physical examination, and voiding cystourethrography identify causes of secondary megaureters and refluxing megaureters as well as the prune-belly syndrome.

B If the voiding cystourethrogram (VCUG) shows no reflux, then follow-up evaluation depends on the grade of the hydronephrosis. The Society for Fetal Urology grading scale is used (Table 72-2):

### Table 72-1 Classification of Megaureter

<table>
<thead>
<tr>
<th>Refluxing</th>
<th>Secondary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary</td>
<td>Neuropathic bladder</td>
</tr>
<tr>
<td>Primary reflux</td>
<td>Hinman syndrome</td>
</tr>
<tr>
<td>Megacystis-megaureter</td>
<td>Posterior urethral valves</td>
</tr>
<tr>
<td>Ectopic ureter</td>
<td>Bladder diverticulum</td>
</tr>
<tr>
<td>Prune-belly syndrome</td>
<td>Postoperative</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Obstructed</th>
<th>Secondary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary</td>
<td>Neuropathic bladder</td>
</tr>
<tr>
<td>Intrinsic (&quot;primary obstructed megaureter&quot;)</td>
<td>Hinman syndrome</td>
</tr>
<tr>
<td>Ureteral valve</td>
<td>Posterior urethral valves</td>
</tr>
<tr>
<td>Ectopic ureter</td>
<td>Ureteral calculus</td>
</tr>
<tr>
<td>Ectopic ureterocele</td>
<td>Extrinsic</td>
</tr>
<tr>
<td>Postoperative</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Nonrefluxing, Nonobstructed</th>
<th>Secondary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary</td>
<td>Diabetes insipidus</td>
</tr>
<tr>
<td>Nonrefluxing, nonobstructed (&quot;primary megaureter&quot;)</td>
<td>Infection</td>
</tr>
<tr>
<td></td>
<td>Persistent after relief of obstruction</td>
</tr>
</tbody>
</table>

### Table 72-2 Renal Sonogram*

<table>
<thead>
<tr>
<th>Grade of Hydronephrosis</th>
<th>Central Renal Complex</th>
<th>Renal Parenchymal Thickness</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Intact</td>
<td>Normal</td>
</tr>
<tr>
<td>1</td>
<td>Slight splitting</td>
<td>Normal</td>
</tr>
<tr>
<td>2</td>
<td>Evident splitting, complex confined within renal border</td>
<td>Normal</td>
</tr>
<tr>
<td>3</td>
<td>Wide-splitting pelvis</td>
<td>Uniformly dilated</td>
</tr>
<tr>
<td></td>
<td>diluted outside renal border</td>
<td></td>
</tr>
<tr>
<td></td>
<td>and calyces (calyces may appear convex)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Further dilatation of pelvis</td>
<td>Thin</td>
</tr>
</tbody>
</table>

Primary Megaureter in Children

Child with MEGAURETER

History
Physical examination
Urinalysis

A
VCUG

B
No Reflux

C
Grade 4 hydronephrosis

Follow-up sonogram in 3–6 mo

D
Ureteral reimplantation with tapering

Reflux

Primary reflux

Antibiotic prophylaxis or surgery

Ectopic ureter

Surgical repair

Primary megaureter with reflux

Grade 1, 2, or 3 hydronephrosis

Antibiotic prophylaxis
Circumcision

Grade 4 hydronephrosis

Antibiotic prophylaxis
Circumcision

No reflux

No Reflux

Primary reflux

Antibiotic prophylaxis or surgery

Ectopic ureter

Surgical repair

Primary megaureter with reflux

Grade 1, 2, or 3 hydronephrosis

Antibiotic prophylaxis
Circumcision

Follow-up sonogram in 3–6 mo

No hydronephrosis

No obstruction

Obstruction

Stop; no follow-up

Antibiotic prophylaxis

No hydronephrosis

Flank pain, UTI, stone disease

MAG-3 diuretic renogram

No obstruction

Obstruction

History
Physical examination
Urinalysis

No obstruction

Obstruction

Antibiotic prophylaxis
Circumcision

Stop; no follow-up

Antibiotic prophylaxis
With grade 1, 2, or 3 hydronephrosis and a nonrefluxing megaureter, it is quite unusual for obstruction to be present. Antibiotic prophylaxis is prescribed for children with grade 2, 3, or 4 hydronephrosis. In the neonate, amoxicillin or cephalexin is prescribed. Beyond 2 months of age, trimethoprim/sulfamethoxazole, trimethoprim, or nitrofurantoin is used. In addition, circumcision in boys is recommended to minimize the risk of UTI. Prophylaxis should be continued until the hydronephrosis grade decreases to 0 or 1.

C In a MAG-3 diuretic renogram, a small dose of technetium-labeled MAG-3 is injected intravenously. During the first 2 to 3 minutes, renal parenchymal uptake is analyzed and compared, allowing computation of differential renal function. Subsequently, excretion is evaluated. After 20 to 30 minutes, furosemide is injected intravenously, and the rapidity and pattern of drainage from the kidneys to the bladder are analyzed. If no obstruction is present, half of the radionuclide should be cleared from the renal pelvis within 10 to 15 minutes; this represents the half-life or $T_{1/2}$. If there is significant upper tract obstruction, the $T_{1/2}$ is generally greater than 20 minutes. A $T_{1/2}$ between 15 and 20 minutes is indeterminate. The images generated usually provide an accurate assessment of the site of obstruction. Numerous variables affect the outcome of the diuretic renogram. For example, newborn kidneys are functionally immature, and in some cases normal kidneys may not demonstrate normal drainage following diuretic administration. Dehydration prolongs parenchymal transit and can blunt the diuretic response. Giving an insufficient dose of furosemide may result in inadequate drainage. If vesicoureteral reflux is present, continuous catheter drainage is mandatory to prevent radionuclide from refluxing from the bladder into the dilated upper tract, which would prolong the washout phase. Because of the numerous variables, the Society for Fetal Urology and the Pediatric Nuclear Medicine Club jointly developed a standardized method for performing diuretic renography in infants and children, termed the “well-tempered renogram.” The MAG-3 diuretic renogram is considered superior to the excretory urogram in infants and children with hydronephrosis because bowel gas and immaturity of renal function often cause the intravenous pyelogram (IVP) images to be suboptimal. In addition, the diuretic renogram provides an objective assessment of the relative function of each kidney.

D When a megaureter is repaired, several surgical options are available. The key aspects are to excise the adynamic segment or distal ureteral stricture and to tailor the ureter sufficiently to achieve a 4:1 to 5:1 length-to-width ratio in the intramural tunnel. The ureter may be tailored by excisional tapering or by plication. With tapering, the Hendren technique generally is used. Allis clamps are placed laterally to define redundant ureter while preserving the medial vascular supply of the ureter. A 10F or 12F catheter is kept in the ureter. The ureter is tapered to a level several centimeters above the bladder. The ureter typically is reimplanted with a psoas hitch to allow a long intramural tunnel. In some centers an extravesical approach is used with excellent results. The ureter is stented for 1 to 2 weeks postoperatively. The ureter also may be tailored using the Starr or Kalicinski plication techniques; these should not be used for extremely wide ureters.
Additional Readings


The major morbidities caused by primary congenital vesicoureteral reflux (VUR) in both sexes are hypertension and renal insufficiency—in children and later in adulthood. In addition, maternal reflux during pregnancy is associated with higher rates of perinatal maternal urinary tract infection (UTI), pyelonephritis, premature labor, and fetal loss. Many data exist to suggest that the recognition and management of VUR have considerably reduced the incidence of these morbidities in contemporary populations. Thus, it is important to remain aware of the demographics of presentation and the means of diagnosis. Finally, although management, both medical and surgical, continues to change and evolve, the underlying principles remain the same. This chapter serves to outline the major aspects of diagnosis and treatment.

Pathophysiology
The backwards flow of urine from the bladder to the kidney is not normal in humans, although it is normal in several animal species. Further, it is not normal at any age, even in premature newborns. The mechanism that prevents reflux is the flap-valve, created by the ureter as it traverses between the bladder mucosa and the muscle at the ureterovesical junction (Figure 73-1A). It is believed that most children born with VUR have anatomic deficiencies at this junction (Figure 73-1B). Voiding dysfunction in utero—abnormalities of the bladder and the sphincteric innervation and coordination—may also play a role in some children being born with reflux by causing higher than normal voiding pressures. These pressures can overcome a minimally competent valve or may deform the valve, resulting in reflux. Children can outgrow reflux, either because the flap-valve elongates with growth and becomes functional or because voiding dysfunction improves over time, thereby lowering voiding pressures. Both factors may also improve with growth and maturation.

Vesicoureteral reflux can cause “reflux nephropathy” or renal scarring seen radiographically as defects in the renal parenchyma—thinning of the cortical mantle (Figure 73-2). Some children with high-grade reflux are born with these defects, which histologically contain elements of renal dysplasia. As a result, in a minority of instances, high-grade VUR associates with renal developmental anomalies, which occurred prenatally. Most renal scars, however, are a result of postnatal pyelonephritis. Loss of the antireflux mechanism allows bacteria to more easily ascend from the bladder and cause serious kidney infections. Reflux without infection, regardless of grade,
Patient with VESICOURETERAL REFLUX

A  Children with history of UTI
    Sibling with reflux
    Prenatal hydronephrosis
    Voiding dysfunction
    (older, toilet-trained children)

B  Imaging studies:
    VCUG
    Renal, bladder ultrasonography
    Radionuclide renal scan
    (only if reflux found)

Initial recommendations (if reflux present):

C  Medical management
    Grades I, II, II
    Grades IV, V (< age 4 years)
    Daily prophylactic antibiotics
    Correction of toilet habits
    Urine cultures every 4 months
    Repeat VCUG every 18 months

Surgical management
    Grades IV, V
    (> age 4 years)
    Breakthrough infection
    Poor compliance
    Antibiotic intolerance
    Family preference
    Reaching adolescent age
is harmless to the kidney. These infection-related scars can be the source of renin-mediated hypertension, and if extensively present bilaterally, they cause renal insufficiency.

A Children with primary reflux can present in several ways: (1) with UTI, (2) as asymptomatic siblings, (3) as newborns with abnormal prenatal sonograms, or (4) as older toilet-trained children with voiding dysfunction. Most children with VUR present with a UTI, either symptomatic or asymptomatic. Children with either febrile infections or simple cystitis are at risk for reflux. Up to 50% of all boys or girls—even after one infection—can have reflux. Voiding dysfunction often coexists in these children. VUR is inherited as an autosomal dominant trait with variable penetrance, so up to one-third of asymptomatic siblings who have no history of infection may also have reflux. After finding that one child in the family has VUR, clinicians recommend that siblings be screened; however, the sibling age at which screening should be stopped is controversial. The most common cause of prenatally detected hydronephrosis is VUR; thus, clinicians should evaluate all newborns with this history for reflux, even if the postnatal sonogram shows no hydronephrosis. Finally, older children who are well beyond the age of toilet training and who still have daytime wetting, even without a history of UTI, may also have associated VUR, thus requiring evaluation. As already mentioned, abnormally high voiding pressures in these children can be associated with reflux. These children tend to hold both urine and stool for long periods of time and are often constipated as well. Obtain a toileting history from every child with reflux, with or without a history of associated UTI.

B No reliable noninvasive means of diagnosing reflux exists. A voiding cystourethrogram (VCUG) in an awake child, which requires catheterization, is necessary. Other studies that avoid catheterization, such as renal sonograms or radionuclide renal scans, will exclude many children with VUR. Most often, a renal and bladder sonogram accompanies the VCUG in any evaluation of a child’s urinary tract because other congenital urologic anomalies may exist. Either iodinated contrast or a radionuclide can be instilled during a VCUG, but it is the contrast cystogram that provides the grade of reflux, using the International Scale of Vesicoureteral Reflux (Figure 73-3). Reflux is graded on a scale of 1 to 5. Renal scarring is best seen with radionuclide imaging, which should be obtained after ascertaining the presence of VUR to see if any reflux nephropathy exists.

C The principles of management include (1) sterile reflux is not harmful to kidneys and has no clinically significant effect upon kidney function, (2) children can outgrow reflux, although this is more likely in the lower grades, and (3) continuous low-dose antibiotic prophylaxis can be maintained for many years while reflux is present and is as effective as antireflux surgery in protecting kidneys from ascending UTI.

The likelihood of spontaneous cessation with growth is grade dependent (Table 73-1); as a result, most children with low-grade reflux (Grades I, II, III) are immediately placed on low-dose, continuous daily antibiotic prophylaxis. The most common agents prescribed are trimethoprim-sulfamethoxazole and nitrofurantoin. Spontaneous cessation may take years and might not occur until adolescence; for this reason, families must be prepared to stay on medication for a long time. Further, these children must have surveillance urine
cultures approximately three times yearly, and the VCUG is repeated every 18 months. Hence, compliance with such a regimen is key to its success. Reluctance to remain on a long-term regimen and “breakthrough” infection are reasons to recommend corrective surgery. Higher-grade reflux (Grades IV, V) can resolve over time in a few children, but this is more likely in infants under the age of 2 years. In older children—especially older than age 4 or 5 years—this likelihood diminishes. Long-term antibiotic prophylaxis is acceptable in these children, but make families aware that reflux most likely will persist, thus necessitating surgery. Finally, once an adolescent reaches adult height, spontaneous cessation is also unlikely.

Inquire about and suggest altering voiding and overall toileting dysfunction, if possible. Encourage patients who void infrequently to void more often. Treat constipation by instituting changes in diet and medication, if necessary.

There are many available alternatives for surgical correction, and this is an evolving area of investigation and innovation. The standard for surgical correction is open ureteral reimplantation by various methods. These techniques all recreate the natural “flap-valve” mechanism within the bladder (Figure 73-4). Surgical success rates approach 98%, especially in the lower grades. More recently, cystoscopic procedures not requiring an abdominal incision or prolonged hospital stay have been devised. When performing these procedures, surgeons use a bulking agent, which is injected, under direct vision, near the refluxing ureteral orifice. By compressing the orifice and changing its shape, reflux is stopped. These agents include polytetrafluoroethylene (Teflon) paste, cross-linked bovine collagen, polydimethylsiloxane paste (Macroplastique), and dextransomer microspheres (Deflux). The success rates are not as high as those with open surgery, nor are they as durable. There are relatively few long-term studies. These procedures are performed on a 1-day stay ambulatory basis and can be repeated if reflux persists.

### Additional Readings


Ureteroceles are cystic dilations of the terminal portion of the ureter distal to its entry into the bladder. In children, ureteroceles are most commonly associated with a duplicated collecting system. The orifice of the ureterocele is usually stenotic, and obstruction is almost always present. Ureteroceles occur four to seven times more frequently in females and are more common in Caucasians. Bilateral ureteroceles are identified in 10% of cases.

A The majority of ureteroceles are now identified prenatally. The natural history of the asymptomatic ureterocele is unknown, but, historically, most ureteroceles presented with infections. Imaging is obtained as part of a postnatal evaluation of antenatally detected hydronephrosis or evaluation of urinary tract infections or because of physical examination abnormalities.

The radiologic evaluation usually includes a sonogram, voiding cystourethrogram (VCUG), and renal scan. A sonogram typically reveals a well-defined cystic intravesical mass that is associated with the posteri or bladder wall. This can be followed into a dilated ureter in the bony pelvis. A duplex renal unit with upper pole hydroureteronephrosis is usually present. The thickness and echogenicity of the renal parenchyma should be evaluated because ureteroceles are often associated with dysplasia and poor function.

A VCUG is obtained in all patients. Up to 50% of the ipsilateral lower pole and 25% of the contralateral renal units have vesicoureteral reflux.1 With poor detrusor support, the ureterocele may evert with voiding and mimic a diverticulum, or the periureteric weakness may give the appearance of a Hutch diverticulum. Rarely, the thin ureterocele will intussuscept back into the large ureteral hiatus without reflux up to the kidney.

Renal scans may be used to evaluate the function of all renal segments. Most of the obstructed upper pole segments will contribute less than 5 to 10% of total renal function. This may serve as a preoperative baseline but is not a good predictor of the degree of recoverable renal function, which is usually negligible. Sen and colleagues reported the largest review of functional and anatomic findings.1

B The current recommended nomenclature classifies ureteroceles as either intravesical (entirely within the bladder) or ectopic (some portion is situated permanently at the bladder neck or in the urethra).2 Observation without antibiotics has been successful in a small number of patients with only the ureterocele moiety affected.3 The infection rate is relatively low in children placed on preventive antibiotics pending surgical intervention (3 to 8%).4,5 Ureterocele decompression in the neonatal period does not necessarily decrease the infectious complications (9% in one series).3

C Single-system ectopic ureteroceles are very rare. Because of the ectopic ureteral position distal to the bladder neck, the function of the affected moiety is almost always poor. A nephroureterectomy is usually the definitive procedure in these children as long as contralateral reflux is not present. Most single-system ureteroceles are intravesical and have excellent function. Several reports show that endoscopic incision is a definitive procedure in single-system intravesical ureteroceles.6,7 This is presumably related to significantly better detrusor support and a low incidence of iatrogenic reflux after incision.

D Most ectopic ureteroceles are associated with the upper pole moiety of a duplex system. The ureterocele moiety may be the isolated abnormality, or the ipsilateral lower pole or contralateral unit may be affected. This variability increases the potential complexity of the anomaly. Because of the variability, many management options exist.

E Early intervention is indicated in the presence of bladder outlet obstruction or urosepsis. In general, bladder outlet obstruction is rare because most ureteroceles decompress during micturition. Hydronephrosis of the ipsilateral lower pole or the contralateral renal moiety in the absence of reflux should increase the suspicion of bladder outlet obstruction. Most children that present with a febrile urinary tract infection improve on antibiotics, but if fevers are unrelenting or the infant is toxic in appearance, decompression of the ureterocele is indicated. The most expeditious technique is endoscopic incision. An upper pole partial nephrectomy is equally successful but is a potentially major undertaking in a sick infant.

F The presence of vesicoureteral reflux increases the potential complexity of ureterocele management. This reflux is usually higher grade and may be into the lower pole of a duplicated system. This reflux rarely resolves and may be a risk factor for recurrent urinary tract infections. Management options include endoscopic incision, upper pole partial nephrectomy, or complete
reconstruction. With the first two options, lower tract pathology (reflux and ureterocele) is observed while the child is maintained on preventive antibiotics. If infections occur or high-grade reflux persists, a subsequent lower tract reconstruction is performed.

It is now apparent that an initial upper tract approach should usually be reserved for patients with only low-grade or absent reflux. Historically, an upper pole partial nephrectomy was the initial procedure of choice for all ureteral duplications and ureteroceles (the simplified approach). Nearly all of the ureter can be removed through the flank incision, and in the absence of reflux into the ureterocele, the distal ureter is left open to facilitate decompression. If there is preserved upper pole function, it can be preserved with a ureteropyelostomy,
but this can be technically challenging. Ureteropelvostomy is associated with a higher reoperative rate than upper pole partial nephrectomy and potentially places the lower pole ureter and pelvis at risk. Vascular injury to the lower pole of the kidney is a potential complication with both approaches. Large series show that the need for additional surgery after an upper tract approach is directly related to the number of renal moieties with reflux.1,6,8 If no reflux was present at diagnosis, 0 to 18% of patients had bladder level surgery. When low-grade reflux (less than 2/5) was present in one ureter, 40 to 50% had surgery, whereas nearly 100% of the rest of the population had bladder level surgery. The published data suggest that those cases with a ureterocele alone and no evidence of vesicoureteral reflux can usually be cured by the “simplified” upper pole approach.

Historically, endoscopic ureterocele incision was viewed as only a temporizing procedure because of the nearly 100% incidence of iatrogenic reflux.9 Incision regained popularity in the early 1990s when a low transverse puncture at the bladder neck level was described.10 In over 240 patients, hydrenephrosis has been successfully relieved 85% of the time. Reflux into the ureterocele moiety occurred in 45% of children after incision, and nearly 70% of the children eventually required a bladder level operation consisting of a ureterocele excision and ureteral reimplantation.11 If reflux was present into other moieties at the time of incision, nearly all children required subsequent surgery. Most children with ectopic ureteroceles fall into this refluxing subset.1 Some question the benefit of endoscopic incision because it is rarely a definitive procedure.8 Incision usually eliminates the need for upper tract surgery and probably facilitates subsequent lower tract reconstruction because ureteral caliber decreases and eliminates the need for ureteral tailoring.7 The indications for partial nephrectomy decrease if it is accepted that a nondilated, nonfunctioning, nonrefluxing moiety can be left in situ.12

Patients are observed on preventive antibiotics after ureterocele incision. A postincision sonogram confirms decompression. A cystogram can be obtained postoperatively to detect iatrogenic reflux. Iatrogenic reflux rarely resolves, but lower grades of preexisting reflux can be managed medically and may not require bladder level surgery. Depending on patient selection, 50 to 80% of children with ectopic ureteroceles managed endoscopically subsequently undergo ureterocele excision and ureteral reimplantation.6,7,11

Complete reconstruction, including ureterocele excision, reimplantation, and potential bladder neck reconstruction, is a definitive approach to ureterocele management. Removal of the upper pole moiety may be included. A primary success rate of > 85% and a complication rate of < 10% have been reported.8,13 This is technically challenging in infants, but a recent report from the Children’s Hospital of Michigan showed 100% success without complications in 18 children averaging 1 year of age.8 This approach assumes that ureterocele excision is important in the management of all children. Based on available data, some patients do not require open bladder level surgery to eliminate future infectious concerns.

A large concern with complete reconstruction is that resection of the entire ureterocele might damage the bladder neck continence mechanisms. However, many patients with ectopic ureteroceles have bladder dysfunction that may be an integral part of the disorder and not a result of the surgical procedures. The most common abnormality is a high-capacity bladder with incomplete emptying.14 Up to 50% of the patients void on an infrequent basis and 10% had urinary incontinence. Certainly this is a challenging procedure, but the incidence of postoperative incontinence is small and may be a primary abnormality.

References

SECTION 9
THE BLADDER
Vesicovaginal and Ureterovaginal Fistula

Martin B. Richman, MD, and Howard B. Goldman, MD

Vesicovaginal fistula (VVF) and ureterovaginal fistula (UVF) represent abnormal channels between the vagina and either the urinary bladder or one of the ureters that result in leakage of urine. In the developed world, most of these fistulas occur as a result of elective gynecologic surgery for benign disease and lead to complete incontinence of urine.

Fistulas between the urinary and vaginal tract have been reported for hundreds of years; however, the first modern description of VVF repair was by Sims in 1852. He emphasized the general principles of fistula repair, including adequate operative exposure, a tension-free closure, and adequate, continuous postoperative drainage to permit healing.

Approximately 90% of VVFs and UVFs in developed countries are attributable to prior pelvic surgery, with abdominal hysterectomy for benign disease accounting for 70% of these. The remaining 10% of urinary-vaginal fistulas in developed countries are the result of radiation, infection, foreign bodies, and pelvic malignancies (Table 75-1).

In underdeveloped countries, most VVFs result from obstetric trauma. Pressure necrosis of the bladder and vagina can occur during prolonged labor when these structures are pressed between the head of the infant and the maternal pubic bone.

Most urinary-vaginal fistulas are found approximately 10 days after pelvic surgery, although some can be discovered in the first few postoperative hours or while still in the operating room. The mechanism of fistula formation is frequently owing to an unrecognized iatrogenic bladder or ureteral laceration. A pelvic urinoma develops and then spontaneously drains through the vaginal cuff suture line. Other potential mechanisms of injury include cautery use or inadvertent suture placement during the control of intraoperative bleeding, which can lead to necrosis and urinary extravasation with subsequent fistula formation.

Radiation-induced necrosis causes 3% of all urinary vaginal fistulas, most of which are VVFs. These fistulas can occur months to years after the termination of therapy, and prior to repair, recurrent cancer must be ruled out with a biopsy of the fistula margin.

Surgical repair of a VVF is performed by either an abdominal or vaginal approach, and UVF repair is done with ureteroneocystostomy.

A Clinical presentation: Evaluation of a suspected urinary-vaginal fistula begins with a complete history and physical examination. Past medical history can reveal previous pelvic surgeries and malignancies with or without radiation therapy. Ask patients with prior pelvic surgery if the incontinence began immediately after surgery or if it began days or weeks later. A patient with a missed postoperative fistula may present months later with a diagnosis of stress or urge incontinence. With further questioning and evaluation, the clinician may associate the onset of incontinence with prior pelvic surgery. With small VVFs and most UVFs, the patient continues to void urine from the bladder but also constantly leaks urine from the vagina. Most UVFs involve only one ureter, whereas the other remaining ureter drains to and fills the bladder.

A complete pelvic examination, including speculum and bimanual evaluation, is essential when evaluating a potential fistula. The presence of urine in the vaginal vault is highly suspicious for a urinary-genital fistula. Observing a hole or an area of granulation tissue at the vaginal cuff or apex may localize a fistula, and with a large lesion, a defect may even be palpated during a digital vaginal examination.

B Dye tests: Identify and localize a urinary-vaginal fistula with various dye tests. Confirm suspicion of a fistula by placing a vaginal pack or tampon in the vagina and giving the patient oral pyridium or intravenous indigo carmine. Finding orange or blue staining on the proximal half of the vaginal pack or tampon indicates a fistula. The fistula can then be characterized as vesicovaginal or ureterovaginal with the double-dye test. This test is most commonly performed by first giving the patient oral pyridium 24 hours prior to the test. Then, in the office, place a vaginal packing or tampon in the vagina and place a urethral catheter into the blad-

Table 75-1 Etiology of Vesicovaginal and Ureterovaginal Fistula

| Iatrogenic injury from pelvic surgery | Gynecologic surgery | Obstetric surgery | Urologic surgery |
| Radiation injury | Pelvic malignancy | Pelvic trauma | Obstetric trauma from prolonged labor | Vaginal or vesical foreign body |
Patient with FLUID LEAKING FROM THE VAGINA

A. History
   Physical examination

   Double-dye test

   Cystogram

   Abnormal

   Suspect VVF

   Intravenous urogram (IVU)

   Abnormal

   Cystoscopy/vaginoscopy and retrograde pyelograms

   Normal

   Suspect UVF

   Cystoscopy/vaginoscopy

   Observe

   Attempt JJ ureteral stent

   Unsuccessful

   Successful

   Surgical repair with ureteroneocystostomy

   Persistent fistula

   Leave stent for 6 weeks, then remove and obtain intravenous urogram

   Resolution of fistula

   Immediate repair

   NSF catheter decompression

   Resolution of fistula

B. Intravenous urogram (IVU)

   Abnormal

   Cystoscopy/vaginoscopy

   If you need to delay repair

   Surgical repair

   Vaginal approach

   Abdominal approach

C. Surgical repair

D. Surgical repair with ureteroneocystostomy

   Leave stent for 6 weeks, then remove and obtain intravenous urogram

   Persistent fistula

   Resolution of fistula
Timing of repair: The timing of a VVF repair is contro-

C Timing of repair: The timing of a VVF repair is controversial. Classically, surgeons waited 3 to 6 months after the injury before attempting to close the fistula. This allowed healing of surrounding tissue and reduced inflammation and edema from the prior surgery. More recently, early and immediate repair of postoperative iatrogenic fistulas has become more prevalent, and success rates appear equivalent to delayed repair. Early repair has obvious benefit to the affected patient who is usually otherwise healthy and who may suffer severe mental and physical distress from the VVF. Early repair is not indicated for fistulas that result from obstetric trauma or radiation or for those complicated by pelvic or vaginal cuff infection. These patients have severe inflammation and necrosis of the affected tissues, and a waiting period will allow a better chance at successful repair.

When a waiting period before VVF repair is necessary, a Foley urethral catheter may be placed to diminish the amount of urine leakage. In rare cases, small fistulas can resolve with Foley catheter bladder decompression alone.

Type of repair: Perform a VVF repair by either a vaginal or an abdominal approach. Each method has its advantages and disadvantages for the patient. Surgeon comfort with one route over the other is also an important factor in the approach taken; the first attempt at repair usually has the best chance of success.

The vaginal approach often leads to less morbidity and a quicker recovery because the patient is spared an abdominal incision, and the bladder is left intact. The fistula repair can be reinforced with interposition of tissue between the bladder and vaginal closures. This can be done by translocation of a Martius labial fat pad, gluteal skin flaps, or myocutaneous gracilis muscle flap, or by interposition of adjacent parietal peritoneum.

The abdominal approach to VVF repair, using a low midline or Pfannenstiel incision, allows treatment of concurrent ureteral injury or fistula, or bowel injury or fistula, and the ability to perform augmentation cystoplasty for radiation-induced cystitis. This approach also enables the surgeon to easily interpose omentum to reinforce a large or recurrent fistula. Absolute indications for an abdominal approach over vaginal approach include a scarred or very small vagina, musculoskeletal abnormalities preventing proper positioning, and simultaneous ureteral or rectal fistulas or a fistula that is either close to or involving a ureteral orifice, requiring a ureteral reimplant.

D Managing a UVF: When a UVF is shown with retrograde pyelography, make an attempt to pass a wire and then a JJ ureteral stent into the affected ureter. If this is possible, it often leads to spontaneous healing of the UVF. Leave the stent in place for 6 weeks and then remove and follow with an intravenous urogram. If the fistula has not resolved, surgical repair should be undertaken.

When unable to pass a JJ ureteral stent, or in the rare cases in which stenting does not lead to spontaneous resolution of UVF, a standard ureteroneocystostomy, with or without a psoas hitch, is the preferred method of re-establishing ureteral continuity. If not undertaken immediately, place a percutaneous nephrostomy tube until the time of surgery, which can help alleviate the patient’s symptoms.

References
Bladder exstrophy occurs at a rate of 3.3 per 100,000 live births. Embryologically it is thought to be the result of an abnormal cloacal membrane. In 1962, Muecke presented an experimental model of bladder exstrophy that demonstrated the key role of the cloacal membrane in the development of bladder exstrophy in a chick embryo. A plastic wedge placed above the cloacal membrane prevented normal mesenchymal (the future abdominal wall) migration between the leaflets of the membrane (Figure 76-1). Rupture of this thin cloacal membrane left the posterior surface of the bladder on the surface of the abdominal wall (Figure 76-2).

Goals for the management of classic bladder exstrophy are (1) bladder closure with the achievement of urinary continence and the preservation of renal function and (2) reconstruction of functional and cosmetically acceptable genitalia. Although the goals of management of the patient with bladder exstrophy have not changed since the 1970s, when Jeffs and Cendron described consistent surgical success with a staged approach to closure, a new surgical philosophy has emerged with the complete primary repair of bladder exstrophy and epispadias. This chapter highlights the prenatal diagnosis of bladder exstrophy and the immediate and long-term management of the patient with bladder exstrophy.

A Ultrasonographic criteria for the prenatal diagnosis of bladder exstrophy include nonvisualization of the urinary bladder, a lower abdominal bulge representing the exstrophied bladder, low insertion of the umbilical cord, a small penis with an anteriorly displaced scrotum, and abnormal widening of the iliac crests. Nonvisualization of the bladder is the most common single finding. Prenatal diagnosis allows for family counseling, planned elective delivery at an appropriate facility, and coordination of a multidisciplinary team for postnatal treatment. The family may be directed to the Association of Bladder Exstrophy Children or other available resources for more information and support.

B At birth, the bladder mucosa should be protected by a hydrated gel dressing (Vigilon) or placement of nonadherent plastic wrap over the exstrophied bladder. With each diaper change, the bladder should be gently irrigated with normal saline and the gel or wrap replaced. The umbilical cord clamp should be replaced by a 2-0 silk suture to minimize traumatic contact with the bladder mucosa. A general physical examination should be performed to screen for any other congenital anomalies. Renal ultrasonography is performed to establish a baseline for further evaluation and spinal ultrasonography may be necessary to evaluate any physical findings suggestive of a spinal anomaly. Details of the bladder and genital anatomy should be noted, such as the size of the bladder plate, polypoid nature, location of the ureteral orifices, and, in the male, the size of the phallus and the length of the urethral plate.

C The first step in staged reconstruction is to convert the bladder exstrophy into a complete incontinent epispadias with a degree of outlet resistance that preserves renal function but stimulates bladder growth. Depending on the timing of repair and the plasticity of the pelvis, a pelvic osteotomy may be required. The second stage, epispadias repair, is generally performed between 6 and 12 months of age, after testosterone stimulation if nec-
Patient with UNBORN CHILD

A Prenatal ultrasonography
- Nonvisualization of the bladder
- Lower abdominal wall mass
- Widened pelvic bones

Exstrophy of the bladder
- Family counseling
- Multidisciplinary team

B Newborn assessment
- Protect bladder mucosa
- Baseline renal ultrasonography

Assess bladder plate for closure
- Suitable for closure
- Not suitable for closure

Assess pelvic plasticity
- No osteotomy
- Pelvic osteotomy

C Staged repair
- Primary bladder closure
- Assess genitalia
- Testosterone
- Epispadias repair/genital reconstruction

Assess capacity
- Inadequate
- Adequate

D Complete primary closure
- Hypospadias
- Repair

Assess capacity
- Augmentation cystoplasty, plus:
  - Incontinence procedure/ureteral reimplantation
  - Incontinent: consider bladder neck procedure, artificial urinary sphincter, injectable materials (collagen), bladder neck closure with catheterizable stoma
  - Continent

E Pelvic osteotomy

F Incontinence procedure/ureteral reimplantation
The complete primary repair for bladder exstrophy is based on the premise that the primary defect in exstrophy is an anterior herniation and that the bladder and urethra must be treated as a single unit and relocated posteriorly into the pelvis to achieve optimal bladder function and continence.4 The inclusion of total penile disassembly reduces tension on the bladder neck and urethral repair and decreases the risk of failed closure and dorsal chordee. In the male, the repair begins with dissection of the bladder plate in continuity with the urethral plate, followed by complete penile disassembly. Proximal dissection with deep incision of the intersymphyseal ligaments posterior and lateral to the urethra is then performed to allow for the movement of the bladder and urethra into the pelvis. Primary closure is then undertaken. The pubis is reapproximated and the penile reconstruction is completed. Depending on the available urethral length, the urethra may be matured ventrally to create a hypospadias to be corrected in the future. The rate of urinary continence with complete primary repair compares favorably with the rate for staged repair.

For the failed exstrophy closure, pelvic osteotomy and postoperative immobilization are important considerations to facilitate tension-free successful reclosure of the bladder. Complete primary repair has also been reported for use in older children with failed exstrophy closures.5

In cases of failure to achieve continence, urodynamic evaluation should be undertaken to assess the etiology of incontinence.6 A high-pressure, low-capacity, or unstable bladder may require anticholinergic therapy or augmentation cystoplasty. In the case of bladder neck incompetence, a primary or repeat Young-Dees-Leadbetter procedure may be employed if the urodynamic evaluation reveals a stable bladder with adequate bladder capacity. Collagen injections or implantation of an artificial urinary sphincter may be considered, but success with each of these methods is limited in most reported series. In some cases of failed bladder neck reconstruction, however, the best alternative may be bladder neck closure, augmentation cystoplasty, and creation of a continent catheterizable stoma.

G Inguinal hernias may be present in up to 82% of boys and 10% of girls with bladder exstrophy. Patients should be carefully examined prior to bladder closure and a preperitoneal repair may be performed at the time of bladder closure. Strong consideration should be given to performing a bilateral repair because the incidence of synchronous or metachronous contralateral hernia may be as high as 82%.7

Although sexual function and libido are normal in exstrophy patients, male patients with genital reconstruction and closure of the urethra may be at high risk of infertility and may require the use of assisted reproductive techniques, including gamete intrafallopian transfer (GIFT) or intracytoplasmic sperm injection (ICSI), to achieve pregnancy.8 In pregnant female exstrophy patients, cesarean section should be planned to avoid traumatic injury to the urinary sphincter mechanism and the pelvic floor, which may lead to uterine prolapse.

Ureterosigmoidostomy was a common method of urinary diversion in the past for patients with bladders thought to be inadequate for closure. The mixture of urine and feces is a predisposing factor for the development of neoplasia in these patients, and they require annual screening colonoscopy for early detection of tumors. Although urinary diversion for patients with bladder exstrophy is no longer widespread, even patients who undergo primary bladder closure may be at an increased risk of developing malignancy; therefore, ongoing surveillance of the bladder and upper tracts should be performed in all patients.
References
Bladder diverticula are commonly discovered incidentally or are found in the course of investigating the source of various unrelated nonspecific lower urinary tract symptoms. Despite presenting symptoms such as lower abdominal swelling or chronic urinary tract infections (UTIs), some large bladder diverticula remain undiagnosed for many years. Bladder diverticula are the result of a herniation of the transitional cell epithelium through the muscularis propria of the bladder wall. They may be congenital or acquired because of bladder outlet obstruction and/or neurogenic bladder. When congenital, they may be located lateral and cephalad to the ureteral orifice or at the dome in some patients with prune-belly syndrome or posterior urethral valves. If the diverticulum is located near the ureteral orifice in the setting of a neurogenic bladder and vesicoureteral reflux, it is termed a “Hutch” diverticulum.

Bladder diverticula may often be found incidentally in the radiographic investigation of recurrent UTIs or other nonspecific lower urinary tract symptoms. Voiding cystourethrography may be more revealing than intravenous urography; however, if the neck of the diverticulum is obstructed, cross-sectional imaging may be required for diagnosis.

A Bladder diverticula do not produce specific symptoms. Retrospectively, symptoms such as incomplete bladder emptying, lower abdominal fullness, and double voiding may be attributed to some large bladder diverticula. Most bladder diverticula are, in fact, diagnosed incidentally during radiographic or endoscopic evaluation of the lower urinary tract. A voiding cystourethrogram (VCUG) (Figures 77-1A and 77-1B) with anterior-posterior, oblique, and lateral images provides information with respect to anatomy, location, size, associated vesicoureteral reflux, and, importantly, emptying of the bladder diverticulum with voiding. Endoscopically, thoroughly examine the interior of the bladder diverticulum for stones or abnormal-appearing epithelium. In addition, during endoscopic examination, send urine cytology from the diverticulum.

B Perform a biopsy on any abnormal-appearing epithelium or lesions within the diverticulum. Take extreme care during the biopsy to prevent perforation; the wall of the diverticulum is very thin owing to the lack of a muscularis propria layer. The overall incidence of cancer within a bladder diverticulum has been reported to be between 4% and 11%.

C Often the pathologist encounters considerable difficulty in assessing depth of invasion and confirming invasive lesions (> Ta). Further, owing to the lack of a muscu-

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**Figure 77-1** This image, which was taken from a cystogram (A), shows a large posterior bladder diverticulum. Both the bladder (seen on the left with the filling catheter demonstrating the location of the bladder neck) and the bladder diverticulum have air-fluid levels. We clearly see the connection between the bladder and the diverticulum. Acquired bladder diverticula are not commonly found in females. This 35-year-old female presented with dysuria, recurrent UTIs, and pelvic pain. Urodynamic evaluation demonstrated a high-pressure/low-flow voiding pattern consistent with bladder outlet obstruction. Subsequent imaging (not seen here) revealed a urethral diverticulum. Sagittal T2-weighted MRI of the same patient demonstrating the bladder diverticulum with a connection to the bladder (B).
Bladder Diverticula in Adults

Patient with INCIDENTAL DIAGNOSIS OF BLADDER DIVERTICULUM (TIC)

A. Cystourethroscopy
cytology
VCUG

B. Lesion(s) suspicious for cancer

- Biopsy
  - Benign
  - Cancer

- Determine type, grade, stage
  (metastatic evaluation)
  Image upper urinary tract

C. Direct appropriate
therapy for cancer

- Symptomatic or
  complicated Tic

- Asymptomatic,
  uncomplicated Tic

D. No suspicious lesions

- Upper urinary tract imaging

E. Urodynamics (UDS)

- Normal
- Abnormal

F. Unresolved
HUN

- Treat LUT
abnormality

- HUN due to Tic

- HUN not due to Tic

G. Evaluate and treat
other causes of HUN

H. Review patient
history and lower
urinary tract (LUT)
symptoms

- Normal
- Hydroureteronephrosis
  (HUN)

I. Urodynamics (UDS)

- Normal
- Abnormal

J. Treat UDS abnormality

K. Surveillance

- Develops complications,
symptoms, or HUN

- Symptomatic, or
  complicated Tic

- Asymptomatic, uncomplicated Tic

L. Assess surgical candidacy for bladder diverticulectomy

- Resolved symptoms, no complications
- Persistent symptoms, complications

M. Surveillance

N. CIC

M. Bladder diverticulectomy

Good

Poor
laris propria layer, it is generally accepted that invasive lesions may progress through the bladder wall and into the surrounding soft tissues of the pelvis relatively early. Thus, cancer found within a diverticulum is often treated aggressively. Following staging (Figure 77-2), surgical treatment may include surveillance and repeat biopsy, intravesical immunotherapy or chemotherapy, transurethral resection, bladder diverticulectomy, partial cystectomy, or radical cystectomy.

**D** Imaging of the upper urinary tract may include intravenous pyelogram (IVP), ultrasonography, computed tomography (CT), or magnetic resonance imaging (MRI). In the absence of hematuria or a known or suspected urinary tract malignancy, the goal of imaging is to evaluate for asymptomatic or silent hydronephrosis.

**E** Hydronephrosis may relate to the bladder diverticulum itself, an underlying urodynamic abnormality that resulted in the formation of the diverticulum or may be completely unrelated to the bladder diverticulum. A thorough multichannel urodynamic study, combined with a VCUG or, alternatively, a videourodynamic study is useful in this setting.

**F** Possibly, the clinician will encounter asymptomatic hydronephrosis unrelated to the bladder diverticulum. Evaluate appropriately and pursue therapy concomitantly.

**G** Bladder obstruction, impaired compliance, and/or neurogenic voiding dysfunction resulting in hydronephrosis will become evident following a well-done urodynamic study. Treating the underlying lower urinary tract urodynamic abnormality via medical or surgical means may reverse or resolve the hydronephrosis. Alternatively, large or well-placed bladder diverticula may cause deviation or compression of the lower ureteral segment, which results in upper urinary tract dilation. Similarly, a bladder diverticulum that encompasses the ureteral orifice may create a functionally shortened intramural ureteral segment and result in vesicoureteral reflux, thus possibly necessitating excision of the bladder diverticulum with ureteroneocystotomy.

**H** Although voiding symptoms are rarely directly attributable to bladder diverticula, complications may include recurrent UTIs, incomplete bladder emptying, bladder calculi, and vascular or rectal obstruction. Recurrent UTI may be attributable to large residual urine. Bladder calculi may occur secondary to stasis and/or infection, although they occur uncommonly.

**I** Symptomatic patients, or those with complicating factors, should undergo urodynamic evaluation to assess for bladder outlet obstruction and impaired bladder contractility. Importantly, bladder contractility may appear diminished on urodynamics because of the “pressure-sink” effect of the bladder diverticulum. This artifact occurs as the detrusor contracts and the intravesical contents are decompressed through the path of least resistance into the bladder diverticulum, as opposed to the urethra. Videourodynamic may help to assess the significance of this possibility.

**J** Successful treatment of the urodynamic abnormality may improve bladder emptying and may potentially result in resolution of the symptoms and/or complications. In this setting and in the absence of future complicating factors, surveillance of the bladder diverticulum may be all that is needed. If symptoms remain, however, or the bladder diverticulum does not empty after treatment of the primary lower urinary tract abnormality, resulting in ongoing complications, then, excising the bladder diverticulum may be warranted.

**K** Asymptomatic patients without complicating factors may be followed closely. This includes periodic urine cytology, endoscopic examination of the bladder diverticulum, and upper urinary tract imaging. Controversy exists about whether prophylactic excision of asymptomatic bladder diverticula should be carried out to prevent malignant transformation or whether close observation is sufficient. Cytologic techniques and endoscopic examination allow for excellent follow-up, but clinicians have reported the rapid development of carcinoma during close observation, and the prognosis and treatment of established lesions remain poor.

**L** Excision of bladder diverticula is most often elective. Prior to considering the procedure, ensure that the patient is in relatively good health and is a low surgical risk. Assess preoperative medical status and correct
and/or optimize reversible risk factors (ie, nutritional, cardiac, and pulmonary). Patients who are prohibitive risks owing to concurrent medical illness or other factors should not undergo surgical excision.

M Management options in treating bladder diverticula include endoscopic incision of the diverticular neck, transurethral fulguration, and open surgical excision.\textsuperscript{15-23} Likewise, there have been some reports of laparoscopic bladder diverticulectomy.\textsuperscript{24} Open excision is usually performed through a transvesical approach, although extravesical and intraperitoneal approaches have been described. Often, the surgeon places ureteral stents to facilitate dissection and avoid ureteric injury. Careful dissection is required to avoid ureteral injury as many bladder diverticula are located adjacent to the ureter or may be adherent to it. Excising the diverticular sac and closing the bladder wall are usually curative, provided that the lower urinary tract abnormality that was originally responsible for developing the diverticulum was identified and treated.

N Manage patients who have poor bladder emptying and who are unable or unwilling to undergo surgical excision of the bladder diverticulum with clean intermittent catheterization.

References
Bladder diverticula, formed when bladder mucosa herniates between fibers of the detrusor muscle, are most common at sites of potential weakness in the detrusor. These locations are paraureteric, where the ureteral, trigonal, and detrusor muscles coalesce near the urachus (bladder dome). The walls of bladder diverticula therefore contain few muscle fibers. Bladder diverticula may be acquired or be congenital in origin.

Congenital diverticula in children are more common than are the acquired variety. They are more common in males and, in most cases, are solitary and are located in smooth-walled bladders without outlet obstruction, functioning at normal voiding pressures. Most are paraureteric in location and have been associated with deficiency in Waldeyer’s sheath, which surrounds the distal ureter and interdigitates with the trigonal musculature to form the effective ureterovesical mechanism (Figure 78-1).

Although most congenital diverticula occur sporadically, they may also be found in association with several clinical syndromes, including Menkes’ (kinky-hair syndrome), a sex-linked neurodegenerative disorder of copper metabolism, Ehlers-Danlos (a disorder of collagen synthesis), Williams (elfin facies, cardiac disease), and cutis laxa (a deficiency of elastic tissue).

Urachal diverticula are located at the dome of the bladder, appear sporadically, and are not uncommon in the prune-belly syndrome. Related urachal anomalies include urachal cyst, urachal sinus, patent urachus, and alternating urachal sinus. These lesions are thought to result from anomalous regression of normal urachal structures.

Acquired diverticula are commonly multiple and associated with vesical trabeculation, which in itself is secondary to either functional or structural vesical outlet obstruction. The elevated vesical pressures, created in the face of outlet obstruction, serve to force bladder mucosa through weaknesses in the detrusor muscle, resulting in formation of diverticula. Anterior or posterior urethral valves, urethral stricture, ureterocele, and other sources of urethral obstruction may cause structural infravesical obstruction. Functional outlet obstruction may be secondary to neurovesical dysfunction or dysfunctional voiding (in its most severe manifestation, the Hinman-Allen syndrome).

Iatrogenic diverticula have been described as a consequence of surgical procedures, notably ureteral reimplantation.

Bladder diverticula may remain asymptomatic or may be the cause of urinary tract infection, vesicoureteral reflux (VUR), ureteral obstruction, calculus formation, or bladder outlet obstruction. Because diverticula vary in size and location—some with a narrow neck and some with a wide neck—the spectrum of pathologic disorders may vary considerably, depending on the site and size of the diverticulum. Large diverticula and those with a narrow neck are more likely to empty poorly and to promote urinary infection, owing to residual urine remaining in the diverticulum after voiding or because of aberrant micturition, with a large amount of urine filling the diverticulum during micturition and subsequently refilling the bladder. Paraureteric diverticula may result in vesicoureteral reflux or may merely be associated with vesicoureteral reflux. Although the presence of a paraureteric diverticulum might be associated with a lessened potential for spontaneous regression of VUR, it has been demonstrated that reflux may resolve spontaneously in the presence of a paraureteric diverticulum. Factors that might influence this potential for regression include the size of the diverticulum (the size of the detrusor defect) and the anatomic position of the diverticulum in relation to the intramural tunnel of the ureter.

Although a large diverticulum might be visualized by ultrasonography or urography, the voiding cystourethrogram (VCUG) is the key to diagnosis. Both voiding during the imaging study and a postvoid film are helpful in delineating the presence of a diverticulum, its location in the bladder, and the presence of both postvoid residual urine in the diverticulum and aberrant micturition with refilling of the bladder after voiding has occurred. A plain film taken before the instillation of contrast will rule out the presence of a calculus in either bladder or diverticulum. Imaging of the urethra during voiding is imperative to rule out intrinsic urethral obstruction.
A trabeculated bladder with diverticula should raise a concern about infravesical obstruction. In certain cases, the appearance of the posterior urethra in a boy requires differentiation between a posterior urethral valve and the failure of the external sphincter to relax during micturition. The latter dyssynergia (discoordination) may be neurogenic in origin or may represent involuntary or voluntary discoordination of the sphincter and detrusor (the Hinman-Allen syndrome).25–27 The detrusor or sphincter discoordination seen in cases of the Hinman-Allen syndrome can be severe and may mimic severe urethral obstruction or true neurovesical dysfunction. Cystoscopy may be required to rule out urethral pathology, and urodynamic investigation may be appropriate.

The primary treatment of children with acquired diverticula involves management of the vesical outlet obstruction or discoordination that caused diverticulum formation. This may include resecting urethral valves, treating urethral stricture, or managing the neurovesical dysfunction or dysfunctional elimination syndrome that resulted in abnormal bladder function.28–30 Treat expectantly multiple diverticula associated with Menkes’ and other clinical syndromes because vesical function may be disordered. In addition, detrusor muscle is so abnormal in many of these connective tissue disorders that diverticulometry may be associated with the formation of other diverticula in many sites in the bladder. Solitary congenital diverticula, when small and asymptomatic and associated with little postvoid residual urine, may be treated expectantly. It is important to follow these children longitudinally, however, because some will develop urinary tract infections or other symptoms that refer to the diverticulum. Others may remain asymptomatic while the diverticulum gradually enlarges to a size significant enough to produce aberrant micturition. In fact, some diverticula may reach an impressive size. If diverticulometry is elected, the surgical approach may be intravesical, extravesical, or a combination of the two. When the diverticulum is in close proximity to the ureter and reflux is not present, note the course of the ureter with a ureteral catheter, so inadvertent ureteral injury does not occur during diverticulectomy.

Paraureteric diverticula associated with ureteral obstruction or VUR require ureteral reimplantation, combined with diverticulectomy. In fact, most paraureteric diverticula represent merely an enlarged muscular hiatus at the ureterotrigonal junction; thus, diverticulectomy and repair of the muscular defect are accomplished in most cases by routine ureteroneocystostomy. Take care to preserve the ureteral blood supply; the bladder (diverticular) mucosa is closely applied to the ureter in most cases, and separation of the two layers can be tedious.

Urachal diverticula may be wide-mouthed and uro-dynamically insignificant. In these cases, surgical intervention is usually unnecessary. When symptomatic diverticula or other urachal lesions are found, when excising the diverticulum, remove a small cuff of the detrusor and excise all urachal remnants that extend to the umbilicus. This is important because of the potential for malignant degeneration in the epithelial tissue, which may persist in the urachal remnant.31,32

References

Stress urinary incontinence (SUI) is the involuntary loss of urine through the urethra, associated with increases in intra-abdominal pressure. Generally, it is attributed to either (1) a failure of the normal transmission of increases in intra-abdominal pressures to the bladder neck and proximal urethra, owing to poor anatomic support of this region (urethral hypermobility or anatomic incontinence); (2) malfunction, damage, or injury to the intrinsic urethral sphincteric unit (intrinsic sphincter deficiency [ISD]); or (3) a combination of these. Recently, it has been suggested that all patients with SUI have some degree of ISD and that urethral hypermobility is associated with or contributes to the risk of developing SUI.

A A satisfactory history, physical examination, and urine analysis can often accurately establish the diagnosis of SUI in an otherwise healthy, uncomplicated, female without neurologic illness or prior pelvic surgery.1

B Only rarely does surgery have the initial role in managing uncomplicated stress urinary incontinence. When secondary complications from the incontinence are not present (eg, skin breakdown, infection), and coexisting ailments requiring surgery are not present, base the decision to surgically treat symptomatic SUI primarily on the premise that the degree of bother or lifestyle compromise to the patient is great enough to warrant an elective operation and that nonoperative therapy is either undesired or has been ineffective.

C Provided that the therapy being considered for the treatment of SUI is completely reversible, noninvasive, safe, and inexpensive, it is unnecessary to proceed with more invasive or expensive testing, such as urodynamics (UDS) or endoscopic examination, of the lower urinary tract. In most patients with uncomplicated SUI, the initial management usually involves various noninvasive measures, including behavioral modification (fluid and dietary management, timed voiding) and pelvic floor exercise, with or without biofeedback, and other accessory teaching aids that include weighted vaginal cones.2–4

D If symptomatic improvement remains unsatisfactory, apply the following, either in isolation or in combination: pharmacologic therapy (alpha agonists, estrogens),5 compressive and occlusive devices (vaginal pessaries, urethral inserts), electrical stimulation, and various other interventions.

E Patient satisfaction is determined by each individual patient and may not relate to the complete resolution of urinary incontinence. General guidelines have been suggested to objectively determine outcomes, but, ultimately, it is the patients and their family who decide success.6

F Patients may become dissatisfied with these noninvasive therapies because of cost, discomfort, inconvenience, and lack of efficacy or related complications, such as urinary tract infection (UTI). Surgical treatment of SUI in these patients then assumes the primary role in treatment. The goal of SUI surgical treatment is to provide sufficient urethral resistance to prevent the egress of urine from the urethra during increases in intra-abdominal pressure, while preserving voluntary, low pressure and complete bladder emptying.

G Because SUI surgery is essentially elective, prior to considering the procedure, ensure that the patient is in relatively good health and is a low surgical risk. Assess preoperative medical status and correct and/or optimize reversible risk factors (nutritional, cardiac, pulmonary).

H Defining the etiology and coexisting and underlying factors that contribute to the urinary incontinence is critical in determining the appropriate surgical approach. A careful preoperative evaluation, including urodynamics and cystoscopy when appropriate, can be essential in understanding and confirming the type of urinary incontinence and thus directing appropriate surgical therapy.

I If objective evidence of SUI has not been demonstrated (via physical examination, UDS), then the diagnosis of SUI may be incorrect. Document definite evidence of SUI prior to proceeding with irreversible therapy, such as surgery.

J Over 100 different operations have been designed to treat SUI in females, and, in general, any number of procedures may be considered an option for the “index” patient, who is otherwise healthy, who desires surgical SUI correction, and who has not undergone prior anti-incontinence surgery. However, consider many factors when determining the optimal surgical therapy for the SUI patient, including etiology and type of urinary incontinence; bladder capacity; severity of the leakage; the presence of associated conditions, such as vaginal prolapse, and concurrent abdominal or pelvic pathology that requires surgical correction. Surgical correction of female stress incontinence is directed toward either (1) repositioning the urethra and/or creating a backboard of support or stabilizing the urethra and bladder neck in a
well-supported retropubic (intra-abdominal) position, which is receptive to changes in intra-abdominal pressure; or (2) creating coaptation and/or compression or otherwise augmenting the urethral resistance with (ie, sling) or without (ie, periurethral injectables), affecting urethral and bladder neck support (Table 79-1).8

K ISD or Type III SUI has been described as a nonfunctional proximal urethral segment or fixed open bladder neck at rest in the absence of a detrusor contraction, usually implying a low Valsalva leak-point pressure and severe SUI symptoms. Historically, bladder neck suspensions (transvaginal and transabdominal) have an unacceptably high failure rate in this group of patients.9,10 For many years, the pathophysiology of SUI was attributed to either urethral hypermobility or ISD or a combination of both. However, clearly, there exist many patients with urethral hypermobility who are not incontinent. For this reason, it has been suggested that perhaps all patients with SUI have some degree of ISD and that urethral hypermobility simply represents a cofactor for SUI development in those patients with any degree of ISD. ISD therefore may represent a spectrum of relative urethral incompetence, and those patients with high-volume SUI symptoms and low urethral resistance are at one end of the severity spectrum (Figures 79-1 and 79-2).

L Assessing anterior vaginal wall prolapse is usually done preoperatively in the lithotomy position at maximal Valsalva. The posterior vaginal wall is retracted with a speculum to maximally accentuate the degree of prolapse. Anterior vaginal wall prolapse to the distal vagina and beyond usually suggests that a concomitant cystocele repair should be performed with the anti-incontinence procedure to avoid postoperative voiding dysfunction.

M Urologists have used the transabdominal approach to vesicourethropexy for many years.11 The advantages to this approach include (1) the familiarity of retropubic anatomy to most urologists, (2) excellent operative exposure and access to the key anatomic elements for the surgery, (3) long-term data suggesting its durability, and (4) the opportunity to repair coexistent abdominal pathology through the same or slightly extended incision. Disadvantages include a large incision, prolonged hospital stay and recovery period, suboptimal results in patients with ISD, and the inability to access and repair coexistent vaginal pathology through the same incision.

N For a patient without ISD or significant prolapse, any of these options are satisfactory, with each having distinct advantages and disadvantages that the clinician should discuss with the patient. An alternative to the retropubic operations for urethral incontinence owing to vesicourethral hypermobility is the transvaginal approach or needle suspension. These techniques have evolved as a minimally invasive alternative to the retropubic procedures. Armand Pereyra in 1959 described the original

Figure 79-1 Rest/strain sequence from the videourodynamic study of a 52-year-old woman with a history of a failed anti-incontinence surgery. The left image demonstrates an open bladder neck at rest. The right image demonstrates urinary bladder neck incompetence with Valsalva maneuver. The leak-point pressure measurement was very low, consistent with severe ISD. There is very limited mobility of the proximal urethra and bladder neck with straining.

Figure 79-2 Rest/strain sequence from the videourodynamic study of a 48 year-old woman with symptomatic urinary incontinence. Note the rotational descent of the bladder neck and proximal urethra with straining in the right image, compared with the resting image on the left. There was no incontinence demonstrated on the videourodynamic study.
Patient with URINARY INCONTINENCE

A. History
   Physical examination
   Urine analysis

B. Patient desires surgical therapy
   Consistent with SUI
   Not consistent with SUI

C. Patient desires nonsurgical therapy
   Not consistent with SUI
   Consider other diagnosis

D. Initiate nonsurgical therapy
   Patient still desires nonsurgical therapy
   Unsuccessful or patient not satisfied with results

E. Unsuccessful or patient satisfied with results
   Successful and patient desired with results
   Continue nonsurgical therapy

F. Unsuccessful or patient dissatisfied with results
   Not a surgical candidate
   Revisit nonsurgical therapy or initiate palliative measures: catheters, pads, etc.

G. Assess surgical risk
   Good surgical candidate
Diagnosis of Stress Urinary Incontinence (SUI)

1. **No objective evidence of SUI**
   - Consider other diagnosis

2. **Objective demonstrable SUI**
   - Proceed with surgical correction

3. **UDS/endoscopic examination**
   - **No intrinsic sphincter deficiency**
     - No or mild anterior vaginal-wall prolapse (cystourethrocele)
       - Coexisting abdominal pathology requiring surgery
         - RP
       - No other coexisting abdominal pathology requiring surgery
         - Sling or RP or PBNS or periurethral injectable (collagen)
     - No or mild anterior vaginal-wall prolapse (cystourethrocele)
     - Moderate to severe anterior vaginal-wall prolapse
   - **Intrinsic sphincter deficiency**
     - No or mild anterior vaginal-wall prolapse (cystourethrocele)
     - No or mild anterior vaginal-wall prolapse (cystourethrocele)
     - Moderate to severe anterior vaginal-wall prolapse

4. **Sling or retropubic suspension or percutaneous bladder neck suspension and cystocele repair**

5. **Sling or periurethral injectable**

6. **Sling and cystocele repair**

7. **Other diagnosis**
transvaginal needle suspension and used stainless steel wires to suspend the paraurethral tissues to the abdominal wall fascia. Since then, urologists have reported many modifications of the original procedure. The common feature with each of these procedures is that the anterior abdominal wall fascia is not incised and that the suspending sutures are passed through the retropubic space from the vagina to the anterior abdominal wall with a specialized long ligature (suture) passer. Advantages to the transvaginal approach include avoidance of a large, transfascial abdominal incision (and its attendant morbidity, especially in the obese patient); shorter operative times; less postoperative discomfort; shorter hospital stay; and the ability to repair coexisting vaginal pathology (ie, prolapse) through the same or slightly extended incision. The disadvantages are as follows: a potentially lower long-term “cure” rate, poor intraoperative visualization, risk of injury to the bladder and urethra during blind passage of the needles through the retropubic space, risk of significant bleeding in the retropubic space with poor operative access from the vaginal incisions, and, finally, if suture buttresses (ie, Stamey operation) are used, infection or erosion of a foreign body. Each of the transvaginal urethropexy procedures differs from one another with respect to the method of anchoring, as well as to the tissues incorporated on the vaginal side of the procedure, that is, whether or not the endopelvic fascia is detached from the tendinous arc of the obturator and whether to use buttresses or bolsters to hold the suture in the vaginal tissues.

Q Originally described almost 100 years ago, slings of various types have had resurgence in popularity over the past several years.13–16 We can attribute this surge in popularity to several factors, including a change in surgical philosophy with respect to pathophysiology of urethral incontinence in the female (ie, many surgeons now believe that all patients with urethral incontinence have some degree of intrinsic sphincteric deficiency regardless of the presence or absence of urethral hypermobility) and a perceived, if not actual, decrease in morbidity of sling surgery in the modern era. Rather than the transabdominal or transvaginal approach to urethropexy, the goal of sling surgery is not only to provide a “backboard” of support for the vesicourethral junction but also to create some degree of urethral coaptation or compression (Figure 79-3). Nonetheless, it is important to tie any type of sling with minimal or no tension to prevent bladder outlet obstruction and/or urinary retention. The synthetic slings, such as TVT®, that comprise primarily polypropylene mesh are placed at the level of the midurethra on absolutely no tension and probably provide their anti-incontinence effect by reducing urethral mobility during increases in intra-abdominal pressure or by producing a dynamic kink in the urethra at these times.17
References


Spina bifida, or myelodysplasia, a group of complex developmental anomalies, is caused by neural tube closure defects. This condition, affecting 1 in 1,000 births in the United States, is associated with the following lesions: (1) spina bifida occulta (a bony defect); (2) meningocele (a meningeal sac without neural components); (3) spina bifida cystica or myelomeningocele (skin-covered sac with neural components); and (4) spina bifida aperta (an open sac). Major advances in the medical and surgical treatment of these individuals have markedly increased their life expectancy and have improved certain aspects of their quality of life. Over 90% of all the open spinal dysraphic states are due to myelomeningocele.

There are many urologic manifestations of patients with myelomeningocele, including urinary retention, urinary incontinence, urinary tract infections (UTIs), and vesicoureteral reflux. Two factors that may contribute to these conditions are neurogenic bladder dysfunction and constipation. To properly treat these patients, the clinician should address both conditions. All patients with myelomeningocele should undergo periodic urine analysis/cultures, imaging, and urodynamic evaluation.

A After closing the spinal defect, urologic evaluation is essential for managing these children. The evaluation consists of assessing the spinal level of the myelomeningocele, the upper tracts by renal ultrasonography, and the lower tract by bladder ultrasonography and voiding cystourethrogramraphy (VCUG). Perform a baseline urodynamic study when it is safe to place the child on his back. Patients can be divided into five groups: (1) normal evaluation, (2) urinary retention, (3) hydronephrosis, (4) UTI, and (5) pathologic high-pressure urodynamic studies (ie, elevated leak-point pressure or bladder-sphincter dyssynergia). More than one of these problems can coexist.

B Children with a minor neurologic defect may be able to spontaneously void and to maintain normal upper tracts. The clinician should determine a postvoid residual; a value < 5 mL is considered within normal limits in the newborn period. These children require close observation with urine cultures every 3 months and with periodic ultrasonography because the bladder dynamics may change.

C Urinary retention or high residual urines can occur after spinal closure. Clean intermittent catheterization (CIC), which effectively treats this condition, should be performed every 4 hours during the day. Use anticholinergics (AChs), in addition to CIC, if the urodynamic evaluation demonstrates a pathologic high-pressure bladder. Many children will begin to self-void, resulting in the transient use of CIC and AChs. Check postvoid residuals prior to discontinuation of therapy and perform periodic urine analysis/cultures, radiographs, and urodynamics.

D Incontinence in the infant is easily managed with diapers. Managing bowel function, however, is important in helping to achieve continence. Constipation therapy can include fiber supplements, mineral oil, enemas, polyethylene glycol 3350, anal stimulation, and manual disimpaction. When all therapies have failed, arrange an evaluation with a gastroenterologist; in fact, an ACE (antegrade continence enema) procedure may be necessary.

However, when continence is desired in the older child, the clinician can successfully implement CIC and AChs to achieve continence. Carry out a urodynamic re-evaluation in these children with continued incontinence. Perform spinal magnetic resonance imaging (MRI) to evaluate for a tethered cord, especially in those with secondary enuresis or with changes in voiding pattern. If children do not achieve continence with these nonsurgical modalities, continence surgery is necessary.

E Hydronephrosis is commonly seen in children with myelomeningocele from either vesicoureteral reflux or a neurogenic bladder. To treat vesicoureteral reflux, prescribe antibiotic prophylaxis until the radiograph confirms that the reflux has resolved. Decreasing the intravesical pressure further may necessitate adding AChs. This therapy is usually successful in children with low-grade reflux but more commonly unsuccessful in those with high-grade reflux. Children with high-grade reflux frequently require temporary diversion (eg, vesicostomy) to preserve the upper tracts. High-grade reflux usually requires eventual ureteral reimplantation and often needs bladder augmentation to increase the bladder capacity and reduce the intravesical storage pressures.

F Myelomeningocele patients are susceptible to recurrent UTIs. The common causes for these infections are constipation (refer to D) and impaired bladder emptying. Impaired bladder emptying may be due to constipation, reflux, and high intravesical pressure. The primary therapy comprises CIC and antibiotics, with the addi-
tion of AChs as indicated. Asymptomatic bacteriuria occurs commonly in CIC patients and does not predispose them to febrile UTIs or renal damage in the absence of reflux, thus not requiring therapy. Febrile UTIs are commonly due to reflux and therefore require VCUG. Recurrent infections are commonly due to failure to catheterize, resulting in high bladder volumes and overdistention. If the patient is compliant with CIC, perform urodynamic re-evaluation.

G A baseline urodynamic evaluation is essential not only to allow for comparison with future urodynamic results but also to select those infants who may benefit from immediate CIC and AChs in the attempt to preserve the bladder and upper tracts. For patients with pathologic urodynamics, clinicians should follow up closely with urodynamic evaluations.

H Before the 1980s, little had been written on the subject of sexual function of the spina bifida patient because only a small number of these individuals lived into adulthood. Now, however, spina bifida patients routinely live into adulthood, owing to recent medical and surgical advances. For this reason, sexual dysfunction has become a well-recognized associated medical disorder in both men and women. Hence, conversations with respect to sexuality should not wait until adulthood but should begin during adolescence.

Erectile dysfunction is a common problem in this patient population. The first study to demonstrate that erectile dysfunction in the spina bifida male is a medically treatable condition involved the use of sildenafil citrate. Clinicians can implement the same treatment modalities that are used for the general population for men with spina bifida. Nonsurgical modalities should be the first line of therapy. The lowest effective medication dose should be used in these men with neurogenic erectile dysfunction.

Additional Readings


Patient with MYELOMENINGOCELE

A

History
Physical examination
Ultrasonography
VCUG
Serum electrolytes
Urine culture
Postvoid residual
Urodynamics

Determine urologic group

B

Normal
Self-voiding

C

Urinary retention
CIC
ACh

D

Incontinence
CIC
ACh

E

Hydronephrosis
No reflux
CIC
ACh

F

UTI
CIC
ACh
Constipation management
Febrile UTI
VCUG
Recurrent UTI

G

Pathologic urodynamics
CIC
ACh

continued

Constipation management
Diapers

Reflux
VCUG
Recurrent UTI

ACh

ACh

ACh

ACh

ACh

ACh

ACh

ACh
Neurogenic bladder (NGB) is a general term that is used to describe various lower urinary tract voiding dysfunctions resulting from neurologic disease or conditions. A wide variety of neurologic conditions may impact on the lower urinary tract, including spinal cord injury or disease (lumbar disc disease, etc), spina bifida, multiple sclerosis, Parkinson’s disease, ischemic or hemorrhagic stroke, and Alzheimer’s disease. The goal when evaluating the patient with NGB is to provide an accurate diagnosis or at least classification of the voiding dysfunction and assess the potential risk to the upper urinary tract. One such classification system is the Functional Classification system outlined below.1 Therapeutic interventions in patients with neurogenic voiding dysfunction should ideally result in low-pressure storage of urine with intermittent, voluntary, and complete low-pressure bladder emptying. Other considerations in patients with NGB include cost, quality of life, preservation of the upper urinary tract, and prevention of complications such as calculi, infection, and malignancy.

A The clinical evaluation of the patient with neurogenic voiding dysfunction includes a thorough history, physical examination (including pelvic and rectal examinations), a directed neurologic examination, and a urine analysis. In addition, assess physical disabilities that may limit future therapies. For example, patients with limited use of their upper extremities will most likely be unable to perform clean intermittent catheterization per urethra.

B An upper tract radiographic study that reveals hydrourteronephrosis necessitates further investigation and mandates therapy of the NGB condition if the upper tract changes are attributable to a lower urinary tract condition. In those patients with hydrourteronephrosis, reviewing the urodynamic tracing, the voiding cystourethrogram (VCUG) (Figure 81-1), and the endoscopic studies will usually reveal the etiology of the dilated urinary tract. Considerations include vesicoureteral reflux, poor compliance, bladder outlet obstruction, calculis disease, and malignancy (especially in those with long-term indwelling catheters).

C Most patients will not present with upper urinary tract changes. Thus, in the absence of complications, such as urinary tract infection (UTI), calculi or reflux, or urodynamic findings, which place the upper urinary tract at risk (ie, impaired compliance), the initiation of therapy in these patients is elective. Most patients will choose to undergo therapy because of the disabling symptomatology associated with NGB, including urinary incontinence and overactive bladder symptoms such as frequency of urination.

D Patients who elect to have no therapy should be carefully monitored. Many neurologic conditions are progressive or may evolve over time (ie, multiple sclerosis). Although no universally accepted algorithm exists for monitoring patients with NGB, annual or biannual upper urinary tract imaging, symptom assessment, physical examination, and serum chemistries is a reasonable surveillance protocol (Figure 81-2).

E Although there are numerous classification systems for NGB and voiding dysfunction, the Functional Classification system is practical and relatively simple to understand.1 Voiding dysfunction is classified according to whether the primary problem is one of urinary filling and storage (“failure to store”) or urinary emptying (“failure to empty”). Each of these groups is then further subdivided into those whose voiding dysfunction is attributable to problems of the bladder itself or to the bladder outlet (including the urethra and sphincter apparatus) or to a combination of both bladder and outlet problems.
Failure to store urine may be attributable to problems with the bladder or the bladder outlet.

Detrusor overactivity is a common source of NGB symptoms. Involuntary contractions of the detrusor muscle result in urinary urgency, frequency, nocturia, and incontinence. Therapy is directed at abolishing or otherwise diminishing these involuntary contractions. As with all therapies for NGB, therapy should start with the least invasive, least expensive, least morbid, and most reversible treatment that will be effective for the underlying condition. Therapies are changed or added as efficacy, cost, or side effects of ongoing treatment are deemed unacceptable. Constant reassessment is often necessary. For patients with bladder overactivity, therapy often starts with behavioral modification (timed voiding, fluid and diet management, and pelvic floor exercises). Pharmacologic therapy in the form of anticholinergics is commonly added to a program of behavioral modification to optimize efficacy. Use tricyclic antidepressants and estrogens in selected patients.

When nonsurgical measures are deemed ineffective and the patient desires additional therapy, surgical intervention may be warranted. Bladder overdistention under anesthesia and denervation procedures (ie, Ingelman-Sundberg) have been reported to improve symptoms in some studies. Neuromodulation (Interstim, Medtronics Corporation, Minnetonka, MN) is a novel intervention for the treatment of some types of refractory voiding dysfunction. Finally, consider using enlargement cystoplasty (augmentation cystoplasty) in select patients who are refractory to other forms of therapy. Patients being considered for augmentation cystoplasty should be good surgical candidates and be willing and able to perform intermittent urethral catheterization.

Nonsurgical therapy for enhancing outlet resistance includes pelvic floor exercises, electrical stimulation, and pharmacologic therapy. Pharmacologic therapy for improving outlet resistance comprises α-adrenergic agonists, estrogen therapy, and tricyclic antidepressants. The clinical utility of these agents is somewhat limited owing to relatively poor efficacy and widespread adverse side effects. Selected female patients may benefit from the use of supportive (ie, incontinence pessary) and/or occlusive devices (urethral inserts, plugs, or patches). Although these devices can be effective in certain patients, issues of individual attitudes toward the intermittent genital manipulation needed to properly use these devices, as well as cost and comfort, have prevented widespread use.

There are multiple methods by which outlet resistance may be augmented surgically (see Chapter 79, “Stress Urinary Incontinence”). To create continence in some patients, intentional overcorrection of the outlet, which, in effect, abolishes voluntary bladder emptying, may be necessary. In these patients, initiation of intermittent urethral catheterization will be required to allow bladder emptying.

If satisfactory continence cannot be achieved by other means, or if safe, low-pressure urine storage cannot be maintained, then urinary diversion away from the urethra is an option. In patients with NGB being considered for urinary tract reconstruction or diversion, incorporation of the native bladder is preferred—especially in those with nonrefluxing native ureterovesical junctions. In patients for whom other measures are unable to create satisfactory urethral resistance to prevent stress urinary incontinence, surgical division and closure of the urethra at the level of the bladder neck or proximal urethra can be performed and urinary emptying maintained by creation of an alternative continent catheterizable channel to the abdominal wall (ie, Mitrofanoff) or incontinent urinary diversion (ie, ileovesicostomy). Alternatively, for patients with significant vesicoureteral reflux, a Bricker bilateral ureteroileostomy or colon conduit may be fashioned.

Circumventing the problem in patients with NGB implies the application of measures that do not directly
Patient with VOIDING DYSFUNCTION (VD) DUE TO NEUROLOGIC DISEASE/CONDITION

A History
Physical examination
Urine analysis

B Upper tract study

Hydronephrosis due to NGB

Classify pathophysiology:
failure to store vs
failure to empty vs
combined

E Patient desires
therapy for VD

Patient desires
no therapy

No complications or
risk factors for HUN

D Surveillance

Failure to store

Due to bladder

Inhibit bladder
contractility

Nonsurgical treatment
Behavioral therapy
Pelvic floor physiotherapy
Pharmacologic therapy
Electrical stimulation
Other

Failure to empty

Due to outlet

Circumvent
the problem

Enhance outlet
resistance

Nonsurgical treatment
Pelvic floor physiotherapy
Electrical stimulation
Pharmacologic therapy
Devices:
supportive, occlusive
Other

Combined deficit:
failure to store
and failure
to empty

R Treat
primary
defect

G

I

F

M

L

No hydronephrosis


Neurogenic Bladder

Urinary diversion: incontinent vs continent

Failure to empty

Due to bladder
- Enhance bladder/intravesical pressure
  - Pharmacologic therapy
  - External compression
  - Valsalva
  - Crede
  - Reflex contractions
  - Neuromodulation

Due to outlet
- Decrease outlet resistance
  - Biofeedback
  - Pharmacologic therapy
  - Androgenic receptor antagonists
  - Antiandrogens
  - GnRH agonists/antagonists
  - Other
  - TURP/TUIBN/etc
  - Urethral stricture repair
  - External sphincterotomy
  - Urethral stent
  - Other

Circumvent the problem

Intermittent catheterization
Continuous catheterization

Intermittent catheterization
Continuous catheterization
treat the underlying lower urinary tract pathology but that result in a functional improvement in the condition. For example, urinary retention or “failure to empty” for whatever reason may be treated in some patients by continuous bladder emptying (indwelling urethral catheterization) or by intermittent catheterization effectively bypassing the underlying condition (bladder or bladder outlet abnormality) responsible for the voiding dysfunction.

M Failure to empty may be due to problems with the bladder or bladder outlet.

N Impaired bladder contractility is often difficult to treat. Although the goal is to improve bladder contractility, few treatments have been shown to be successful. Commonly, clinicians treat these patients with intermittent catheterization, continuous catheterization, or urinary diversion.

O Bladder outlet obstruction may be anatomic (benign prostatic hypertrophy (BPH), prostate cancer, urethral stricture) or functional (striated sphincter dyssynergia, bladder neck dysfunction) (Figure 81-3). In either case, the goal of therapy is to reduce outlet resistance sufficiently to permit satisfactory, low-pressure bladder emptying.

P Few, if any, published randomized, placebo-controlled trials exist that demonstrate a definite improvement in bladder emptying with any pharmacologic agent, includingbethanechol.21 Patients with decreased outlet resistance may be able to empty satisfactorily with Valsalva or Crede’s maneuver, although these measures may concomitantly increase outlet resistance, resulting in inefficient emptying. This is not recommended in patients with significant vesicoureteral reflux. Some patients with NGB can willfully and predictably induce a coordinated bladder contraction with intermittent or rhythmic tapping in the suprapubic region. Finally, neuromodulation has been found to alleviate some types of chronic idiopathic urinary retention.9

Q Identifying the source of bladder outlet obstruction is essential to directing appropriate therapy. Clinicians can accomplish reduction of outlet resistance both medically and/or surgically depending on the clinical situation.

R For those patients with both bladder and bladder-outlet problems contributing to a failure to store urine, it is reasonable to treat both the bladder and bladder outlet concomitantly or alternatively attempt to primarily treat whichever is contributing to most of the symptomatology.

References

Figure 81-3 Voiding image from a voiding cystourethrogram (VCUG) in a patient with NGB and suspected detrusor external sphincter dyssynergia. This image demonstrates a heavily trabeculated bladder, dilated proximal urethra, and poor opacification beyond the membranous urethra.
Urinary incontinence after prostatectomy is problematic and is not uncommon. Incontinence occurs in 0.5 to 1.0% of all patients undergoing prostatectomy for benign disease; higher rates (5 to 30%) are associated with radical prostatectomy. Urine leakage can have a major impact on quality of life. In the immediate postoperative period, stress and urgency incontinence are common. This has been attributed to the varying degrees of edema and inflammation present in the healing prostatic urethra. Only in those instances when incontinence persists beyond the healing period (6 to 12 months) is complete urologic evaluation warranted.

Postprostatectomy incontinence may be caused by sphincter malfunction and/or bladder dysfunction. Urinary control in the adult male depends on the integrity of both the internal and external urinary sphincters. The internal sphincter, consisting of smooth muscle fibers of the bladder neck and prostatic urethra, is innervated by the autonomic nervous system and provides for passive continence. The distal urinary sphincter, comprising striated muscle and smooth muscle fibers, is under voluntary control. In the presence of stable bladder function, either sphincteric mechanism alone is sufficient to maintain urinary continence. During prostatectomy, the internal sphincter mechanism is virtually destroyed. Thus, postprostatectomy stress incontinence, or even total passive incontinence, may result if the external sphincter is also damaged or destroyed.

Bladder dysfunction is characterized by detrusor instability and impaired compliance. Urgency incontinence, a frequent preoperative symptom in the presence of outflow obstruction, may persist into the postoperative period when due to uninhibited bladder contractions. Recent studies have concluded that sphincter dysfunction is the main cause of postprostatectomy incontinence, although some form of bladder dysfunction is also present in 34 to 45% of patients.

Obstruction after prostatectomy, resulting from an anastomotic stricture or residual prostatic tissue (post–transurethral resection of the prostate), may also play an important role in the development of postprostatectomy incontinence. Obstructing strictures often cause overflow incontinence, urge incontinence, and/or a weak urinary stream.

A An appropriate history and physical examination can provide valuable information regarding the etiology of postprostatectomy incontinence. Urgency incontinence and dysuria are frequent complaints in patients with a urinary tract infection and usually resolve with appropriate therapy. A complaint of stress incontinence, which can be witnessed during the physical examination by asking the patient to perform a Valsalva maneuver, highly suggests the presence of sphincteric dysfunction.

B Perform cystourethroscopy to rule out the presence of correctable pathologic changes involving the external sphincter, prostatic urethra, and bladder neck. Residual apical tissue and/or stricture formation may interfere with complete closure of the external sphincter, resulting in incontinence. In the absence of other pathologic changes, assess the functional integrity of the external sphincter by observing under direct vision the voluntary closure of the sphincter.

C Urodynamic evaluation is mandatory for patients with no obvious anatomic abnormality and in those with suspected sphincteric damage. Urodynamic testing helps in distinguishing between bladder and sphincteric causes for incontinence. Assessment of the abdominal leak point pressure, which is calculated as the total bladder pressure in the absence of a detrusor contraction at which leakage occurs, may help quantify the degree of sphincteric dysfunction.

D Treatment of bladder dysfunction includes fluid restriction, timed voiding, and anticholinergic medications. Consider neuromodulation or augmentation cystoplasty in severe cases that do not respond to simpler methods.

When stress incontinence secondary to sphincteric dysfunction persists beyond the postoperative healing period, a trial of medical management is indicated. The use of sympathomimetic agents such as ephedrine, in conjunction with sphincteric exercises, frequently proves therapeutic in cases of mild incontinence. Patients who remain incontinent despite optimal medical management are candidates for surgical intervention.

E Of the current surgical options available (Table 82-1), transurethral collagen injection is the simplest to perform and the least morbid. However, the overall effectiveness and durability of response to injected collagen for postprostatectomy incontinence have been disappointing. Obtain the best results by selecting patients with milder degrees of incontinence (<3 pads per day) and an abdominal leak point pressure >60 cm H2O. Most patients initially require multiple injections to obtain continence, with periodic reinjections at longer intervals to maintain dryness. Collagen injection therapy offers a less invasive form of treatment as a first-line...
Patient with POSTPROSTATECTOMY INCONTINENCE

A History and physical examination
Urinalysis and urine culture

Urinary tract infection
Treat infection

Sterile urine

Incontinence persists

B Uroflometrics
Cystourethroscopy

Normal or suspected sphincter damage

Urethral and/or bladder neck stricture

Residual prostatic obstruction

Urodynamic evaluation (urethral pressure profilometry, cystometrogram, pressure-flow studies)

Detrusor instability

Appropriate therapy (behavioral modification, anticholinergics)

Damaged external sphincter

Trial of medical therapy, pelvic floor exercises, biofeedback

Incontinence resolved

Persistent incontinence

Injection therapy with bulking agent
Implantation of artificial urinary sphincter (AUS)
Male sling
External compression or collecting device
therapy before considering a male sling or artificial urinary sphincter.

F Compared with injection therapy, artificial urinary sphincter (AUS) implantation achieves higher continence rates in a shorter period of time.\textsuperscript{8,9} However, drawbacks of an AUS include the morbidity of an operation and a surgical revision rate of 15 to 40%.\textsuperscript{1,7–9} Patients must have adequate manual dexterity and mental competence to operate the device. Social continence rates of approximately 80% and patient satisfaction rates of 90% have been reported with the AUS.\textsuperscript{9–11}

G In the last 5 years, a novel compressive sling has been developed to treat postprostatectomy incontinence. The placement of a sling at the level of the bulbar urethra, anchored to the pubic rami or rectus fascia, has been demonstrated to be an effective treatment in the short term.\textsuperscript{12–14} The long-term durability of this technique is unknown. The major advantage of the sling is that it does not require any mechanical manipulation.

Table 82-1 Surgical Treatment for Postprostatectomy Incontinence

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Injection of bulking agents</td>
<td>Performed under local anesthesia, minimal morbidity</td>
<td>Multiple procedures required, limited durability, less effective than other procedures</td>
</tr>
<tr>
<td>Artificial urinary sphincter</td>
<td>Very effective, immediate results</td>
<td>Morbidity from surgery, possibility of infection or erosion, reoperation required in 15 to 40%, requires manual dexterity</td>
</tr>
<tr>
<td>Male sling</td>
<td>Very effective</td>
<td>New technique, long-term outcome unknown, perineal discomfort</td>
</tr>
</tbody>
</table>

References
SECTION 10

THE URETHRA
Faulty embryogenesis of the cloacal region gives rise to the variety of abnormalities labeled anorectal malformations (ARMs). This usually involves a failure of the caudal migration of the urorectal septum or incomplete development of the proctodeal structures. ARM occur in 1:4,000 to 1:5,000 live births (M > F). Urogenital sinus malformations represent a combination of anomalies for which the true incidence is difficult to estimate; however, vaginal agenesis occurs in 1:4,000 to 1:5,000 live female births, and cloacal anomalies occur in 1:50,000 live births. The incidence of cloacal extrophy, which is associated with ARM, is approximately 1:200,000 to 1:400,000 live births. Infants with these anomalies are at risk for urosepsis and aspiration pneumonia. Mortality, although uncommon, is usually secondary to sepsis, cardiac anomalies, and renal failure.

Patients with anorectal or cloacal malformations may have a constellation of recognizable anomalies.

- VACTERL association: vertebral, anorectal, cardiac, tracheoesophageal, radial/renal, and limb anomalies
- Rokitansky-Küster-Hauser syndrome: vaginal agenesis, skeletal and renal anomalies
- MURCS association: müllerian duct aplasia, renal aplasia, and cervicothoracic somite

Patients with ARM have varied presentations:

- Abnormal prenatal sonogram (demonstrating renal anomalies, myelomeningocele, hydrocolpos, or extrophy)
- Abnormal neonatal examination (absence of anus, abnormal genitalia, perineal fistula)

Three groups of children with malformations may be recognized:

- Those with normal external genitalia and no perineal fistula
- Those with normal external genitalia and an obvious perineal fistula
- The rare group of females with a single perineal opening or cloaca

Up to 80% of male infants with supravelator anomalies have urinary tract fistulas. Depending on where the fistula opens into the urinary tract, it can affect the relationship of the ejaculatory ducts and the verumontanum. Up to 87% of female infants with supravelator anomalies have a fistulous communication with the genital tract. A rectovesical fistula is quite rare and is encountered in 6 to 13% of male patients and 1% of female patients with ARM.

A The goals of management of these patients are as follows:

- Stabilize the patient clinically and perform diagnostic evaluation to determine the level of the ARM and identify associated anomalies
- Commence initial therapies to normalize the anorectal anatomy, protect the upper urinary tracts, ensure low-pressure urinary drainage, and minimize any neurologic sequelae of treatable spinal cord pathology (ie, tethered cord)
- Normalize the anatomy and establish urinary and fecal continence

B Based on the physical findings and radiographic evaluation, the lesions can be divided into high, intermediate, and low lesions (Figure 83-1). A widely accepted classification system is the Wingspread Conference classification (Wingspread 1984). This classification is helpful in planning treatment and predicting the outcomes in terms of continence and also has the added advantage of allowing a better understanding of the embryogenesis of the various defects. The diagnostic evaluation of a baby with suspected ARM varies depending on the sex of the child.

If an external opening is visible in the perineum (indicative of a low malformation [infralevator]), one can predict the presence of an anocutaneous fistula or anal stenosis.

With the finding of a cleft (bifid scrotum) or a proximal hypospadias and/or complete absence of gluteal folds, a high (supravelator) lesion should be suspected.

Abdominal sonogram: Between 33% (low-level lesions) and 40% (high-level lesions) of these patients have urologic abnormalities (ie, vesicoureteral reflux [VUR] [20 to 47%], renal agenesis [5 to 19%], duplication anomalies, or neurogenic bladder).
Voicing cystourethrogram (VCUG)): A VCUG, as opposed to a radionuclide study, should be obtained as it provides additional anatomic details and can demonstrate the presence of a rectourinary or rectogenital fistula. Additionally 1 to 2% of these patients also have other urethral pathology.

Spinal sonogram: Ultrasonography can be used to evaluate the spine to demonstrate occult spinal cord abnormalities (25% incidence in these patients). After 6 months of age magnetic resonance imaging (MRI) is indicated owing to ossification of the vertebral bodies.

Invertogram: Demonstrates the location of the rectal pouch relative to the levator complex.

Fistulography.

A careful study of the female perineum will allow prediction of the nature of the lesion. The most common anomalies seen in the female are anovestibular fistula, anocutaneous fistula, and anal stenosis (high lesions are more common in males). If only a single orifice is seen at the level of the vulva, it represents a cloaca (constituting a common opening for the urethra, vagina, and rectum, which occurs in approximately 10% of all ARMs).

Radiographic evaluation should include the following:
- Abdominal ultrasonography to evaluate the urinary tract as well as the internal genitalia
- VCUG
- Spinal ultrasonography
- Fistulography

Invertograms are rarely indicated in females because very few patients have noncommunicating lesions.

Male or female infants with anal stenosis or anocutaneous or anovestibular fistula can usually have an anoplasty performed in infancy.

### Table 83-1 Classification of Anorectal Malformations

<table>
<thead>
<tr>
<th></th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perineal fistula</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Rectourethral fistula</td>
<td>Yes</td>
<td>Usually not</td>
</tr>
<tr>
<td>Bulbar</td>
<td></td>
<td>Persistent cloaca</td>
</tr>
<tr>
<td>Prostatic</td>
<td></td>
<td>Imperforate anus without fistula</td>
</tr>
<tr>
<td>Rectovesical fistula</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>(bladder neck)</td>
<td></td>
<td>Rectal atresia</td>
</tr>
<tr>
<td>Imperforate anus without fistula</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Rectal atresia</td>
<td>Yes</td>
<td></td>
</tr>
</tbody>
</table>

**Complex Defects**


Infants with intermediate- or high-level fistulas should undergo a fully diverting colostomy. Be aware that patients with an enterourinary fistula and a large segment of defunctionalized colon are at risk for developing hyperchloremic metabolic acidosis secondary to absorption of urine via the colonic mucosa.

Depending on the level of the lesion (infralevator versus supralevator), either a posterior sagittal anoplasty or a posterior sagittal anorectoplasty (Peña procedure [PSARP]) is undertaken.

If a rectourethral or rectovaginal fistula is present, it is addressed at the time of the PSARP. During the PSARP, while excising the urinary fistula, caution must be exercised to avoid narrowing the urethral lumen and creating a urethral stricture (keep in mind that a high percentage of these patients have congenital urethral strictures).
Anorectal Malformation

Associated genitourinary anomalies

Cause-specific therapy (next page)

Patient with low ARM
Patient with intermediate or high ARM
Cloacal anomaly
Cloacal exstrophy

Perineal procedure in infancy
Neonatal diverting colostomy
Panendoscopy

Posterior sagittal anoplasty (PSAP)
Posterior sagittal anorectoplasty (PSARP) (performed when patient is suitable)
Urinary fistulas repaired at this time
Anal dilation
Take down of colostomy

Short urogenital sinus (< 3 cm)
Perineal pull-through procedure with “W” or “U” flap

Long urogenital sinus (> 3 cm)
Abdominoperineal procedure to separate the vagina from the UG sinus. Vaginoplasty with/without continent urinary tract reconstruction

Initial goals are to stabilize the patient and then to determine the level of ARM diagnostic evaluation

History

Physical examination to determine if any associated anomalies are present
Serum electrolytes (renal panel) (correct any fluid and/or electrolyte abnormalities)
Urinalysis and urine culture (may see meconium in urine)
Abdominal and perineal ultrasonography
Spinal ultrasonography (if patient older than 6 months will need MRI)
VCUG: check postvoid urinary residual (PVR)
Invertogram (not required if meconium present) with/without Fistulogram
with/without Formal urodynamic evaluation (any patient scheduled for PSARP)
Patients with a large postvoid residual urinary volume might need to be started on clean intermittent catheterization (CIC) and antibiotic prophylaxis until the function of the urinary bladder can be appropriately studied.

Patients diagnosed with vesicoureteral reflux (VUR) should be started on antibiotic prophylaxis initially and the VUR managed expectantly. In some instances the child may need to be started on CIC (or in cases of high-grade VUR [grades IV–V] consider a vescostomy). (Manage the VUR as per Chapter 73, “Vesicoureteral Reflux”).

Female patients with cloacal or urogenital sinus anomalies should undergo panendoscopy prior to any surgical procedure.

Urogenital sinus anomalies should be addressed by a vaginoplasty procedure.

Patients with cloacal anomalies require a combined PSARP and vaginoplasty.

References
Patient with ASSOCIATED GENITOURINARY ANOMALIES

Cause-specific therapy

Vesicoureteral reflux
  - Antibiotic prophylaxis
  - Vesicostomy for grade V VUR
  - Ureteral reimplantation

Neurogenic bladder
  - Refer to neurosurgery for possible detethering
  - Antibiotic prophylaxis
  - CIC
  - Vesicostomy

Obstructive uropathy
  - Ureteropelvic junction, ureterovesical junction with/without megaureter
  - Antibiotic prophylaxis
  - Identify levels of obstruction (Lasix scan)
  - Site-specific treatment

Hypospadias
  - Undescended testes
  - Surgery
Folds or membranes that are embryologically obscure in origin and sometimes devastating in effect are the most common cause of congenital obstruction in the male urethra. These are usually called urethral valves, but this term is a misnomer that arose largely because of their endoscopic appearance. A better term might be congenitally obstructing urethral membrane, as suggested by Dewan.1 If the urethra is opened longitudinally on its anterior aspect at the time of autopsy, as it usually is, the lesion will appear as folds, rather than a membrane. If, however, the prostatic urethra is opened by excising its anterior wall, the lesion will show itself as a membrane that extends obliquely from the posterior to the anterior urethral wall with its lumen often eccentrically placed.2 The most common location for these membranes extends from a point just distal to the verumontanum, posteriorly, to the anterior urethral wall slightly distal to this point. This membrane is thought to be a wolffian remnant that should have involuted in utero but instead persists and produces an obstructing membrane.3 The mechanism by which this lesion, which has been termed type I urethral valves by Young and colleagues,4 produces its characteristic radiographic appearance is as follows: the obstructing lesion is a relatively fixed point as is the bladder neck while the prostatic urethra between these two points can dilate. This produces a characteristic radiographic appearance. Young also described two other lesions, but type II valves are not considered true obstructing lesions.5 Type III valves, oriented perpendicularly across the lumen of the urethra, depending on their location, merge into what have been called anterior urethral valves.6 Anterior urethral valves are much less common and, as the name implies, are located in the anterior urethra, most often in the bulbous urethra.7 They can also be found in the pendulous urethra and in the fossa navicularis.8 Although anterior urethral valves can be an obstructing membrane across the urethra and indistinguishable from a congenital urethral stricture, more often it seems to be the distal edge of a urethral diverticulum that is elevated and thereby obstructs as the urethra distends with urinary flow.

**Early Management**

**A** Many cases of posterior urethral valves are now detected antenatally.9 In the past, we hoped that, with early detection, in utero intervention might reverse the outcome in many of these boys. With that hypothesis, there have been in utero attempts at percutaneous drainage of the bladder,10 cutaneous vescostomy,11 and even endoscopic ablation of the valves.12 Unfortunately, no human evidence exists that such maneuvers have altered the eventual renal function of the boys, while the maternal and fetal risk has been significantly increased.13 Antenatal diagnosis, however, has allowed for prompt intervention once the infant is delivered. Some boys still present with palpable abdominal masses, urinary infection, poor stream, and day and night wetting, rarely with renal failure.14 Generally, boys presenting at a young age do not have poorer long-term renal outcome than do those presenting later.15

**B** The diagnosis of both posterior and anterior urethral valves is best made radiographically.5 The clinician will suspect the diagnosis on ultrasonography by the presence of hydronephrosis and a thickened bladder wall; sometimes the dilated posterior urethra is identified, producing what has been called a keyhole sign.14 The posterior urethral valve is best demonstrated with a voiding cystourethrogram, in which the voided stream is viewed in the oblique projection. The bladder neck will appear as an indentation between the bladder (which is usually heavily trabeculated) and a dilated prostatic urethra. There will be an abrupt change in caliber between the dilated prostatic and much smaller membranous urethra. An anterior urethral valve will usually appear as a saculation that ends in an abrupt reduction in urethral caliber but sometimes is manifest as a diaphragm across the anterior urethra. Once the diagnosis is suspected, it is important to assess the patient’s renal function and electrolyte balance and determine whether infection is present. A Tc 99m dimercaptosuccinic acid (DMSA) renal scan may help if one kidney is markedly hydronephrotic.16 Generally, boys presenting at a young age do not have poorer long-term renal outcome than do those presenting later.15

**C** If the patient is azotemic, place a catheter in the bladder to decompress it. Treat infection and correct any electrolyte imbalances.7 After the patient has been stabilized, the treatment depends on the nadir serum creatinine.

**D** If the nadir creatinine is < 1.0 mg/dL, infection has been controlled with antibiotics, and the urethra accepts an appropriate-sized endoscope without the necessity for urethral dilation, transurethral incision of the obstructing membrane is the treatment of choice.5,17 Avoid urethral dilation to permit introduction of the endoscope; it will likely produce a urethral stricture, which further complicates management.18
Patient with URETHRAL VALVES: EARLY MANAGEMENT

Antenatal diagnosis

Suspected infravesical obstruction

Voiding cystourethrogram and ultrasonography

Blood urea nitrogen, creatinine, electrolytes
Urine culture, renal scan in selected cases

Normal renal function, no infection (or urinary tract infection treated)

Azotemic, infected, or unstable

Catheter drainage, metabolic stabilization; treat infection

Creatinine stable < 1 mg%  Creatinine stable > 1 mg%

Yes

Urethra accepts endoscope without dilation

Endoscopic ablation of valves

Hydronephrosis improves

Yes

Hydronephrosis does not improve

Observe

Negative

Whitaker test

Positive

Pyelostomy or ureterostomy

No

Yes

Vesicostomy
E Conversely, if the creatinine is significantly elevated, if infection cannot be controlled, or if the urethra will not accept an appropriate endoscope, urinary diversion by cutaneous vesicostomy is the easiest and most efficacious modality. Whether the valves are primarily resected or a vesicostomy has been employed, it is important to observe the patient over time to ensure that hydronephrosis improves and azotemia is minimized. If hydronephrosis does not improve or if azotemia increases, it is important to rule out obstruction at the ureteropelvic or the ureterovesical junction with a diuretic renal scan or even a Whitaker pressure perfusion test. Although invasive, the Whitaker test, in this instance, may prove more reliable because the poorly functioning kidney may not respond well enough to a diuretic to give reliable results.

F If these show positive results, supravesical diversion with cutaneous pyelostomy or loop or end cutaneous ureterostomy would be indicated.

G Long-Term Management

If the nadir creatinine remains elevated and the patient is adequately diverted so that obstruction has been relieved, eventually this will necessitate considering reconstruction in preparation for eventual renal transplantation. However, if the urinary tract is intact or diverted and no ongoing obstruction is present, dietary management is necessary to forestall the need for dialysis and transplantation for as long as possible.

H During periods of observation, it is important to monitor hydronephrosis and serum creatinine. If these should increase, rule out correctable factors such as obstruction, infection, and decreased bladder compliance and, if any of these are present, correct them to minimize their impact on the kidneys.

I In the intact patient, as the patient is being observed over time, hydronephrosis or serum creatinine may increase, thus making it important to determine whether the bladder itself is at fault. To accomplish this, place a Foley catheter in the bladder for a short period of time (a few days to a week) to determine if the hydronephrosis and creatinine improve.

J If Foley catheter drainage does not result in improvement in upper tract dilatation, a Whitaker pressure perfusion test may be necessary to prove that no obstruction has developed at the ureterovesical or the ureteropelvic junctions. A Mag-3 renal scan with diuretic washout likely would not suffice for this purpose because renal function would be too poor to respond.

K In the event that there is no ongoing lower tract obstruction and no ureterovesical or ureteropelvic obstruction, videourodynamic can determine if there is vesicoureteral reflux and decreased bladder compliance to explain the increase in hydronephrosis. The clinician may treat decreased vesical compliance with anticholinergics, but often this does not suffice. Therapeutic choices at this point include urinary diversion or augmentation cystoplasty. Although the intestine or the stomach has been used in the past, these have definite disadvantages. If one kidney is not functioning, as shown by DMSA renal scan, the clinician can proceed to a nephrectomy, and the ureter can be used to augment the bladder.

L If the nadir creatinine is normal and the patient is diverted, the urinary tract should be reconstructed.

M Once the urinary tract is intact, it is important to periodically monitor serum creatinine and hydronephrosis to ensure that no new or ongoing problems have occurred that might impact renal function. At times, it may be necessary to place a Foley catheter to determine whether a full bladder is adversely affecting renal function. Similarly, a Whitaker test or videourodynamic may be needed to assess obstruction or compliance.

N For vesicoureteral reflux that is present in the intact patient with hydronephrosis and a normal serum creatinine level, treatment with anticholinergics and prophylactic antibiotics will occasionally result in resolving the vesicoureteral reflux. If it does not and there is a functioning renal unit, consider ureteroneocystostomy. Conversely, if the ipsilateral renal unit is nonfunctional, consider nephroureterectomy.
Another issue in long-term management is continence. Assuming that patients achieve normal urinary control, they should be observed over time to monitor renal function. A significant number of boys, however, either do not achieve or, over time, lose urinary control. With respect to renal function, this is often a poor prognostic sign. Ongoing obstruction, decreased vesical compliance, and infection must be ruled out. These can be treated and, perhaps, result in continence. Sphincter damage from previous treatment is fortunately rare and, as long as the bladder neck is intact, usually does not result in incontinence. Hyposthenuria as a result of nephrogenic diabetes insipidus is difficult to control.

Urinary diversion has been suggested as a temporizing measure in these patients.\textsuperscript{23}

Whether renal function is normal or abnormal, continence is often a long-term problem for these boys. If incontinence is present, it is important to rule out urinary infection and ongoing infravesical obstruction, as well as to correct decreased bladder compliance. Hyposthenuria, if present, is a difficult problem to manage and often results in urinary incontinence. Damage to the urinary sphincter, although possible, is not a frequent cause of incontinence as long as the bladder neck is intact.
References
Successful hypospadias repair requires a broad understanding of surgical options and, as such, does not always lend itself to an algorithmic pathway. Nevertheless, recent advances in hypospadias repair have streamlined our approach to this complex reconstructive challenge.

A Careful use of androgen stimulation can be very helpful when the glans size is inadequate. We administer intramuscular testosterone enanthate (25 mg) 5 weeks prior to the hypospadias repair followed by a repeat dose 2 weeks later if required.

B The artificial erection is critical to determine the presence or absence of chordee. Although this is usually performed after degloving the penis, it can be performed as the initial step according to the surgeon’s preference. It is cosmetically beneficial to incorporate inner preputial flaps ventrally.

C Should chordee remain following takedown of the skin, it is usually the result of corporal disproportion. If penile length is adequate, the most direct means to correct this is through plication of the tunica albuginea. The tunica albuginea must be incised, either longitudinally or transversely, prior to plication to ensure that the plicated edges heal together permanently. Care must be exercised not to injure the ventral neurovascular bundle. One option is to elevate the bundle using a Freer elevator prior to plication.

D In the presence of severe chordee, penile length can be compromised following plication of the tunica albuginea. The patient is better served by dividing the urethral plate and ventral tunica albuginea of both corporal bodies. This tissue defect is then covered by the interposition of autologous dermis or other suitable tissue replacement. We have had excellent results using commercially available porcine lamina propria. A second-stage procedure is then performed in 6 months.

E Several options are available for a glanular repair. In mild cases, all that may be needed is a meatoplasty in conjunction with removal of the dorsal hooded foreskin and the incorporation of ventral skirt flaps. If the meatus is more proximal in location, an M inverted V glansplasty (MIV) repair or the meatal advancement glanuloplasty (MAGPI) can be employed. Both require a relatively mobile meatus to be successful. For the megameatus variant, we prefer the glans approximation procedure (GAP) repair.

F The Thiersch-Duplay method can be used for all repairs proximal to the glans. Where the urethral plate width is inadequate, this can be incised in the midline to “hinge” the tissue, facilitating closure. Although this approach can be used for penoscrotal, scrotal, and perineal hypospadias, these variants may have severe chordee, necessitating a two-stage repair. To minimize fistula formation, a second tissue layer must overlay the repair. Our preference is a subcutaneous pedicle flap harvested from the dorsal foreskin. Others report good success using abortive spongiosum, as well as with tunica vaginallis coverage.

G When the repair is performed in an infant, a urethral stent is usually optional. Our preference is to not use them except in toilet-trained boys to obviate the risk of urinary retention. Preoperative and postoperative phenazopyridine has allowed us to perform stentless repairs in these boys.

Good surgical technique is as important as choice of repair in obtaining a successful outcome. Surgical magnification employing either a microscope or 3.5× loupes is critical. Also important is careful tissue handling with precise placement of all sutures.

Additional Readings
Current Approach to Hypospadias

**Patient with HYPOSPADIAS**

A. **Assess glans size**

- **Testosterone Stimulation**
  - Inadequate
  - **Deglove penis and perform Gittes test**
    - Significant persistent chordee
      - Tuna albuginea plication
        - **Assess penile length**
          - Adequate
            - Wait 6 months to permit maximal wound healing
              - Divide urethral plate and ventral corporal bodies followed by corporoplasty using dermis or porcine lamina propria
                - **Meatal position**
                  - No chordee
                    - **Glanular meatus**
                      - Coronal meatus
                        - Midshaft and distal penile meatus
                          - **Penoscrotal, scrotal, or perineal hypospadias**
                            - **1. GAP procedure for megameatus variant**
                              - **2. MIV repair**
                                - **3. MAGPI repair**
                                  - **4. Meatoplasty**

- **Adequate**

B. **Deglove penis and perform Gittes test**

- No chordee
  - **Tunica albuginea plication**
  - **Assess penile length**
    - Adequate
      - **Wait 6 months to permit maximal wound healing**
        - Divide urethral plate and ventral corporal bodies followed by corporoplasty using dermis or porcine lamina propria
          - **Meatal position**
            - No chordee
              - **Glanular meatus**
                - **Coronal meatus**
                  - Midshaft and distal penile meatus
                    - **Penoscrotal, scrotal, or perineal hypospadias**
                      - **1. GAP procedure for megameatus variant**
                        - **2. MIV repair**
                          - **3. MAGPI repair**
                            - **4. Meatoplasty**

C. **Significant persistent chordee**

- **Tunica albuginea plication**
  - Adequate
    - **Wait 6 months to permit maximal wound healing**
      - Divide urethral plate and ventral corporal bodies followed by corporoplasty using dermis or porcine lamina propria
        - **Meatal position**
          - No chordee
            - **Glanular meatus**
              - **Coronal meatus**
                - Midshaft and distal penile meatus
                  - **Penoscrotal, scrotal, or perineal hypospadias**
                    - **1. GAP procedure for megameatus variant**
                      - **2. MIV repair**
                        - **3. MAGPI repair**
                          - **4. Meatoplasty**

D. **Assess penile length**

- Inadequate
  - Divide urethral plate and ventral corporal bodies followed by corporoplasty using dermis or porcine lamina propria
    - **Meatal position**
      - No chordee
        - **Glanular meatus**
          - **Coronal meatus**
            - Midshaft and distal penile meatus
              - **Penoscrotal, scrotal, or perineal hypospadias**
                - **1. GAP procedure for megameatus variant**
                  - **2. MIV repair**
                    - **3. MAGPI repair**
                      - **4. Meatoplasty**

E. **Meatal position**

- **No stent**
  - Toilet trained or on phenazopyridium
    - Toilet trained or reoperation
      - **Glanular meatus**
        - **Coronal meatus**
          - Midshaft and distal penile meatus
            - **Penoscrotal, scrotal, or perineal hypospadias**
              - **1. GAP procedure for megameatus variant**
                - **2. MIV repair**
                  - **3. MAGPI repair**
                    - **4. Meatoplasty**

F. **Divide urethral plate and ventral corporal bodies followed by corporoplasty using dermis or porcine lamina propria**

- Not toilet trained or on phenazopyridium
  - Toilet trained or reoperation
    - **Glanular meatus**
      - **Coronal meatus**
        - Midshaft and distal penile meatus
          - **Penoscrotal, scrotal, or perineal hypospadias**
            - **1. GAP procedure for megameatus variant**
              - **2. MIV repair**
                - **3. MAGPI repair**
                  - **4. Meatoplasty**

G. **No stent**

- Toilet trained or reoperation
  - **Stent x 3–5 days**
A urethral diverticulum is an epithelial-lined, sac-like outpouching of the urethral wall that results from either a congenital defect or, more commonly, an acquired insult. The reported incidence of urethral diverticula is between 1.4 and 5%. The true incidence is probably higher due to the large number of asymptomatic women who are overlooked during the evaluation of patients with lower urinary tract symptoms. Urethral diverticula were first described by Hey in the beginning of the nineteenth century. It was not until the 1950s, with the advent of positive-pressure urethrography, that they became more commonly recognized. Urethral diverticula are usually found in women between ages 25 and 60 years, with a mean age of 40 years at diagnosis. Although some older studies support a higher incidence in African American women compared with Caucasian women, newer studies are less conclusive.

Urethral diverticula are generally believed to be an acquired process. There are reports of congenital diverticula, which are thought to be due to either faulty union of primordial folds, development of Gartner’s ducts, müllerian duct cysts, or agenesis of the muscular component of the urethra. Most cases, however, are thought to be due to infection resulting in obstruction of the periurethral glands and in formation of suburethral cysts. These cysts then dilate and eventually rupture into the urethra, allowing urine to enter and pool within the cyst. Epithelialization ensues, and the diverticulum is formed. The infection can originate from several sources, including vaginal flora, enteric flora, and sexually transmitted diseases such as gonorrhea. Stagnation of the urine with an active infectious process can lead to recurrent urinary tract infections (UTIs), stone formation, development of fistulas, and even malignancy.

Urethral diverticula can present in many ways. The three Ds—dysuria, dyspareunia, and dribbling—are common symptoms. Nocturia, frequency, urgency, hematuria, vaginal mass, suprapubic or vaginal pain, incontinence, or urinary retention may also be the initial form of presentation. As many as 20% of women with urethral diverticula are asymptomatic. In those with abscess or fistula formation, severe pain, fever, and purulent discharge are common. Table 86-1 lists the differential diagnosis of periurethral masses. A thorough physical examination is an important part of evaluating for urethral diverticula. Palpable masses can be found in the most women with urethral diverticula. On pelvic examination, a soft or hard suburethral mass can be palpated, which can be tender or nontender. On compression of the urethra, purulent material or urine can often be expressed from the meatus. Table 86-3 lists the differential diagnosis of periurethral masses.

Table 86-1: Common Symptoms in Patients with Urethral Diverticula

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency</td>
<td>Urge incontinence</td>
</tr>
<tr>
<td>Urgency</td>
<td>Suprapubic pain</td>
</tr>
<tr>
<td>Dysuria</td>
<td>Perineal pain</td>
</tr>
<tr>
<td>Recurrent UTI</td>
<td>Hesitancy</td>
</tr>
<tr>
<td>Postmicturition dribbling</td>
<td>Vaginal/urethral discharge</td>
</tr>
<tr>
<td>Dyspareunia</td>
<td>Urinary tenderness</td>
</tr>
<tr>
<td>Hematuria</td>
<td>Incomplete voiding</td>
</tr>
<tr>
<td>Stress incontinence</td>
<td>Urinary retention</td>
</tr>
</tbody>
</table>

UTI = urinary tract infection.

B Multiple modalities can be used to confirm the diagnosis of urethral diverticula (Table 86-4). Although controversial, the voiding cystourethrogram (VCUG) remains the initial imaging technique of choice in terms of sensitivity, specificity, availability, comfort, and cost. Perform under fluoroscopy with the patient in a standing position (Figure 86-1). If a diverticulum is not visualized, a retrograde positive-pressure double balloon catheterization (PPU) can be performed. PPU is more sensitive than a VCUG, but it is generally more uncomfortable for the patient (Figure 86-2). An air-fluid level is commonly seen in large diverticula. A filling defect within the diverticulum may suggest a neoplasm, a calculus, or an inflammatory mass.

A third tool that aids in the diagnosis of urinary diverticula is urethroscopy. A zero-degree lens can

Table 86-2: Differential Diagnosis for Symptoms Similar to Urethral Diverticulum

<table>
<thead>
<tr>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacterial cystitis</td>
</tr>
<tr>
<td>Interstitial cystitis</td>
</tr>
<tr>
<td>Detrusor instability</td>
</tr>
<tr>
<td>Bladder or urethral carcinoma in situ</td>
</tr>
<tr>
<td>Vesicovaginal or urethrovaginal fistula</td>
</tr>
<tr>
<td>Bladder stone</td>
</tr>
<tr>
<td>Hypertreflexic neurogenic bladder</td>
</tr>
</tbody>
</table>
Urethral Diverticula in the Adult Female

Patient with SUSPECTED URETHRAL DIVERTICULUM

A
History
Physical examination

B
Voiding cystourethrogram
Positive pressure urethrogram
Urethroscopy
Endoluminal MRI
Ultrasonography
Intravenous pyelography

Urethral diverticulum confirmed

C
Urodynamic evaluation if indicated

Conservative treatment
Surgical treatment

D
Asymptomatic
Poor general condition
Risk for incontinence

Large ostium
Uncomplicated diverticulum

Postvoid stripping
Observation
Biopsy if indicated

Small ostium
Abscess

Aspiration
Local/systemic antibiotics

E
Symptomatic
Failure of conservative treatment
Calculus
Fistula

Transurethral diverticulotomy
Transvaginal marsupialization
Total excision of diverticulum
Consider paravaginal flap
Biopsy

F
Malignancy

No malignancy

Observation

Poor surgical candidate
Observation

Surgical candidate
Wide local excision and/or radiation
Cystourethrectomy
Anterior exenteration
Adjuvant therapy

Biopsy if indicated
The diverticula during urethroscopy, the anterior wall of the vagina can be massaged, resulting in expression of purulent material or urine.

In recent years, endoluminal magnetic resonance imaging (MRI) has become the new gold standard to document the presence of diverticula\(^26,27\) (Figure 86-3 and Figure 86-4). It is especially useful when diverticula are strongly suspected but not visualized using other diagnostic techniques. It can also be used to define the extent and complexity of the diverticula and to aid in planning definitive surgical management.\(^28\)

Transrectal, transperineal, or even endovaginal ultrasonography provides a quick, noninvasive, and accurate way to diagnose diverticula. Ultrasonography can also help distinguish multiple diverticula from a single, large septated diverticulum.\(^29-31\) An intravenous pyelogram (IVP) may be indicated when an ectopic ureterocele is suspected.\(^32\) In addition, diverticula can sometimes be visualized on the postvoid films from an IVP.

Once a diverticulum has been confirmed, urodynamic evaluation of the urethra with assessment of the urethral pressure profile will assist in the choice of surgical repair.\(^33,34\) The urethral pressure profile in patients with diverticula shows a biphasic curve. It also identifies diverticula that are located near the peak urethral clo-

**Table 86-3** Differential Diagnosis for Suburethral Mass

<table>
<thead>
<tr>
<th>Diagnosis</th>
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<tbody>
<tr>
<td>Urethral diverticulum</td>
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<tr>
<td>Gartner's duct cyst</td>
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<tr>
<td>Skene gland infection</td>
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<tr>
<td>Ectopic ureter</td>
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<tr>
<td>Vaginal wall leiomyoma/schwannoma</td>
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<tr>
<td>Urethral neoplasm</td>
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<tr>
<td>Cystourethrocele</td>
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<tr>
<td>Mucosal prolapse</td>
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<tr>
<td>Urethral caruncle</td>
</tr>
</tbody>
</table>

**Figure 86-1** Voiding cystourethrogram showing small female urethral diverticulum (arrow). (Courtesy of Robert F. Spataro, MD, Rochester, NY.)

**Figure 86-2** Large female diverticulum. Note catheter balloon in the bladder (large arrow), multiple stones in the diverticulum (double small arrows), and positive-pressure double balloon catheter (single small arrow). (Courtesy of Robert F. Spataro, MD, Rochester, NY.)

**Figure 86-3** MRI showing coronal view of a urethral diverticulum (arrow). (Courtesy of Howard B. Goldman MD, Cleveland, OH.)
sure pressure segment, in which case, marsupialization is contraindicated as it can result in incontinence. Urodynamic evaluation can also diagnose stress incontinence, which affects surgical treatment. The urodynamic evaluation may be omitted in patients who are not candidates for surgical treatment.

If the patient is asymptomatic, is mildly symptomatic, has poor general health, or is at high risk for developing incontinence with surgical management, initially employ conservative treatment. If the patient has a large ostium in an otherwise uncomplicated diverticulum, postvoiding vaginal stripping of the urethra will decrease the risk of infection and may relieve some of the symptoms. If the diverticulum has a small opening and an associated abscess, treat with aspiration and antibiotics. This is also the first option for treatment in patients who are at high risk for incontinence. Consider a biopsy in those patients at risk for malignancy.

Surgical treatment is the option of choice in patients who are symptomatic, are unresponsive to medical treatment, have calculi, or have a fistula. Different classification systems have been formulated to group diverticula and aid in this management. Transurethral endoscopic diverticulotomy, transvaginal diverticulotomy, or total excision of the diverticulum with urethral reconstruction and biopsy are the standard procedures for definitive treatment. Patients with additional stress incontinence should have a concomitant vaginal sling procedure at the time of diverticular surgery.

Marsupialization is appropriate in patients with distal diverticulum or when the diverticulum has a small opening with an associated abscess. Total excision, the treatment of choice for urethral diverticula, offers the best long-term outcomes in those patients who are candidates. The goal of this surgery is to excise the entire diverticulum and obtain a watertight closure. All available techniques use a transvaginal approach with multiple-layer closure of the urethra and vagina to avoid overlapping of suture lines.

Complications from any of the above surgeries include urethrovaginal fistulas, recurrent diverticula, and secondary stress incontinence. In patients with recurrent diverticula or peridiverticular inflammation, a paravaginal flap is often needed to prevent breakdown or recurrence.

Urethral carcinoma is a rare entity that has been reported in fewer than 100 patients with urethral diverticula. Adenocarcinoma is the most common form, although transitional cell and squamous cell carcinoma have also been reported. Presentation may vary, but irritative voiding symptoms and urethral spotting or bleeding are the most common presenting signs. MRI is the imaging study of choice. Management and prognosis of a diverticular malignancy vary depending on the size, location, and extent of disease, as well on the general medical condition of the patient. Surgery and radiation are the mainstays for primary and adjunctive treatment of urethral diverticular carcinoma. In patients who have bulky disease or are good surgical candidates, treatment consists of cystourethrectomy and anterior exenteration with or without adjunctive treatment. If patients have small, localized disease or are poor surgical candidates, wide local excision with radiation is also an option. Chemotherapy is a treatment of last resort for urethral diverticular malignancies. New regimens are currently being tested, and it is hoped that in the future more effective treatments may be found.

References
Urethral strictures are stenosing regions in the urethra that occur as a result of injury, with varying locations, length, and thickness. The injury causes fibrotic scar formation, which replaces the normal urothelium with possible involvement of the surrounding corpus spongiosum. Presentation, symptoms, and treatment of the stricture depend on the extent, etiology, and location.1

Urethral strictures can be traced back to sixth century BC, where ancient Hindoo writing described acts of urethral lithotomy and dilation.2 Although there have been many similarities over the centuries in presentation and treatment, urethral stricture management has undergone significant changes over the last 50 years. With the advent of endoscopic and open surgical intervention, invasive management is now more widely practiced.

Table 87-1 lists the causes of urethral strictures in the adult male. Previously, gonococcal urethritis was the most prevalent cause of strictures. With the advent of early detection and treatment with antibiotics, however, trauma has become the most common cause.3 Traumatic injuries include straddle injuries, injury because of urethral instrumentation, and injuries to the pelvis and perineum. Trauma generally leads to short, dense strictures with healthy adjacent urethra, whereas infection results in long and irregular strictures with diffuse proximal involvement.4 Infectious causes include balanitis xerotica obliterans (BXO), gonorrhea, and chlamydia. BXO affects the genital skin of the prepuce and presents with white, thickened plaques on the surface of the glans. It usually causes meatal stenosis and phimosis but also can cause penile urethral strictures.5 Prolonged urethral catheterization and the use of latex catheters may result in local ischemia and possible stricture disease, although studies are inconclusive.6,7 As a preventive measure, plastic and silicone catheters, and even suprapubic catheterization, are now used instead of latex catheters at some centers for patients undergoing surgeries where prolonged catheterization is expected. A congenital origin of stricture disease has been reported in the literature; however, other causes must first be ruled out before considering this etiology.8,9

Knowledge of the anatomy of the genitourinary system plays an important role in understanding stricture presentation and instituting appropriate treatment. The male urethra extends from the bladder neck to the external meatus, passing through the body of the prostate gland and urogenital diaphragm.10 The penis is divided into two regions. The anterior region extends from the inferior aspect of the urogenital diaphragm to the external meatus and consists of the bulbomembranous, bulbar, pendulous, and submeatal regions of the urethra. The posterior region comprises the membranous and prostatic regions. Stricture disease usually involves the anterior urethra, with the bulbar region being the most common location. There is a different location and depth of surrounding spongiosal tissue along the course of the urethra. This affects the extent of injury and the treatment management. The penis receives its blood supply from the bulbar arteries and the dorsal artery of the penis, forming a biaxial system. This dual blood flow supplies both the genital skin and corpus spongiosum. This allows manipulation and transfer of tissue without injuring the penis and urethra.

A Diagnosing a urethral stricture in a patient requires a complete history and a physical examination. Urethral strictures manifest with a wide array of symptoms (Table 87-2). Patients commonly present with obstructive voiding symptoms and a decreased force, with or without spraying of urinary stream.11 Patients with urethral strictures can present with secondary urinary tract infection (UTI), epididymitis, or prostatitis. If left untreated, major complications could arise (Table 87-3). Stricture symptoms are similar to symptoms encountered in other conditions; thus, a wide differential should be entertained (Table 87-4). Spontaneous urethral bleeding should lead to concern for urethral carci-

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**Table 87-1** Etiology of Urethral Strictures

<table>
<thead>
<tr>
<th>Traumatic</th>
<th>Straddle injury</th>
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<tbody>
<tr>
<td></td>
<td>Iatrogenic</td>
</tr>
<tr>
<td></td>
<td>Pelvic fractures</td>
</tr>
<tr>
<td>Inflammatory</td>
<td>Gonorrhea</td>
</tr>
<tr>
<td></td>
<td>Chlamydia</td>
</tr>
<tr>
<td></td>
<td>Balanitis xerotica obliterans</td>
</tr>
<tr>
<td>Ischemic</td>
<td></td>
</tr>
<tr>
<td>Congenital</td>
<td></td>
</tr>
</tbody>
</table>

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**Table 87-2** Symptoms in Patients with Urethral Stricture

<table>
<thead>
<tr>
<th>Decreased force of stream</th>
<th>Spontaneous urethral bleeding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nocturia</td>
<td>Hesitancy</td>
</tr>
<tr>
<td>Dysuria</td>
<td>Postvoid dribbling</td>
</tr>
<tr>
<td>Frequency</td>
<td>Epididymitis</td>
</tr>
<tr>
<td>Recurrent UTIs</td>
<td>Penile pain</td>
</tr>
<tr>
<td>Hematuria</td>
<td></td>
</tr>
</tbody>
</table>

UTIs = urinary tract infections.
Urethral Stricture in the Adult Male

**Diagnostic studies:**
- Uroflometry
- Urethrography
- Urethroscopy
- Ultrasonography

**History**
- Physical examination

**Posterior urethral strictures**
- Status post radical prostatectomy
  - > 2 cm length
  - BXO
  - Primary perineal anastomosis
  - Abdominoperineal repair
  - Endoscopic urethrotomy
  - Serial dilations
  - Laser urethrotomy

**Conservative treatment**
- Urethral dilations
- Internal urethrotomy
- Urethral stent

**Open urethroplasty**
- Trauma
- Uncomplicated failure of conservative treatment
  - Single-stage urethroplasty
  - Cure
  - Observe

- Severe BXO
  - Urethrocutaneous fistula
  - Chronic periurethral infection
  - Multiple-stage urethroplasty
  - Cure
  - Observe
  - Recurrence
  - Conservative treatment
  - Observe
A history of previous prostatectomy should raise the possibility of bladder neck contracture. A history of obstructive voiding symptoms can raise the possibility of benign prostatic hypertrophy or bladder calculi. Severe prolonged obstruction can lead to a high-pressure system, causing vesicoureteral reflux and possibly leading to renal failure. Retention can result from active infection or bleeding.

A physical examination can help with the diagnosis of stricture disease. In some patients with stricture disease, especially those with severe disease, the clinician can palpate a firm nodule around the urethra. Further, evidence of BXO, fistula, or abscess can be detected on physical examination. A digital rectal examination can help evaluate for prostate cancer, benign hypertrophy, or prostatitis. A scrotal examination can help diagnose epididymitis.

Once a stricture is suspected, perform diagnostic studies to confirm this possibility.

Uroflowmetry with a flow of < 10 mL/s (normal 20 mL/s) suggests obstruction. Severe, chronic urethral stricture disease can cause elevated serum creatinine, which suggests urinary retention or renal deterioration. Urine culture can determine if active infection is present.

Retrograde urethrogram, the diagnostic study of choice for anterior stricture disease (Figures 87-1, 87-2), determines the presence, location, length, and multiplicity of disease. Dynamic studies offer better localization of the stricture, and more than one view may be needed to visualize the stricture. Voiding cystourethrography can also help better delineate proximal strictures, as seen in trauma. In patients with suprapubic catheters, antegrade studies are useful. Urethrography can visualize fistulas and diverticuli, but it fails to delineate the depth of stricture disease. Ultrasonography is a quick and noninvasive radiologic study to measure the thickness of an anterior stricture. Ultrasonography can also measure arterial supply, which can be affected in trauma leading to erectile dysfunction. Magnetic resonance imaging (MRI) is useful for urethral disease following pelvic trauma.

Cystourethroscopy can visualize and evaluate the stricture, helping to determine the type of repair. It can also help in placement of a urethral catheter in those with urethral injuries or urinary retention and evaluate the urethra for malignancy in patients with chronic strictures. Take a biopsy of all suspicious lesions.

In all diagnostic studies, it is important to delineate normal urethra, both distal and proximal to the stricture, to avoid recurrence after treatment.

Once a urethral stricture is diagnosed, a treatment plan is made according to location, length, multiplicity, and etiology. Treatment options can be broadly separated into conservative and open surgical treatments. In con-

**Table 87-3 Complications of Untreated Urethral Strictures**

<table>
<thead>
<tr>
<th>Complication</th>
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</thead>
<tbody>
<tr>
<td>Recurrent urinary tract infections</td>
</tr>
<tr>
<td>Chronic epididymitis/prostatitis</td>
</tr>
<tr>
<td>Perirectal abscess</td>
</tr>
<tr>
<td>Urethrocutaneous fistula</td>
</tr>
<tr>
<td>Urethral carcinoma</td>
</tr>
<tr>
<td>Urinary retention</td>
</tr>
<tr>
<td>Bladder calculi</td>
</tr>
<tr>
<td>Bladder diverticuli and decompensation</td>
</tr>
<tr>
<td>Bilateral hydronephrosis and renal insufficiency</td>
</tr>
</tbody>
</table>

**Table 87-4 Differential Diagnosis with Symptoms Similar to Urethral Strictures**

<table>
<thead>
<tr>
<th>Condition</th>
</tr>
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<tbody>
<tr>
<td>Benign prostatic hypertrophy</td>
</tr>
<tr>
<td>Prostate carcinoma</td>
</tr>
<tr>
<td>Bladder neck contracture</td>
</tr>
<tr>
<td>Cystitis</td>
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<tr>
<td>Bladder calculi</td>
</tr>
<tr>
<td>Prostatitis</td>
</tr>
<tr>
<td>Interstitial cystitis</td>
</tr>
<tr>
<td>Urethral carcinoma</td>
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<tr>
<td>Urethral foreign body</td>
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</tbody>
</table>
Urethral Stricture in the Adult Male

Urethral dilation involves the progressive, gentle, and gradual insertion of dilators into the urethra until resistance is met. The goal is to gradually stretch and break the scar without producing injury. This dilation process temporarily enlarges the lumen. Serial dilation is performed until a lumen approximately 24 French diameter is achieved—a process that can take weeks.\(^4\) Filliforms and followers might be needed initially, with the aid of a flexible urethroscope to avoid false passages. Meatal strictures caused by instrumentation are best handled by periodic dilations. Dilations rarely help the patient who fails initial dilation and in those whose strictures extend beyond the urethral mucosa. Complete cure occurs only in superficial lesions. Lengthy or multiple strictures, fistulas, abscesses, and a history of false passages are contraindications and must be ruled out before attempting dilation because dilation can further traumatize the urethra.\(^3\) Failure of treatment can also be seen in patients with decreasing time intervals between dilations and if patients require dilation at intervals of less than 4 to 6 months.\(^12\)

Self-catheterization, a form of dilation that has been used as adjunctive therapy to conservative and to surgical treatments to increase success rates and to increase time interval between repeat treatments, involves a program of initial daily catheterizations with a tapered frequency over an extended 3- to 12-month period until an adequate and stable opening is achieved. This allows the urethra to heal with a lower likelihood of restricture.\(^16\) Studies have shown that clean, intermittent self-catheterization can delay and possibly prevent stricture recurrence provided that it is continued for at least 1 year.\(^17\)

Urethrolotomy is another common regenerative treatment used for urethral strictures. Since 1961, endoscopic direct vision urethrotomy has replaced blind urethrotomy.\(^18\) A cold knife is currently used; laser urethrotomy appears to offer no advantage.\(^19\) With the advent of newer endoscopic equipment, direct vision urethrotomy has become the primary treatment for uncomplicated bulbar urethral strictures. Its success rate has been reported to be between 56 and 95%, depending on the series.\(^20\) It is mainly used in the bulbar region and when stricture length is less than 2 cm. In a recent series of 199 cases of bulbar urethral strictures, 96% of strictures were less than 2 cm, making internal urethrotomy a viable first-line option.\(^21\) Urethrotomy is generally not indicated in the penile urethral region, owing to the high rate of stricture recurrence.\(^20\) Incision is usually made at the 12 o’clock region of the stricture to avoid the penile vasculature. It must include the full length and depth of the stricture.\(^22\) Multiple incisions may be needed for severe strictures, and subsequent incisions are usually done at the 3 and 9 o’clock positions. In severe strictures, a guidewire is needed to prevent the creation of false passages and injury to the surrounding corpora. A catheter is left in place for 2 to 7 days posturethrotomy because studies have shown that leaving a catheter in for longer does not affect lumen re-epithelialization.\(^23\) In fact, if the surgeon does not leave a catheter in, this can make the urethra prone to hemorrhage, which is the second most common complication in urethrotomy after recurrence.

Initial short-term follow-up studies showed promising results, with a 70 to 80% success rate in treatment of urethral strictures. This figure was significantly higher than were other forms of regenerative treatments.\(^10\) Newer studies, however, are inconclusive regarding long-term results. Long-term follow-up has shown similar results with dilation and internal urethrotomy, with recurrence rates as high as 80% depending on the length and extent of disease.\(^15\) These high recurrence rates may be due to either failure of treatment or due to the changing nature of strictures, with more common traumatic strictures being harder to cure than infectious strictures.\(^18\) Studies have also shown that recurrence of strictures after urethrotomy portends lower success rate with each successive urethrotomy. A second urethrotomy (or dilation) for stricture recurrence within 3 months has limited value. Conversely, if the stricture recurs more than 6 months after initial

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**Figure 87-2** Retrograde urethrogram showing a diffuse panurethral stricture (small arrows). A urethrocutaneous fistula can also be seen (large arrow). (Courtesy of Arthur J. Segal, MD, Rochester, NY.)
Surgical repair is used in those patients who fail regenerative treatment or have strictures that are not amenable to conservative management. This includes panurethral strictures, posthypospadias strictures, complex bulbo cavernosum pathology, and strictures with extensive spongiofibrosis.11 Many surgical options are available with no single procedure appropriate for management of all strictures. Options include stricture excision and primary anastomosis, placement of full-thickness graft on incised stricture, placement of tube graft or flap in place of excised stricture, genital flap placement on the incised stricture, and a combination of these options (Table 87-5).

<table>
<thead>
<tr>
<th>Conservative</th>
<th>Surgical</th>
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<tbody>
<tr>
<td>Urethral dilation</td>
<td>Primary anastomosis</td>
</tr>
<tr>
<td>Optical internal urethrotomy</td>
<td>Full-thickness graft/tube graft</td>
</tr>
<tr>
<td>Urethral stenting</td>
<td>Buccal</td>
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<tr>
<td>Intermittent self-dilation</td>
<td>Bladder</td>
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<tr>
<td></td>
<td>Genital</td>
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<tr>
<td></td>
<td>Genital cutaneous island flaps</td>
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<tr>
<td></td>
<td>Scrotal</td>
</tr>
<tr>
<td></td>
<td>Penile</td>
</tr>
<tr>
<td></td>
<td>Combination of above</td>
</tr>
<tr>
<td></td>
<td>Multistage approach</td>
</tr>
</tbody>
</table>

In the elderly and in poor surgical risk patients with a limited life expectancy but obvious morbidities, owing to their urethral stricture, repeated urethrotomy, dilations, self-catheterizations, and possible stenting may be useful to obviate the need for urethroplasty.

A patch graft urethroplasty is another surgical option for treating urethral stricture disease. End-to-end anastomotic urethroplasty is ideal for short bulbar strictures, whereas free grafts are reserved for longer complex strictures. This involves incising the stricture, as well as normal urethra on both sides of the stricture. A full-thickness graft is then placed and sutured for a watertight anastomosis. Split-thickness grafts contract too much and cannot be used for one-stage repairs.4 Obtain the graft from the penis, genital skin, bladder, post-auricular, or buccal regions. If there is adequate skin, penile tissue is usually the first choice due to its tissue properties, proximity to the repair, and postoperative success rate.4 We use buccal mucosa when there is inadequate penile tissue, and it has shown comparable efficacy. Bladder mucosa grafts are also successful, but the tissue is more difficult to harvest. Less success has been found when using scrotal skin because of its moisture retaining and hairy properties. The success rate for free graft urethroplasty in the treatment of urethral strictures varies from 50 to 95%.29 Failure rate is increased with graft extension into the penile urethra. Tubular grafts, or using the full-thickness graft circumferentially with anastomosis to both sides of normal tissue, have shown worse results than their onlay counterparts.5

Table 87-5  Treatment for Urethral Strictures

<table>
<thead>
<tr>
<th>Multistage approach</th>
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<tbody>
<tr>
<td>Combination of above</td>
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</table>

Use genital cutaneous island flaps with very long fibrotic strictures and with extensive local scarring; grafts have a higher potential rate of failure in these instances. They also have better results than do grafts for extensive penile urethral strictures; they reduce both recurrence and chordee.20 Penile fasciocutaneous flaps are the most

Urethral stents are a fairly recent form of conservative treatment for urethral stricture disease. This concept involves the endoscopic introduction of a self-expanding stent composed of titanium or metal alloy that is permanently implanted across the stricture.24 The stent eventually epithelializes within 12 months, thereby avoiding calcification, migration, and recurrent infections.25 Urethral stents may be a good option for postischemic strictures that fail dilation or internal urethroplasty.26 Stent placement is not usually used as a first-line conservative treatment of urethral strictures. Studies are still under way to better assess its efficacy and indications. Although high success rates were initially reported, recent data are less convincing, with higher rates of recurrence at sites proximal and distal to initial stent placement. This necessitates either the cumbersome removal of the stent or the placement of successive stents. Avoid placing stents in the penile urethral region because of associated erectile issues and next to the sphincter, owing to incontinence. Urethral stents are contraindicated in strictures involving layers deeper than the urothelium, in instances of failure of previous substitution urethroplasty, and in traumatic strictures.27

In the elderly and in poor surgical risk patients with a limited life expectancy but obvious morbidities, owing to their urethral stricture, repeated urethrotomy, dilations, self-catheterizations, and possible stenting may be useful to obviate the need for urethroplasty.

Excision of the urethral stricture with primary anastomosis offers the best cure rate and is the urethroplasty treatment option of choice, whenever appropriate.28 Two possible situations are posterior strictures related to trauma and anterior strictures < 3 cm.28 Excision cannot be used for penile urethral strictures > 1 cm because chordee can result. The anastomosis must be clear from stricture, both proximally and distally, or the stricture will recur. Complication rates are reduced with hemostasis, watertight anastomosis, and eradication of UTI prior to the operation.
In strictures that are severe, that are panurethral, that are caused by BXO, that have fistulas or abscesses, or that have had multiple urethroplasties in the past, a multistage approach is the best option. In the first stage, incise and enlarge the strictured area of the urethras by grafting and perform marsupialization to the skin. Place a temporary catheter and a suprapubic catheter in the proximal urethra to avoid damaging the graft. Once both catheters are removed, then do perineal voiding training to ensure graft stability and granulation. As early as 2 months, but usually 6 to 12 months later, depending on what series is reported, the graft is tubularized to form the neourethra with a 24 to 28 F lumen and the perineal area is closed in multiple layers. Because of its high rate of recurrence in genital skin, treat urethral strictures caused by BXO with a two-stage free graft urethroplasty using nongenital skin.

Stricture recurrence following any of these surgical options requires reassessment of the consequent stricture and a new formulation of treatment. Strictures often recur at the limits of the repair because the extent of the stricture is often underestimated. A history of previous surgery and preoperative UTI has a negative outcome on any type of urethroplasty. The subsequent treatment ranges anywhere from a dilation to multistage repair, depending on the location and the extent of the recurrent stricture.

The surgeon places a small catheter in all urethroplasties, and they recommend suprapubic diversion. Placement can be anywhere from 2 to 3 weeks after surgery, depending on the type and extent of the procedure. Perform urethrography before removing the catheter to evaluate for urinary extravasation and proper healing. To assess the repair, perform a retrograde urethrogram at 3 and 12 months postsurgery.

Posterior urethral strictures, a distinct form of stricture, have controversial management and care. Usually owing to trauma, they initially present as detraction defects that scar over time. Traumatic urethral injuries are usually due to major motor vehicle accidents or to falls from great heights. Of pelvic traumas, 10% have associated urethral injuries. Injury can be anywhere from simple shearing that involves only the urothelium to a complete transection of the urethra. Injury predominantly occurs at the prostatomembranous junction by a shearing force that may avulse the apex of the prostate from the urogenital diaphragm. Straddle injuries, however, usually produce bulbar urethral strictures. Suspect posterior urethral injury when the patient presents after a major trauma with inability to void, with blood at the urethral meatus or gross hematuria, with an unstable pelvis, and with a high-riding prostate on physical examination. Avoid diagnostic catheterization because a partial urethral tear might become a complete disruption. Long-term consequences include recurrent strictures, impotence, and incontinence.

There has been controversy over the years about the time to operate, the type of exposure, and the type of operation for posterior urethral trauma. Stretching or contusion of the posterior urethra requires an indwelling catheter for a few days. Partial rupture of the urethra may be managed with endoscopic urethral stenting initially or suprapubic cystotomy at the time of injury. This usually results in a patent urethra or, at most, a short stricture that can be corrected with visual urethrotomy. Attempt an endoscopic approach in those patients with a suspected small distraction defect or nonobliterative stricture as visualized on post-trauma urethrographic studies. Perform this 1 to 2 weeks after injury, before significant scarring occurs. Erectile function should not be adversely affected; there is no manipulation of periurethral or periprostatic tissue. Stricture recurrence is frequent and temporary self-dilation has been suggested to decrease the failure rate.

When there is complete rupture with minimal urethral distraction, the common practice continues to be suprapubic catheter placement and delayed repair 4 to 6 months later. The benefit of delayed repair outweighs the increased risk of impotence, incontinence, and bleeding seen with immediate repair. Stricture always ensues with delayed management. The surgical approach is usually a perineal incision with excision of the strictured area and anastomosis of the healthy urethral tissue, proximally and distally. For longer defects, the urethra might need more extensive mobilization proximally to promote a tension-free anastomosis. This includes mobilizing the urethra from the suspensory ligaments, separating proximal corporal bodies, rerouting the urethra around the corporal bodies, and, if needed, performing an inferior pubectomy. If these approaches do not work, an abdominal approach will provide further...
mobilization. Likewise, an abdominoperineal approach might also be indicated in men with strictures > 2 cm and surrounded by dense fibrosis, strictures with diverticula, false passages, or fistula and/or extensive sphincter damage. The stricture-free outcome with these procedures approaches 100%.40

The proponents of immediate repair state that exploration, clot evacuation, and urethral realignment are safe and effective, prevent strictures, and avoid long-term suprapubic drainage.41 Magnetic devices, interlocking sounds, and manual manipulation aid in reconnecting urethral segments. It is unclear if increased rates of impotence and incontinence relate to damage to the neurovascular bundle from the surgery itself or from the initial injury. In addition, early exploration can lead to rebleeding of the pelvic vasculature that had tamponaded. For this reason, reserve immediate exploration for high-riding bladders, associated rectal tear, and concomitant bladder neck injury or continued bleeding.42

Another option—exploration 7 to 10 days post-trauma—has been reserved for complete rupture with marked urethral separation because there is a high probability that suprapubic cystotomy alone will result in a diffuse, complex stricture that requires not only perineal surgery but also an extensive transpubic repair.39 At 7 to 10 days post-trauma, the bleeding of the initial injury no longer obscures the view, fibrosis has not started to appear, and the patient has stabilized from the initial trauma. An abdominal primary anastomotic closure that had tamponaded. For this reason, reserve immediate exploration for high-riding bladders, associated rectal tear, and concomitant bladder neck injury or continued bleeding.40

Consider two-stage reconstruction in patients with marked scarring of perineum from trauma or previous stricture repairs or with associated damage to the anterior urethra, perineal abscesses, or infected diverticuli or fistulas.43

We generally recommend catheter placement for 2 to 4 weeks postrepair. A suprapubic catheter is used mainly for urinary diversion, and the urethral catheter acts as a stent. Arrange a voiding study for 3 to 4 weeks postrepair and, at this time, clamp the suprapubic tube and schedule its removal a few days later once voiding has been monitored and deemed adequate.23

Posterior urethral strictures can also occur after a radical prostatectomy or transurethral resection of the prostate. Major risk factors in the development of strictures after a radical prostatectomy include prior transurethral resection, a tight anastomosis, vest suture technique, excessive intraoperative blood loss, or prolonged leakage of urine.44 Bladder mucosal eversion reduces stricture rate.45 Because of the proximity to the external sphincter, dilation is usually the initial treatment of choice, and the patient usually needs serial dilations over the years.46 Outcome is generally good due to the superficiality of the stricture. Balloon dilation of the strictured area can be done if serial dilations fail. Internal urethrotomy is generally contraindicated due to the proximity to the sphincter; however, a minor laser or cold knife incision has been used in certain circumstances where dilation is unsuccessful.12 Repeated failure or involvement of the dense stricture into the external sphincter requires an extensive continence-preserving procedure, which Turner-Warwick describes.39

References


SECTION 11
THE PENIS
Combined data from several studies have revealed that the etiology of micropenis is hypogonadotrophic hypogonadism in 50% of patients, hypergonadotrophic hypogonadism in 25% of patients, end-organ insensitivity including growth hormone defects in 15% of patients, and idiopathic in 10% of patients. The diagnostic work-up and treatment of this disorder are based upon this knowledge.

**A** Micropenis is defined as an abnormally small (< 2.5 standard deviations below the established mean value for race and gestational age) but otherwise perfectly formed penis. In a normal full-term gestational male, the absolute stretched penile length should be > 2.5 cm. The initial evaluation should note general characteristics of the infant (rule out abnormal facial features or body habitus consistent with a karyotype abnormality), the stretched penile length, and the location and size of the testes.

**B** In the neonate with micropenis, the possible presence of panhypopituitarism requires emergent evaluation. Serial glucose, sodium, and potassium evaluations are mandatory. Maintain intravenous access with glucose and electrolyte replacement until serial serum determinations are documented as normal.

In addition, perform chromosomal evaluations to rule out the most common types of karyotype abnormalities associated with micropenis: Klinefelter’s syndrome (47,XXY) and Down syndrome (trisomy 21).

Diagnostic determinations of thyroid hormones (thyroid-stimulating hormone [TSH], thyroxine, thyroid-binding globulin), serum cortisol, growth hormone, luteinizing hormone (LH), follicle-stimulating hormone (FSH), testosterone, and dihydrotestosterone values should be obtained at birth and repeat LH, FSH, and testosterone values every 3 weeks through to age 3 months. Failure to obtain these later studies significantly impairs the diagnostic evaluation.

In the neonate under age 3 months, magnetic resonance imaging (MRI) of the brain is usually deferred because it requires heavy sedation and/or anesthesia. In a child who presents at age over 3 months, an MRI at the time of the initial evaluation may significantly accelerate the diagnostic work-up.

**C** If serial serum testosterone values of > 100 ng/dL are noted, a functional hypothalamic, pituitary, gonadal axis is present. Thus, evaluating the hypothalamic and pituitary axis is omitted.

If testosterone values of < 100 ng/dL are found and if findings do not indicate a serial rise in LH and FSH, the etiology is most likely hypogonadotrophic hypogonadal defect. In hypergonadotrophic hypogonadism, findings show a neonatal rise in LH and FSH over the first 3 months of life but no corresponding rise in testosterone occurs.

**D** Perform a short-course trial of human chorionic gonadotropin (hCG) if no rise occurs in the serum testosterone (> 100 ng/dL) in the first 3 months of life. This test verifies the presence of functioning testes. Obtain baseline serum testosterone and administer hCG 100 IU/kg (maximum of 1500 units), given every 48 hours for 3 doses, and 12 hours after last injection, remeasure serum testosterone. With functioning testes, there is a > 10-fold increase in serum testosterone over baseline value.

**E** No rise or blunted rise to short-course hCG could be attributable either to absent testes or to substrate depletion in a chronically understimulated hypogonadotropic male. Arrange a chronic trial of hCG. Administer a similar dose of hCG (see D) every fifth day for 6 weeks. Obtain a serum testosterone value on the forty-second day after the initial injection; we consider a value < 200 ng/dL as abnormal.

**F** Abnormal response to long-course hCG indicates testicular failure. The most frequent causes are Klinefelter’s syndrome, Robinow syndrome (brachy-mesopcephalic dwarfism), vanishing testes syndrome, and LH receptor defects. Nonpalpable testes may necessitate a laparoscopy to verify their presence or absence. If testes are present, perform a biopsy of the testes for further evaluation and prognosis.

**G** Findings of an increased serum testosterone after hCG stimulation are consistent with either hypothalamic or hypopituitary etiology.

**H** Clinicians frequently recommend a Gn-RH (gonadotropin-releasing hormone) test. An appropriate rise in LH in response to Gn-RH stimulation indicates that the diagnosis is pituitary malfunction; however, failure of LH to rise may also be attributable to chronic depletion of the pituitary of substrate, owing to understimulation of this organ. Because chronic Gn-RH injections to rule out the latter phenomenon are not clinically feasible, most authorities omit this test and go straight to an MRI of the brain.
If the MRI reveals a pituitary abnormality, the infant is diagnosed as having a pituitary cause for the micropenis. If the MRI indicates no pituitary abnormality, then the infant is diagnosed as having a hypothalamic etiology for the micropenis. Testosterone ethanate is the mainstay of treatment; infants < age 3 months are prescribed 15 mg IM every 3 weeks for 4 injections, and infants over 3 months are given 25 mg IM every 3 weeks for 4 injections.

If stretch penile length does not normalize (> 2.5 cm), this may be due to partial androgen receptor defects or partial postandrogen receptor defects that can be overcome by increasing androgen dosage. In these situations, we double the initial dose of testosterone and repeat the injections, again every 3 weeks for four injections.

For persistent micropenis that is present after high-dose testosterone, recommend genital skin biopsy for testosterone and 5α-reductase receptor analysis.

In patients who do not respond to high-dose testosterone therapy, we do discuss the pros and cons of sexual conversion with the family. It should be noted, however, that most patients with persistent micropenis into adulthood have identified sexually to the male gender and are successfully cohabiting with members of the opposite sex.

**Additional Readings**


Peyronie’s disease (PD), a self-limited connective disease characterized by the progressive formation of fibrous plaques within the tunica albuginea and underlying erectile tissue, can be a physically and emotionally debilitating disease. The consequent curvature and deformity of the erect penis may interfere with penile erection and thus precipitate erectile dysfunction. Described as early as 1561 by Fallopius, Francois Gigot de LaPeyronie (1678–1747) is credited for popularizing knowledge of the disease. The first surgeon to King Louis XV, LaPeyronie described patients with “rosary beads of scar tissue extending the full length of the dorsum of the penis.” Despite medical advances over the next 250 years, PD remains a therapeutic dilemma, owing to its obscure etiology and the absence of a specific, curative medical therapy.

Incidence
The incidence is generally estimated to be 1%, affecting primarily Caucasian men aged 45 to 60 years, although men in their teens and in their eighties may also be afflicted with the disease. A retrospective study in Rochester, Minnesota, by Lindsay and colleagues reports the incidence of PD to be 26 of 100,000 men and the prevalence to be 389 of 100,000 men. A survey of 4,432 male inhabitants in Cologne, Germany, estimates that the prevalence of PD is 3.2%, with 1.5%, 3.0%, 4.0%, and 6.5% of the men aged 30 to 39 years, 40 to 59 years, 60 to 69 years, and above 70 years affected, respectively. Another recent study of 954 men in Brazil discovered an overall prevalence of 3.7%; demonstrating that PD is more common than previously perceived.

Presentation
The hallmark feature of PD is penile curvature during erection, which is the presenting symptom in 52% of men. The plaque, or fibrotic scar tissue in the tunica albuginea, restricts full expansion and extension of the side affected, thereby causing bending to the side of the plaque. The manifestations of the disease may include (1) an asymptomatic mass or lump in the penis shaft, (2) mass in the penis with pain during erection, (3) penile curvature during erection, with or without pain, (4) erectile dysfunction, (5) lack of penile rigidity during erection distal to the fibrotic plaque, (6) subclinical fibrosis, and (7) painful coitus. PD has been documented to be associated with Dupuytren’s contracture or scarring of the palmar fascia, plantar fibromatosis or Lederhose’s disease, carcinoid syndrome, Paget’s disease of the bone, diabetes, gout, tymanosclerosis, and in men using beta-blockers.

Most patients have a palpable plaque or indurated area on physical examination. The plaque is usually located on the dorsum of the penis, with resultant upward curvature. When confined to the ventral aspect, a downward bend ensues. With concomitant dorsal and ventral plaques, there may be apparent chordée, but penile shortening and a flail penis distal to the plaques may occur. Although ventral or lateral curvatures are less common, they may pose challenges to vaginal penetration and intercourse. The patient most commonly presents with painful erections and penile bending in the active phase of the disease, although one-third of the patients may present with painless curvature. The inflammatory process and irritation of the afferent sensory nerves may cause the pain associated with PD. The pain may resolve spontaneously owing to resolution of the inflammatory process or death of the trapped nerve fibers, and the scar tissue may stabilize over a course of 12 to 18 months, after which the penile configuration may not undergo any further changes. However, spontaneous recovery may result over an average of 4 years as pain regresses followed by gradual softening of the plaque and straightening of the penis.

Although LaPeyronie proposed chronic irritation from sexual practices and venereal diseases as causes of the disease, the etiology remains unclear. Nonetheless, trauma with subsequent fibrosis is commonly perceived as the precipitating event in the pathogenesis of the disease. Acute or repetitive trauma with tissue disruption and microvascular injury may lead to extravascular leakage of blood, thrombus formation, and fibrin deposition, which is associated with fibroblast proliferation and aberrant collagen synthesis. The consequent fibrosis and collagen trapping lead to formation of the Peyronie’s plaque. Devine and colleagues devised a schema for the formation of the plaque. During erection, the sheath of the tunica albuginea and the septal fibers that are interwoven with the tunica are stretched to the limit of their compliance. The midline septal fibers between the corporal bodies confer vertical rigidity, thereby resisting any upward or downward bends. In young men, the high intracorporeal pressure is sufficient to negate any deforming force, while the tissue elasticity prevents any tear in the event of structural deformity. With decreased intracorporeal pressure and compliance in older patients, a tear at the junction of the septum and tunica can result during coitus with subsequent blood vessel disruption. Following such microvascular injury, a fibrotic response, ultimately leading to plaque forma-
tion with the characteristic curvature, may ensue. Despite this proposal of mechanism, not all patients with PD report a history of trauma. Unquestionably, other factors may be pivotal in PD development.

Studies are ongoing in assessing the genetic predisposition for PD. The disease has been associated with tissue surface antigens including HLA-A1, B7, B27 (class I major histocompatibility complex [MHC]), and HLA-DR3, DQ (class II MHC). In 1979, Willscher and colleagues reported a significant association between PD and the HLA-B7 cross-reacting antigens, with 88% of the PD patients possessing an antigen of the B7 cross-reacting group. PD has been suggested as a male-limited, autosomal dominant trait, and a study documented the occurrence of Dupuytren’s contracture in 7 of 9 (78%) PD patients, implying a similar genetic disposition. Conversely, Leffell could not demonstrate a significant correlation between PD and HLA-B7 antigens and propose a heterogeneity of the disease. Using molecular biologic and genetic techniques, Noss and colleagues could not exclude a class II MHC association, while class I MHC antigens may be involved because the expression of class I MHC protein differs in PD patients compared with control subjects. An autoimmune component may be involved in the pathogenesis of PD, with one study demonstrating that approximately 76% of PD patients exhibit at least one abnormal immunologic test compared with 10% among control subjects. The pathogenesis of PD unarguably
involves a cascade of structural, genetic, and immunologic events that necessitate further research to delineate their intricate relationship.

B Smith in 1966 first documented PD as an inflammatory process with lymphocytic and plasmacytic infiltrate in the areolar connective tissue sleeve between the corpus cavernosum and tunica albuginea, ultimately progressing to fibrous involvement of the smooth muscle bundles of the intercavernous septum with calcification and ossification. He also reported subclinical PD with histologic evidence of chronic inflammation and fibrosis in the subtunical sheath in 100 autopsies of asymptomatic patients. The space between the tunica albuginea and erectile tissue has subsequently been referred to as Smith’s space. This space may be responsible for confining the inflammatory process and engendering the Peyronie’s plaque, a stable fibrotic tissue that cannot be resorbed.

Maturation of the scar involves the translocation of collagen fibers into more organized collagen bundles, and the resultant fibers forming the plaque are independent in their connective tissue organization, thereby making the plaque incompatible with adjacent structures. Consequently, the structural network that provides flexibility, rigidity, and tissue strength to the penis is lost, secondary to such changes and deranged formation or fragmentation of elastic fibers. Despite the role of collagen in the pathogenesis of PD, Rhoden and colleagues failed to demonstrate any association between the serum markers of collagen diseases and PD.

Implicated in chronic fibrotic diseases affecting the lung and liver, transforming growth factor-β (TGF-β) protein expression is also shown to be significantly associated with PD. TGF-β can increase transcription and synthesis of collagen, proteoglycans, fibronectin, and tissue inhibitors of collagenase and can induce angiogenesis and control of cytokine production and other inflammatory mediators. Inhibition of TGF-β activity can therefore be therapeutic in PD patients by interfering with the modulation of inflammation, fibroblast activity, and fibrin deposition. P53, a proapoptotic factor and regulator of cell cycle, may also play a role in the pathogenesis of PD. An aberration of the p53 pathway has been suggested to promote the overproliferation of fibroblasts seen in PD and malignant cells. Recently, the advent of DNA microarrays may shed light on potential novel approaches to combat tissue fibrosis by defining the complex interplay among biochemical pathways in PD. Other regulatory factors implicated in the pathogenesis of PD include osteoblast factor 1, monocyte chemotactic protein 1, procollagenase IV, and nitric oxide and nitric oxide synthase isoforms.

The structural alterations in the tunica albuginea that the Peyronie’s plaque causes can contribute to erectile dysfunction. Ralph and colleagues reported decreased blood flow beyond the plaque in patients with distal penile flaccidity. Veno-occlusive dysfunction has been proposed to contribute to erectile dysfunction that is secondary to a decrease in the compliance of the tunica albuginea. The impaired compliance may render the tunica ineffective in compressing the emissary veins, consequently precipitating venous leakage and loss in penile rigidity.

C As the initial step in the evaluation process, the clinician should perform a complete history and physical examination, with primary attention toward sexual and genital development, as well as identifying any vascular or connective tissue abnormalities. In addition, the clinician should include a well-documented, detailed history of time of onset, course of disease, trauma, erectile dysfunction, previous urologic instrumentation, and medication abuse. During physical examination, define the location, size, and character of the plaque. Grasp the glans penis with one hand and stretch the penis to the limit in order to palpate the lesion more precisely. Examine the patient for Dupuytren’s or Lederhose’s disease. A plain radiograph can aid in discerning calcification in the plaque, although that diagnosis is easily made by palpation. Although ultrasonography can assist in monitoring the progress of the disease by revealing the site and size of the plaque, it adds little to a thorough physical examination. Similarly, magnetic resonance imaging (MRI) is expensive and is not generally indicated unless a detailed anatomy visualization is needed prior to surgery. Color duplex ultrasonography and dynamic pharmacocavernosometry/ cavernosography, however, are valuable in assessing the penile circulation and collateral arteries and detecting any veno-occlusive dysfunction, respectively. To help confirm the diagnosis, document the deformity before therapy, and increase compliance with the request, ask the patient to bring a digital or Polaroid picture of his erect penis that illustrates the degree and direction of angulation and character of the erection. Erection can also be induced by prostaglandin E1 or papaverine injection to elicit the curvature.

After the diagnosis of PD is established, it is imperative to reassure the patient and, if possible, his partner, that the plaque does not represent a malignant process and that the current sexual dissatisfaction from the disease can be remedied. Finally, in the early evaluation of penile curvature or presence of a plaque/lesion, consider other causes of angulation and induration of the penis. Table 89-1 lists the differential diagnoses.

D Given the self-limiting course of PD, the initial therapeutic approach should remain conservative. Offer reassurance without any further testing or treatment to those patients with minimal curvature not interfering with sexual function, without pain or discomfort, and with no erectile dysfunction. However, patients who can have intercourse but complain of pain or sexual diffi-
Table 89-1  Differential Diagnosis of Penile Curvature of Plaque

<table>
<thead>
<tr>
<th>Condition</th>
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<tbody>
<tr>
<td>Congenital curvature of the penis</td>
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<tr>
<td>Sclerosing lymphangitis</td>
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<tr>
<td>Thrombosis of the dorsal penile artery</td>
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<tr>
<td>Cavernosal thrombosis caused by hereditary hemoglobinopathies</td>
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<tr>
<td>Leukemic infiltration of the corpora cavernosa</td>
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<tr>
<td>Ventral curvature secondary to urethral stricture disease</td>
</tr>
<tr>
<td>Late syphilitic lesions</td>
</tr>
<tr>
<td>Fibrosis secondary to severe urethritis with abscess</td>
</tr>
<tr>
<td>Penile infiltration with lymphogranuloma venereum</td>
</tr>
<tr>
<td>Benign or malignant primary or secondary tumors</td>
</tr>
</tbody>
</table>

culity for less than 1 year and progression of the plaque may be offered medical therapy. In addition, consider patients who are not interested in surgery candidates for medical therapy. Unfortunately, the patient should be informed that there is no definitive treatment modality. LaPeyronie initially proposed that mercury and mineral water were remedial. Since then, various treatment options have been suggested (Table 89-2).36

Vitamin E, a tocopherol with antioxidant properties, is an oral agent commonly used in the treatment of PD. Scardino and Scott first reported the beneficial effects of vitamin E in 1949, with a 78% decrease in curvature and a 91% decrease in plaque size.37 However, in a study of 105 patients treated with vitamin E that was presented at the National Institutes of Health (NIH) Conference on PD, it was reported that only 13% of PD patients had improved in sexual function or curvature.38 Nonetheless, offer vitamin E therapy as an initial treatment option for PD patients because of its mild side-effect profile and low cost.

Potassium para-aminobenzoate (POTABA) is another oral agent reported to be effective in treating fibrotic diseases. Its mechanism of action is via its increased oxygen use at the tissue level and enhanced oxygen-dependent monoamine oxidase activity, which decreases serotonin effect at the tissue level. Zarafonetis and Horrax first documented the applicability of POTABA in PD in 1959 when they demonstrated a 100% decrease in pain reduction, 82% curvature improvement, and 76% plaque resolution in their study of 21 patients.39 However, its expense ($1,000 yearly), frequent dosing requirement, and associated gastrointestinal upset have limited its popularity. Oral colchicine has been recently proposed to be therapeutic in PD patients, with Akkus and colleagues reporting that about 50% of patients experienced a decrease in plaque size and curvature improvement.40 An inhibitor of inflammatory cells and fibroblasts, colchicine can increase collagenase activity and reduce collagen synthesis, and has been suggested to be given in the early phase of the disease.41 Colchicine has a potential side effect of bone marrow suppression.

Other venues of medical treatment for PD include intralesional therapy and topical agents. Collagenase injection was performed by Gelbard and colleagues in 1985, who reported no significant improvement in more severe curvature, and this form of therapy should be reserved for patients with minimal disease.42 Steroid injection is not recommended because of possible tissue atrophy and difficulty in performing subsequent surgery.43 Persistent, severe pain can be alleviated with low-dose radiotherapy (1,000 cGy) by decreasing inflammation. Intralesional interferon α2b has been proposed as an effective therapeutic option, and patients placed on this regimen may experience reduction in penile curvature, diminished pain with erection, and decreased plaque size.43 Finally, Levine showed that intralesional application of verapamil is therapeutic in PD, with 97% of patients reporting pain reduction, 72% sexual function improvement, 86% deformity reduction, and 54% curvature reduction.44 The only injectable calcium channel blocker, verapamil, modifies cytokine expression involved in wound healing and increases the proteolytic activity of collagenase, thereby postulated to stimulate remodeling and degradation of extracellular matrix in tissue by altering the metabolic pathways of fibroblasts.33,44 Our study suggests that verapamil may be applied to PD patients with noncalcified plaque and penile angulation of < 30 degrees.45 Patients with bends of more than 30 degrees or with a plaque for more than 1 year are more appropriate candidates for surgical intervention.

No surgery should be undertaken until the penile curvature and sexual dysfunction have stabilized, usually over a period of at least 12 months. Reserve surgical therapy for patients who fail conservative measures and for those with such severity that precludes normal coitus. In general, the surgical options are classified into three categories: tunica-shortening procedures (plication), tunica-lengthening procedures (excision/incision with graft), and penile prosthesis placement. Patients with adequate penile length, good potency, and curvature of < 60 degrees are candidates for plication tech-

Table 89-2  Medical Treatment for Peyronie’s Disease

<table>
<thead>
<tr>
<th>Treatment Option</th>
<th>Author</th>
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<tbody>
<tr>
<td>Mercury and mineral water</td>
<td>LaPeyronie1</td>
</tr>
<tr>
<td>Vitamin E</td>
<td>Scardino and Scott37</td>
</tr>
<tr>
<td>Cortisone injection</td>
<td>Teasly42</td>
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<td>Potassium para-aminobenzoate</td>
<td>Zarafonetis and Horrax49</td>
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<td>Ultrasoundography</td>
<td>Heslop and colleagues48</td>
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<td>Steroid iontophoresis</td>
<td>Rothfield and Murray64</td>
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<td>β-Aminopropionitrile</td>
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<tr>
<td>Collagenase injection</td>
<td>Gelhard and colleagues65</td>
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<td>Laser ablation</td>
<td>Puente de la Vega and colleagues66</td>
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<td>Prostacyclin</td>
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<td>Interferon α2b</td>
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<td>Tamoxifen</td>
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<td>Verapamil</td>
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<tr>
<td>Colchicine</td>
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</tbody>
</table>
niques. In 1965, Nesbit originally described a popular technique for congenital abnormalities. The Nesbit plication procedure involves the excision of an ellipse of tunica albuginea opposite the plaque to straighten the penis. The width of the ellipse excised should be 1 mm per 10 degrees of curvature. Although Pryor reported a satisfaction rate of 82% in 359 patients, a shortcoming of the procedure is penile shortening, limiting its feasibility in some patients. Modifications of the Nesbit plication have been reported, including transverse closure of vertical incisions in the tunica and closure with permanent suture knots buried beneath the tunica in a running looped fashion. We prefer the modification employing the partial-thickness shaving rather than conventional excision of a wedge of tunica albuginea, thereby reducing intraoperative bleeding, negating cavernous tissue damage, and optimizing adhesion of plicated tunical layers. With this amended technique, 78% of the 26 patients in our study reported a good to excellent outcome.

Excision or incision with graft can be an optimal therapeutic alternative for men with penile curvature > 60 degrees or complex curvatures, hourglass deformity or hinge effect, good potency, and suboptimal penile length. Various autologous tissues and synthetic materials have been used, including tunica vaginalis, rectus muscle aponeurosis, fascia lata, free fat pad, dura mater, temporal fascia, dermis, dorsal and saphenous veins, cadaveric pericardium, polytetrafluoroethylene, and Dacron. Cadaveric pericardium is commercially available in various sizes with randomly oriented fibers similar to host tissues that heal easily. In addition, it is deemed to be a good substitute for the excised tunica albuginea. Because some studies report failure and high incidence of erectile dysfunction associated with plaque excision with dermal patch, surgeons use incision of the plaque with venous graft. Incision with graft placement is justified because of less tunica and underlying erectile tissue manipulation, thus promoting better postoperative rigidity. Lue believes that saphenous vein grafts are the most optimal physiological substitute for the tunica albuginea; the saphenous vein has the following properties: the endothelium prevents hematoma formation by releasing anticoagulation factors, similar thickness to the tunica albuginea, good elasticity, and the < 1 mm wall thickness establishes blood supply from the corpora and prevents graft contracture from ischemia. Plaque incision with saphenous vein graft has been reported to yield satisfactory to excellent results in 92% of patients.

Finally, impotent patients or those with penile flaccidity distal to the plaque may require penile prostheses. Various studies report that malleable and inflatable penile implants are safe and effective therapeutic treatments for impotent PD patients. If curvature persists despite prosthesis placement, modeling the erect penis has been reported to rectify the deformity. The maneuver involves forcibly bending the erect penis in the direction opposite to the curvature and held for 90 seconds during the operation. Too much force, however, may cause fracture of the tunica, thus requiring immediate intraoperative repair. Our experience with the chordee present after the insertion of either a semirigid or inflatable prosthesis is that the prosthesis will cause the penis to straighten, usually within 6 months, thereby negating the need for modeling maneuvers.

Conclusion

PD is a disease with higher incidence than previously thought. Despite more than 250 years of medical advances since its first description, the etiology of PD remains unknown. This challenge is reflected by the various treatment options available and the absence of a specific, successful medical therapy. Most patients only require reassurance or conservative medical therapy, whereas the remainder require surgical intervention to accomplish satisfactory sexual intercourse. Future strategies for combating PD include gene profiling, tissue engineering, development of a specific animal model, and further research on the genetics and pathogenesis associated with PD.

References


Sexual differentiation is a well-regulated sequence of events. Developmentally, chromosomal sex determines gonadal sex, which then determines phenotypic sex. A patient with an intersex disorder may have ambiguous genitalia, normal-appearing external genitalia (female or male), or a minor abnormality such as hypospadias and an undescended testis. A straightforward organizational scheme for intersex disorders is based on the histology of the gonads (Figure 90-1). The basic classifications are

- **Female pseudohermaphroditism**: 46,XX karyotype with partial virilization; this is the most common cause of ambiguous genitalia. Typically, the disorder results from a 21-hydroxylase or 11β-hydroxylase deficiency (congenital adrenal hyperplasia [CAH]). Another cause is excessive androgen production from the mother.

- **Male pseudohermaphroditism**: chromosomal male (46,XY) with normal testes who is incompletely virilized; this may include a defect in testosterone synthesis, 5α-reductase deficiency, a receptor defect (complete or incomplete), a defect in testicular differentiation, or a defect in production of müllerian-inhibiting substance (MIS).

- **Mixed gonadal dysgenesis**: chromosomal mosaicism with a 45,XO/46,XY karyotype. Internal genitalia include a unilateral streak gonad; persistent müllerian duct structures (fallopian tube, uterus, and vagina) ipsilateral to the streak; a contralateral testis, which may or may not be undescended; and frequently a fallopian tube on the side of the testis. This is the second most common cause of ambiguous genitalia. Nearly all are incompletely virilized. Patients reared as females typically have genital ambiguity with phallic enlargement, a urogenital sinus, and varying degrees of labioscrotal fusion.

- **True hermaphroditism**: the gonads contain both ovarian and testicular tissue. This disorder is the least common cause of ambiguous genitalia. Patients may have an ovotestis on one side and an ovary or testis on the other (unilateral), bilateral ovotestes (bilateral), or a testis on one side and an ovary on the other (lateral). The most common finding is an ovary on the left side and a testis on the right. Nearly all patients have a urogenital sinus and most have a uterus. The ductal system usually follows the ipsilateral gonad: a fallopian tube on the side of the ovary and an epididymis on the side of the testicle. If an ovotestis is present, the adjacent ducts may be wolffian, müllerian, or both. If an ovotestis is present, it may be anywhere along the course of normal testicular descent and often is associated with an inguinal hernia. The appearance of the external genitalia is variable. Nearly all have incomplete virilization, that is, they have hypospadias. At puberty, 80% of patients develop gynecomastia and 50% menstruate. Individuals reared as males may show cyclic hematuria. Ovulation is more common than spermatogenesis, but both are uncommon. Sixty percent of the patients have a 46,XX karyotype, but the SRY gene has been detected in many. Twenty percent have a 46,XY karyotype; the remainder demonstrate mosaicism or chimerism.

The child with ambiguous genitalia should be evaluated by a team consisting of a geneticist (dysmorphologist), pediatric endocrinologist, pediatric urologist, and ethicist. Decisions regarding the evaluation, gender assignment, and long-term management need to be made jointly based on the diagnosis and the future potential for successful gender identity and sexual and reproductive function.

A thorough history taking and physical examination must be performed, with full attention given to the history of the pregnancy, the family history, and the pedigree. Identically afflicted relatives should be identified, because many intersex disorders have a strong familial history. Sudden infant death, infertility, amenorrhea, hirsutism, and variant forms of sexual development in any relative should be investigated. The mother should be questioned about any medication, especially hormones, taken during pregnancy.

On physical examination, the genitalia should be carefully examined and documented; one important finding is a gonad located in the scrotum or the labioscrotal fold. Any phenotypic male with bilateral non-palpable testes or subcoronal hypospadias and cryptorchidism should undergo full evaluation as CAH may be the etiology. Rectal examination may disclose a cervix. Other potential findings include hyperpigmentation of the areola and labioscrotal folds (CAH), palpation of the uterus as a thickened structure, hypertension, signs of dehydration and failure to thrive, and associated congenital anomalies.

Laboratory analysis provides an important tool for the evaluation and treatment of these conditions. An initial study is a karyotype determination. Testing of multiple tissues (blood lymphocytes, skin fibroblasts) may
Figure 90-1 Diagrammatic scheme of sex determination and differentiation.

- **Intersex Disorder**
  - **Gonad(s) palpable**
    - **Müllerian structures absent**
      - Ultrasound
        - 17-Hydroxyprogesterone
          - Karyotype
            - XY
              - Gonads
                - Testis
                - Ovary
              - Mixed gonadal dysgenesis
            - XO/XY mosaic
              - Testis and streak
              - Ovary and testis and/or ovotestis
            - XX;XY; XX/XY mosaic
              - Ovary
              - Ovary and testis and/or ovotestis
              - With/without testis
              - Male pseudohermaphroditism
              - Mixed gonadal dysgenesis
              - Nonadrenal female pseudohermaphroditism
            - Normal
              - Male pseudohermaphroditism
              - True hermaphroditism
              - Congenital adrenal hyperplasia
            - Elevated
              - Male pseudohermaphroditism
              - True hermaphroditism
              - Congenital adrenal hyperplasia
  - **Gonad(s) impalpable**
    - **Müllerian structures present**
      - Normal
      - Elevated
      - Male pseudohermaphroditism
      - True hermaphroditism
      - Congenital adrenal hyperplasia
    - **Müllerian structures absent**
      - Male pseudohermaphroditism
      - True hermaphroditism
      - Congenital adrenal hyperplasia
be necessary if chromosomal mosaicism is suspected. Evaluation for Barr bodies in a buccal smear may be inaccurate in the newborn and is generally not obtained.

Voiding cystourethrogramy and retrograde genitography determine whether the uterus, cervix, and vagina are present. Abdominopelvic ultrasonography should be performed to study the pelvic organs for the presence of a uterus, the inguinal area for the presence of gonads (testes or ovotestes), and for the size and presence of the kidneys and adrenal glands. If the bladder is empty during the study, it should be filled by means of a small feeding tube to allow visualization of the pelvic structures. Inability to discern the cervix or vagina by radiography does not exclude their existence. Endoscopy, cystourethroscopy, and vaginoscopy allow more complete examination of the genitalia, and if these tests are performed with contrast under fluoroscopic control, the anatomy may be defined more accurately.

If the gonads are nonpalpable, the serum 17-hydroxyprogesterone level should be measured. Serial serum electrolyte levels should also be determined because the most common cause of intersex disorder, CAH (21-hydroxylase deficiency), may cause life-threatening salt wasting (hyponatremia, hyperkalemia, acidosis). Steroid profiles, such as testosterone, androstenedione, adrenocorticotropic hormone (ACTH), plasma renin, and 11-deoxycortisol determinations, may on occasion be necessary.

In the full-term newborn with a 21-hydroxylase deficiency, serum levels of 17-hydroxyprogesterone are typically elevated, ranging from 3,000 to 40,000 ng/dL (normal, 100 to 200 ng/dL); in those with mild forms, the level is at the upper limit of normal. In premature infants, 17-hydroxyprogesterone levels may be normally elevated (false-positive). Measurement of urinary 17-ketosteroid and pregnanetriol level is not usually performed. Salt-losing patients often have hyponatremia and hyperkalemia on a regular or low-salt diet. In newborns with the 11-hydroxylase deficiency, plasma 11-deoxycortisol and 11-deoxycorticosterone levels are elevated. On ultrasonography, 50% of neonates with CAH have adrenal glands that are enlarged or at the upper limit of normal in size.

Because there is no production of testosterone or MIS by the male gonads, the Wolffian structures are absent, and the development of the fallopian tubes, the uterus, and the upper vagina is normal. Only the development of the external genitalia is affected in females. With the mildest forms, there is simply clitoral hypertrophy and a normally positioned vagina; in the most severe forms, there is complete labioscrotal fusion, a long phallus with a urethral opening at its tip, and a high insertion of the vagina on the urethra. The gonads are nonpalpable because the ovaries do not descend into the inguinal canal or labia unless an inguinal hernia is present. The more severe the virilizing effect, the more severe the enzyme deficit.

Initial management is directed at correcting or preventing hypoglycemia, hyponatremia, hyperkalemia, hypovolemia, and shock. In addition to saline infusion and correction of electrolyte abnormalities, hydrocortisone therapy is started. When the child is stabilized and receiving appropriate doses of glucocorticoids and mineralocorticoids, surgical management is considered. The procedure, termed feminizing genitoplasty, involves (1) clitoroplasty, in which the erectile tissue of the clitoris is removed, preserving normal clitoral sensation, and (2) vaginoplasty, in which the lower vagina is exteriorized.

The primary consideration in true hermaphrodites is gender assignment. If the phallus is diminutive, the infant probably should be reared as a female, irrespective of the internal genitalia. If there is both a phallus and a vagina, the sex of rearing should be based on the findings at exploratory laparotomy. If a testis is identified that can be placed in the scrotum and the phallus is satisfactory in size, the infant should be raised as a male. If there are normal müllerian structures on one side that are associated with an ovary, strong consideration should be given to rearing the infant as a female. After gender assignment, the contradictory gonadal tissue and internal ducts should be excised.

Testicular feminization (complete androgen resistance) is an X-linked disorder of patients with a 46,XY karyotype who have an abnormality of the androgen receptor, either qualitatively abnormal or at undetectably low levels. Differentiation of the Wolffian ducts and virilization of the external genitalia are inhibited, and secretion of MIS causes regression of the müllerian ducts. Consequently, affected individuals have bilateral testes, normal female external genitalia with a short, blind-ending vagina, and Wolffian-derived internal duct structures. At puberty, breasts develop, but the patients do not menstruate or develop any pubic or axillary hair. Diagnosis usually occurs at puberty after evaluation for amenorrhea. The diagnosis of testicular feminization may occur when a phenotypic girl undergoing hernia repair is found to have an inguinal or labial testis.

Treatment includes bilateral orchietomy because there is a significant risk of gonadal cancer with age. Estrogen replacement then becomes necessary. If a prepubertal girl is diagnosed with complete androgen resistance, whether to perform bilateral gonadectomy at that time or delay the procedure until pubertal development has occurred is controversial. Because of the underdeveloped müllerian structures, patients are candidates for vaginoplasty, which is usually performed with a segment of large or small bowel.
Patient with AMBIGUOUS GENITALIA

A History
Physical examination

Chromosomal analysis
Genitography
Ultrasonography

46,XX

46,XY

XO

F XO/XY

B 17-OH-progesterone

Normal

Elevated

17-OH-progesterone

Maternal androgens

Electrolytes

Glucocorticoids

Mineralocorticoids

Androgen insensitivity
(partial or complete)

MIS deficiency

No response

Deficiency of androgen synthesis

E Gonadal dysgenesis

C True hermaphrodite
(ovary/testis/ovotestis)

D Male pseudohermaphrodite

Exploratory laparotomy

Gonadal biopsy

hCG stimulation

Testosterone

High DHT

Low DHT

Normal DHT

5α-reductase deficiency

Androgen insensitivity
(partial or complete)

MIS deficiency

No response

Deficiency of androgen synthesis

E Gonadal dysgenesis

F XO/XY

Maternal androgens, tumor

Maternal androgens, tumor

Electrolytes

Glucocorticoids

Mineralocorticoids

Androgen insensitivity
(partial or complete)

MIS deficiency

No response

Deficiency of androgen synthesis

E Gonadal dysgenesis

G XO/XY

(Testis/streak)

Turner’s syndrome

MGD

Male pseudohermaphrodite

True hermaphrodite
(ovary/testis/ovotestis)

17-OH-progesterone

Maternal androgens

Electrolytes

Glucocorticoids

Mineralocorticoids

Androgen insensitivity
(partial or complete)

MIS deficiency

No response

Deficiency of androgen synthesis

E Gonadal dysgenesis

G XO/XY

(Testis/streak)

Turner’s syndrome

MGD

Male pseudohermaphrodite

True hermaphrodite
(ovary/testis/ovotestis)

17-OH-progesterone

Maternal androgens

Electrolytes

Glucocorticoids

Mineralocorticoids

Androgen insensitivity
(partial or complete)

MIS deficiency

No response

Deficiency of androgen synthesis

E Gonadal dysgenesis

G XO/XY

(Testis/streak)

Turner’s syndrome

MGD

Male pseudohermaphrodite

True hermaphrodite
(ovary/testis/ovotestis)

17-OH-progesterone

Maternal androgens

Electrolytes

Glucocorticoids

Mineralocorticoids

Androgen insensitivity
(partial or complete)

MIS deficiency

No response

Deficiency of androgen synthesis

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Turner’s syndrome

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True hermaphrodite
(ovary/testis/ovotestis)

17-OH-progesterone

Maternal androgens

Electrolytes

Glucocorticoids

Mineralocorticoids

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(partial or complete)

MIS deficiency

No response

Deficiency of androgen synthesis

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(Testis/streak)

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True hermaphrodite
(ovary/testis/ovotestis)

17-OH-progesterone

Maternal androgens

Electrolytes

Glucocorticoids

Mineralocorticoids

Androgen insensitivity
(partial or complete)

MIS deficiency

No response

Deficiency of androgen synthesis

E Gonadal dysgenesis

G XO/XY

(Testis/streak)

Turner’s syndrome

MGD

Male pseudohermaphrodite

True hermaphrodite
(ovary/testis/ovotestis)

17-OH-progesterone

Maternal androgens

Electrolytes

Glucocorticoids

Mineralocorticoids

Androgen insensitivity
(partial or complete)

MIS deficiency

No response

Deficiency of androgen synthesis

E Gonadal dysgenesis

G XO/XY

(Testis/streak)

Turner’s syndrome

MGD

Male pseudohermaphrodite

True hermaphrodite
(ovary/testis/ovotestis)
A spectrum of incomplete androgen resistance syndromes, which are X-linked, has been identified. Müllerian development does not occur, and wolffian duct derivatives usually are hypoplastic. In these syndromes (Reifenstein’s), development of the external genitalia is variable and ranges from genital ambiguity to severe hypospadias with chordee. The testes are small and are often undescended. Biopsy of the testes reveals azoospermia. At puberty, there is usually poor virilization, absent or sparse axillary and pubic hair, and gynecomastia. Serum luteinizing hormone, testosterone, and estradiol levels are elevated. Gender assignment of these patients depends on their phenotype and gender identity. Some who have a phenotype of a mild virilized female with clitoromegaly choose not to have any reconstructive surgery. Phenotypic males with severe hypospadias and chordee can undergo satisfactory urethral reconstruction and resemble normal males.

External genital development in the male is stimulated by the 5α-reduced product of testosterone, dihydrotestosterone (DHT). In males with a 5α-reductase deficiency, there is a small phallus or ambiguous genitalia with perineoscrotal hypospadias, a bifid scrotum, and inguinal or scrotal/labial testes. Because the testes produce MIS, there is a blind vaginal pouch that opens into the urogenital sinus or urethra. However, the wolffian duct derivatives are present. In untreated patients, at puberty the female phenotype transforms into a masculine phenotype with penile/phaHlic enlargement, scrotal rugation and pigmentation, enlargement and descent of the testes into the labioscrotal folds, and deepening of the voice. In addition, at puberty, gender identity often changes from female to male in untreated individuals. The diagnosis is suggested by a high testosterone-to-DHT ratio, either under basal conditions or after stimulation with human chorionic gonadotropin (hCG). Genitography shows wolffian duct structures. Also termed hernia uteri inguinale, persistent müllerian duct syndrome is an X-linked condition that results from a defect in the production of MIS, an abnormality in the secretion of MIS, or a lack of response by the müllerian duct to MIS. This form of male pseudohermaphroditism does not cause ambiguous genitalia. The typical presentation is an infant or child with an inguinal hernia and cryptorchidism in whom routine exploration discloses müllerian structures (fallopian tube and uterus) as well as an epidiidymis and vas. In many cases, transverse testicular ectopia is present. Treatment includes removal of the müllerian structures; care must be taken not to injure the wolffian duct derivatives.

Five enzymes are involved in the biosynthesis of testosterone: 20,22-desmolase, 3β-hydroxysteroid dehydrogenase, 17α-hydroxylase, 17,20-desmolase, and 17-ketosteroid reductase. In most patients with the 46,XY karyotype with a disorder in testosterone synthesis, the genitalia are female in appearance or ambiguous. If the sex of rearing is decided to be male, early hypospadias repair and orchiopexy are recommended. If a female gender is assigned, however, gonadectomy and clitoroplasty should be performed and vaginoplasty may be necessary at puberty.

E Gonadal dysgenesis is characterized by abnormal testicular development, and in the 46,XY form, there is a variety of phenotypic differences ranging from normal male to genital ambiguity, depending on the extent of testicular development. It may be sporadic or familial. Swyer syndrome refers to the female phenotype with female internal genitalia, normal or tall stature, and sexual infantilism with primary amenorrhea. These patients have streak gonads, which do not secrete testosterone or antimüllerian substance, and therefore müllerian derivatives develop. All of these patients are at risk for dysgerminoma, seminoma, and gonadoblastoma. Consequently, at laparotomy, gonadectomy (removal of the streak gonads) is recommended. Pubertal development should be initiated by estrogen replacement therapy in patients reared as girls.

F Patients with mixed gonadal dysgenesis (MGD) reared as females typically have genital ambiguity with phallic enlargement, a urogenital sinus, and varying degrees of labioscrotal fusion. Internal genitalia include a unilateral streak gonad; persistent müllerian duct structures (fallopian tube, uterus, and vagina) ipsilateral to the streak; a contralateral testis, which may or may not be undescended; and frequently a fallopian tube on the side of the testis. Individuals reared as females usually have an intra-abdominal testis, whereas in those with a more masculine phenotype, the testis is usually inguinal or scrotal. Approximately 33% of patients have somatic stigmata of Turner’s syndrome with a shield chest, webbed neck, cubitus valgus, multiple pigmented nevi, and short stature. Approximately 60% are reared as females because of the diminutive phallus, which is usually hypospadiac.

Management depends on several factors. First, the testis lacks germinial elements. Second, most patients have significant hypospadias, with a uterus and a vagina. Individuals with a male gender assignment must undergo reconstructive surgery, but usually the appearance of the penis can be relatively normal if the corporal bodies of the penis are sufficiently long. Third, gonadal tumors develop in 25% of patients and include seminoma, gonadoblastoma, dysgerminoma, and embryonal cell carcinoma. Tumors may develop in either the testis or the streak gonad. Approximately 50% of patients will be less than 148 cm in height. For these reasons, most infants with mixed gonadal dysgenesis are reared as females. If gender assignment is female, early exploratory laparotomy and prophylactic gonadectomy are advisable.
Ambiguous Genitalia

Additional Readings
SECTION 12

TESTIS AND EPIDIDYMIS
Vanishing testis syndrome is characterized by the appearance of normal external genitalia in a 46XY male but with the total absence of testicular tissue. Based on the physiology of normal genital development, it is clear that testicular tissue must have been present early in development. As evidence for this, the testes must have secreted müllerian inhibitory substance (MIS) as these children do not have müllerian structures. Similarly, these patients usually have normal wolffian duct derivatives (eg, the vas deferens), so that the testes must have secreted high levels of testosterone locally to stabilize the wolffian ducts. Most conclusively, the development of normal external genitalia is dependent on the peripheral conversion of testosterone to dihydrotestosterone. The testes must have made sufficient levels of testosterone for this to occur. Yet despite these convincing findings of the presence of testes, these children have nonpalpable testes and are confirmed at the time of operative exploration to have anorchia. The etiology is most likely some form of vascular accident (perhaps bilateral testicular torsion) relatively late in gestation. Strong evidence showing that these tissues become infarcted and atrophied secondary to an in utero or neonatal torsion is the pathologic finding of dystrophic calcification and hemosiderin deposition with the presence of vas deferens and vessels in a high percentage of the testicular nubbins.1 Interestingly, some authors suggest that the term “absent” may not be appropriate for every case because the residual germ cells were found in about 5% of specimens in large series.2,3 The other possible cause of an absent testis is testicular agenesis, an extremely rare condition compared with torsion and associated with renal agenesis in almost 30% of cases.4 Moreover, this condition, if bilateral, would not allow the development of normal external genitalia.

In children with normal male external genitalia and bilateral nonpalpable testes, the following workup is recommended. First, it should be considered possible that the child is a female with congenital adrenal hyperplasia. Hence, a chromosome analysis should be performed in the newborn period and the child observed closely for the possibility of mineralocorticoid deficiency (severe salt wasting).

A If the chromosomes are 46XY, anorchia can be diagnosed endocrinologically in several ways. First, children with anorchia have extremely low levels of MIS; hence, MIS levels can be obtained. Unfortunately, the test is not commonly available; in the United States, for example, only a few laboratories can perform it. Another alternative is to measure basal serum gonadotropins (luteinizing hormone [LH] and follicle-stimulating hormone [FSH]) and testosterone levels and then to repeat the testosterone levels after human chorionic gonadotropin (hCG) stimulation. In anorchia, gonadotropin levels are elevated and there is no increase in testosterone in response to hCG. If all of these conditions are met, no surgical exploration is required.3 Unfortunately, during most of childhood after the first 6 months of life, gonadotropin-releasing hormone (GnRH) levels are low; therefore, even in children with anorchia, LH and FSH may be normal.6 If basal gonadotropins are normal, surgical exploration or hormone treatment is mandatory, regardless of the results of the stimulation test.

The hormonal stimulation test can be performed with GnRH or hCG. The dosage may vary depending on the clinician’s choice, but intramuscular (IM) injection of 1,500 IU of hCG on alternate days for three dosages will provide enough stimulation in most cases.

If hormonal studies are inconclusive, radiologic imaging is another alternative. Ultrasonography is noninvasive and easy to perform, but its accuracy for intraabdominal testes is very low.7 Computed tomography and magnetic resonance imaging are techniques with higher rates of sensitivity and specificity than ultrasonography.8–10 However, the need for sedation or anesthesia, radiation exposure, and high costs limit their use. Furthermore, if gonads are seen, operative exploration is needed. If gonads are not seen, the tests are not sensitive enough to exclude testes, and operative exploration will be needed. In practice, radiologic studies are useful only rarely.
Congenital Anorchism: Vanishing Testis Syndrome

**Patient with BILATERAL NONPALPABLE TESTES AND 46XY CHROMOSOMES**

A. **Hormonal assays**
   - Normal
   - Increase FSH/LH
     - No increase in testosterone

B. **Optional hormonal treatment**
   - Nonpalpable
     - No descent
     - Laparoscopy
       - Inguinal testis
         - Inguinal orchiopexy, optional adjuvant hormonal treatment
       - Atrophic testis
         - Removal testicular nubbin; consider prosthesis and testosterone replacement therapy (in bilateral cases) in adolescence
       - Blind ending vessels
         - No testicular tissue; consider prosthesis and testosterone replacement therapy (in bilateral cases) in adolescence
     - Palpable
       - Descent
       - Inguinal orchiopexy, optional adjuvant hormonal treatment

D. **No functional testicular tissue**
   - Vanishing testis syndrome
     - Follow-up by primary care physician
     - Testosterone replacement therapy and prosthesis placement in adolescence
     - Laparoscopic orchiopexy; also consider two-stage Fowler-Stephens in very high testes; optional adjuvant hormonal treatment

C. **Laparoscopy**
B Many clinicians consider giving hormonal therapy in an attempt to make the testes palpable or even to make them descend into the scrotum in rare cases. However, this is not useful unless there is endocrinologic evidence of testicular tissue (see above). A widely accepted protocol consists of the IM injection of 200 IU/kg of hCG weekly for 4 weeks. A total dosage of more than 15,000 IU may cause side effects, but these are generally reversible. Another drug commonly used in Europe, but not approved in the United States, is GnRH (or a GnRH analog in low dosage). Intranasal administration of GnRH 200 µg 6 times daily for 4 weeks provides results similar to hCG treatment.11

C Laparoscopy is now the gold standard for evaluation of children with nonpalpable testes. It is safe and accurate, has a low complication rate, and has the advantage of providing access for bringing the testis down into the scrotum during the same procedure.12–14 In general, 15% of nonpalpable testes are bilateral,15 and the left side predominates in unilateral cases in most series.16,17 Ten to 15% of nonpalpable testes are intra-abdominal and atrophic.18 The incidence of inguinal atrophic remnants is 25 to 30%.15 The incidence of atrophic testes does not differ from left to right.17

D In children with proven bilateral anorchia (vanishing testis syndrome), testosterone replacement therapy should be started during puberty (10 to 14 years of age), at the time serum gonadotropins increase. Many of these patients will request testicular prostheses, and adolescence seems to be the best time for testicular prosthesis placement, generally via an inguinal approach. In those patients who have endocrinologic evidence of bilateral anorchia but who have never been explored, it has been our policy to perform a confirmatory diagnostic laparoscopy while the patient is under anesthesia for prosthesis placement because there are few cases reported in the literature to validate the endocrinologic findings.
## References


A testis that is not found in the scrotum during physical examination may be retractile, maldescended, or absent. A maldescended testis may be located in the abdomen, in the inguinal canal, or between the external inguinal ring and scrotum. An ectopic testis may be distinguished from an incompletely descended testis when it is found out of its normal pathway (superficial inguinal, perineal, penile, femoral, prepubic, or contralateral). Although many substances and structures, such as the gubernaculum, epididymis, processus vaginalis, and androgens, are involved in testicular descent, the exact etiology of cryptorchidism remains unknown in most cases.

The incidence of cryptorchidism is 21% in premature infants (defined as < 2,500 g), 2.7% in newborns, and 0.8% at 8 months of age. Because the incidence in adults is not different from the latter, spontaneous descent is unlikely after 8 months of age. Retractile testes can be difficult to recognize in older children, and the fact that the cremasteric reflex is minimal in the first 6 months of life makes the newborn period an ideal time for documentation of testicular position. Once the diagnosis of cryptorchidism is made and the testes are palpable, no radiologic imaging or hormone stimulation testing is needed.

A There are conflicting results reported for hormonal treatment of cryptorchidism. Children at 3 to 5 years of age with bilateral maldescended testes seem to have the best response. However, the overall success rate is, at best, no more than 25%, and close surveillance is recommended even for testes that descend after successful treatment with human chorionic gonadotropin or gonadotropin-releasing hormone (Gn-RH), because many of them may reascend in time. Furthermore, hormonal treatment should probably not be chosen in cases with an obvious hernia.

B The standard surgical treatment of cryptorchidism is orchiopexy, and it can be performed in most cases via an inguinal approach. A hernia repair should also be done when a patent processus vaginalis or hernia sac is identified (the great majority of cases). In unilateral cryptorchidism, routine exploration for contralateral hernia is not mandatory and should be reserved for patients who have suspicious contralateral scrotal or inguinal swelling. For patients in whom the testis cannot be palpated preoperatively, we choose to perform a diagnostic laparoscopy for localization of the testis. If it is found to be inguinal, it can likely be brought down with a standard groin approach, but if it is intra-abdominal, a laparoscopic dissection is generally needed. In the case of a very high testis, ligation of the testicular artery (Fowler-Stephens procedure) can be performed laparoscopically and a secondary procedure performed 3 to 6 months later to bring the testis into the scrotum, based on the blood supply of the vas deferens and its collateral circulation. Should testicular artery ligation be chosen, it is critical that this approach be decided on prior to extensive dissection as the dissection itself might well destroy the collateral blood vessels. The success rate of inguinal orchiopexy in terms of bringing a viable testis into the scrotum is almost 98%, and complications are few (hydrocele, testicular atrophy). For intra-abdominal testes, the success rate is 70 to 90%.

C Some authors recommend adjuvant treatment with Gn-RH analog in selected cases, even after a successful orchiopexy. This is based on data indicating that patients who exhibit a failure of normal spermatogenic development on biopsy at the time of orchiopexy (having 0.2 or fewer adult dark-type spermatogonia per tubule) may be found later to have reduced fertility index in their semen analysis. Biopsies performed after treatment with Gn-RH analog show significant improvement. Those who propose hormonal therapy recommend biopsy of every cryptorchid testis and then hormonal stimulation of those that appear to have a high risk of infertility. This has not yet become standard practice in the United States.

The incidence of infertility as a result of unilateral cryptorchidism is not significantly increased versus the general population (89% versus 93% for the latter), although it is not clear how much the maldescended testis contributes. However, infertility is a real problem for patients with true bilateral cryptorchidism. Although early intervention (usually before 18 months) is thought to be optimal, the paternity rate in patients with bilateral cryptorchidism is only 65% (versus 93% for normals). This may be owing to failure of normal testicular development, failure of hormonally induced maturation, congenital epididymal abnormalities, or even surgical trauma. The exact cause is not known in most cases.

The incidence of testicular neoplasms in patients with a history of a maldescended testis is higher than in controls. Indeed, 10% of testicular neoplasms arise from cryptorchid testes; in other words, there is a 4.7- to 48-fold increased risk of cancer developing in the maldescended testis. Furthermore, the risk is 4 times greater for abdominal testes than for inguinal ones, and there is an increased risk even for the contralateral, descended testis. There are no clear data to show that surgical intervention alters the risk of neoplasm.
Patient with CRYPTORCHIDISM

A

Optional hormonal treatment

Nonpalpable

Laparoscopy

Palpable

No descent

Descent

B

C

Inguinal orchiopexy, optional adjuvant hormonal treatment

Follow-up by primary care physician

Inguinal orchiopexy, optional adjuvant hormonal treatment

Removal testicular nubbin; consider contralateral scrotal fixation

Monorchia, prosthesis in adolescence if desired

Laparoscopic orchiopexy; also consider two-stage Fowler-Stephens in very high testes; optional adjuvant hormonal treatment

References

Patients are often referred for a urologic evaluation for a scrotal mass. This mass may either have been found incidentally on examination in a primary care physician’s office or may have been brought to the attention of a doctor by the patient because of associated symptoms. The differential diagnosis of a scrotal mass is extensive and requires evaluation to rule out serious pathology.

**A** Evaluation begins with a complete urologic history and physical examination. A complete history will provide clues to the etiology of the problem. Was there recent trauma? Is the mass associated with pain? How long has the mass been present? Is it increasing in size? Are there associated urinary complaints, dysuria, frequency, or fevers? Next, in the physical examination, the physician examines the normal hemiscrotum, first to provide a reference for comparison with any abnormal findings. Tenderness may indicate an inflammatory condition, trauma, incarcerated hernia, or torsion. A painless mass may be testicular, epididymal, or located in the spermatic cord and may be cystic or solid. In general, clinicians are concerned about solid lesions. Perform transillumination in a darkened room with a passage of light through the mass suggesting a cystic nature. Examine the inguinal area for the presence of a hernia. Urinalysis is routinely obtained, and abnormalities may indicate an inflammatory condition. Scrotal ultrasonography may be necessary to further aid evaluation.

**B** In a patient with a history of scrotal trauma, a ruptured testicle should be suspected. Physical examination would reveal some degree of scrotal swelling, tenderness, and hematoma. Scrotal ultrasonography may help and has a sensitivity of 64% and a specificity of 75% for detecting traumatic rupture but should not delay surgical exploration if indicated. More prone to rupture, testicular neoplasms should be suspected in cases of minimal trauma. A history of testicular trauma has been reported in 4 to 20% of all patients with testicular cancer.

**C** A scrotal mass associated with pain is usually due to an inflammatory process; however, we must rule out malignancy and testicular torsion. Pain was reported as a presenting symptom in 33% of patients in a large series of men with testicular cancer. Testicular torsion is a surgical emergency and requires prompt evaluation and surgical correction. Prognosis for torsion is good if an operation is performed within the first 4 to 6 hours. Likewise, torsion of the appendix testis can cause pain. Clinically, this is similar to testicular torsion but can be treated conservatively with nonsteroidal anti-inflammatory drugs (NSAIDs). In addition, it is important not to overlook general surgical emergencies such as a strangulated hernia.

**D** Infectious or inflammatory conditions of the scrotum can be minor and inconvenient (eg, folliculitis) or life-threatening (eg, Fournier’s gangrene/necrotizing fasciitis). The scrotum is susceptible to folliculitis because of friction or rubbing. Treat this conservatively with good skin care, removal of irritants, and medicines when indicated. More serious infections may lead to scrotal abscess formation or cellulitis. Proper antibiotic coverage is necessary to cover both streptococcus and staphylococcal species. Surgical incision and drainage are necessary to aid healing in cases of abscess formation. The most serious complication of an infectious process in the scrotum is the development of necrotizing fasciitis. Predisposing factors include diabetes mellitus, trauma, paraphimosis, extravasation of urine, perirectal or perianal infections, and recent surgery such as herniorrhaphy or circumcision. Fournier in 1883 characterized a rapid and fulminating genital gangrene of idiopathic origin; however, today we can identify a source in nearly all individuals. This indicates immediate, aggressive débridement and antibiotic treatment. Perform retrograde urethrography if urinary extravasation is suspected. If extravasation is confirmed, arrange for urinary diversion in the form of a suprapubic cystostomy.
Patient with SCROTAL MASS

A

History,
Physical examination
Transillumination

Urinalysis

History of trauma
No history of trauma

B

Ruptured testicle

C

Mass with pain

Hernia

Solid testicular mass

G

Testicular mass

Cystic

Hydrocele

Torsion: testicular or appendix testis

D

Inflammatory

E

Painless mass

Spermatic cord mass

G

Spermatocyte

Varicocele

Scrotal abscess

Solid radical orchiectomy vs inguinal exploration
When identifying a painless mass on physical examination, it is important to determine the structure from which the mass originates. Further, it is necessary to determine whether this mass is cystic or solid in nature. All solid masses in the testicle need to be removed or require a biopsy because of the cancer risk. In addition, solid masses in the cord or epididymis need further evaluation. Primary tumors, arising from the epididymis and cord, are rare and usually benign. Benign lesions are adenomatoid tumors, leiomyomas, and papillary cystadenomas. Malignant lesions are rhabdomyosarcomas, leiomyosarcomas, fibrosarcomas, and liposarcomas. In general, prognosis is poor for those with primary malignant tumors of the epididymis or cord.

Varicocele, or dilated vein of the pampiniform plexus, is the most common mass arising from the spermatic cord. A varicocele may be present in 20% of males. This is generally due to incompetent venous valves and is more common on the left side because of the anatomic drainage of the left gonadal vein into the left renal vein. On physical examination, a varicocele is generally described as “a bag of worms” that is more prominent in the standing position. A varicocele that does not decrease in size while supine or presents acutely raises concern about the venous outflow drainage and the possibility of a retroperitoneal mass. In most adults, a varicocele is of no clinical significance, although some may complain of a dull pain. An association between men with varicoceles and infertility exists. Varicoceles have been reported in approximately 30% of infertile men. These individuals tend to have defects in sperm density, motility, and morphology. Surgical repair improves seminal parameters in approximately 70% of patients.

A hydrocele is the most common benign scrotal mass but may be secondary to tumor, trauma, or inflammation. Hydrocele formation results from excessive accumulation of serous fluid secreted by the tunica vaginalis. Physical examination reveals a cystic structure surrounding the testicle or just anterior to the testicle. This cystic structure generally transilluminates on physical examination. A spermatocele is a cystic structure found in the epididymis, possibly caused by infection, trauma, or obstruction. This structure will generally transilluminate on physical examination. Ultrasonography can help to confirm the diagnosis of a hydrocele or spermatocele. Treat both with surgical excision, if large and symptomatic. Some studies have shown a role for sclerotherapy as a treatment option.
References
Following descent of the testis into the scrotum, the processus vaginalis typically obliterates. Failure of complete obliteration results in a potential hydrocele or hernia. Approximately 6% of male infants have a hydrocele and 1 to 4% have an inguinal hernia. Approximately 95% of children undergoing hernia repair are boys, with 60% on the right side, 30% on the left side, and 10% bilateral. In phenotypic girls with an inguinal hernia, testicular feminization syndrome should be considered, although only approximately 1% of girls with a hernia have this condition. The incidence of hydrocele and hernia is higher in premature than in term males.

In most neonates with a hydrocele, the fluid is trapped in the tunica vaginalis in the scrotum and there is no patent processus vaginalis. The vast majority of these hydroceles, particularly those that are small or medium in size, disappear by 12 to 18 months of age. Those that persist typically are found to have a patent processus vaginalis on exploration.

Beyond 1 year of age, hydroceles typically are communicating. Classically, the scrotum is decompressed in the morning, but during the day, with ambulation, the scrotum gradually enlarges, becoming filled with fluid that enters the scrotum through a patent processus vaginalis.

There are three hydrocele variants (Figure 94-1):

- A hydrocele of the cord results if there is a small amount of fluid surrounding the testis and there is a fluid collection contained within the processus vaginalis. Typically these boys have a patent processus extending up to the peritoneal cavity.
- The hydrocele may extend from the scrotum proximally through the inguinal canal into the retroperitoneum, termed an abdominoscrotal hydrocele. Typically these are very large, tense hydroceles, and they do not communicate with the peritoneal cavity.
- A hydrocele may be present in the scrotum in association with an inguinal testis. Boys with this type have a typical patent processus through the internal inguinal ring and should undergo a standard orchiopexy.

Evaluation of a scrotal mass begins with transillumination with a bright light in a dark room. A hydrocele transilluminates, and one should be able to identify the testis if it is in the scrotum. A hernia typically is a smooth, firm mass that emerges through the external ring lateral to the pubic tubercle and enlarges with increased abdominal pressure, particularly with crying and straining. When the child relaxes, the hernia either reduces spontaneously or can be reduced by gentle pressure upward and posteriorly. In contrast, it is unusual to reduce a hydrocele. Another finding in some children with an inguinal hernia is the “silk glove” sign, in which thickening and silkiness of the spermatic cord are appreciated as the spermatic cord is palpated where it crosses the pubic tubercle.

If the hydrocele does not resolve by 12 to 18 months of age, hydrocelectomy is indicated. The procedure should be performed through an inguinal approach, with high ligation of the patent processus vaginalis and drainage of fluid in the tunica vaginalis around the testis. The hydrocele sac does not need to be removed as this may result in injury to the epididymis or vas deferens. If the child has an undescended testis, an orchiopexy should be performed at the time of hydrocelectomy/herniorrhaphy.

Most incarcerated hernias can be reduced nonoperatively, allowing herniorrhaphy to be performed electively. Reduction can be accomplished by placing downward traction on the testicle and gently manipulating the contents of the hernia superolaterally. Depending on the duration of the incarcerated hernia, one may elect emergency inguinal exploration to examine the viability of the bowel and omentum, even with successful reduction of the hernia. Following repair of an incarcerated hernia, approximately 10% develop testicular atrophy.

Whether to perform contralateral inguinal exploration for a nonclinical hernia is controversial. The risk of a contralateral hernia is 5 to 20% and is greatest if the initial hernia is on the left and if the child is less than 2 years of age.
years old. Currently, contralateral laparoscopic observation of the internal inguinal ring is performed by passing the laparoscope through the processus vaginalis into the peritoneal cavity and across to the other side; insufflation may be performed with either carbon dioxide or air. If a contralateral patent processus is found, contralateral inguinal exploration is recommended.

### Additional Readings


Sexual problems are common and are associated with cardiovascular risk factors. The new paradigm in the office diagnosis and treatment of male sexual function encompasses not only assessing erectile function but also libido, ejaculatory disorders, and quality-of-life parameters associated with these problems.

In 1999, Laumann and colleagues analyzed data from the National Health and Social Life Survey, a probability sample of 1,749 women and 1,410 men aged 18 to 59 years. The main outcome measures were the risk of experiencing sexual dysfunction, as well as negative concomitant outcomes. They found that sexual dysfunction was more prevalent for women (43%) than for men (31%) and was associated with various demographic characteristics, including age and educational attainment. Premature ejaculation was the most common male sexual dysfunction (21%). Decreased libido and male erectile dysfunction (ED) were less common (5% each).

In several studies, depression has shown high correlation with erectile dysfunction. Shabsigh and colleagues found that depressive symptoms were reported by 54% of men with ED alone versus 21% of men with benign prostatic hypertrophy (BPH) alone.

A History is crucial in determining the correct sexual diagnosis. The history should clarify the etiology, determine comorbid conditions, direct the treatment, and pinpoint the problem. Completing a series of validated questionnaires is optional but extremely helpful in diagnosing hypogonadism, depression, and ED. Thus, we strongly encourage incorporating these instruments into the sexual dysfunction evaluation. Laumann and colleagues have demonstrated that low libido and ED were comparable in prevalence in their recent publication. Low testosterone is associated with low libido. The androgen deficiency in the aging male (ADAM) questionnaire, authored by Morley and colleagues, is relatively easy to administer and to use. The ADAM questionnaire is considered positive if there is a “yes” response to question 1, a “no” response to question 7, or a “yes” response to any other three questions. Because of the strong associations between ED and depression, we have incorporated the Centers for Epidemiologic Studies Depression (CESD) inventory, a 20-question validated instrument that screens for depression, into our daily office practice.

Alternatives include the Beck Depression Inventory (BDI). The scores for BDI are (14 to 19 = mild, 20 to 28 = moderate, ≥ 29 = severe). The sexual health inventory for men (SHIM) is a useful, validated instrument that verifies the ED state and offers a degree of severity. There are five questions that pertain to sexual intercourse; each question has five possible responses. The scoring system includes the following: 22 and above = normal, 17 to 21 = mild ED, 12 to 16 = mild to moderate ED, 8 to 11 = moderate ED, 0 to 7 = severe ED. There are no validated instruments to detect ejaculatory disorders. We use history to detect rapid ejaculation. Rapid ejaculation that accompanies and is subsequent to the onset of ED is secondary rapid ejaculation. This is a response to the ED. Primary rapid or premature ejaculation is a lifelong problem, wherein the male ejaculates within 1 minute of erection or 1 minute of vaginal penetration.

B The urologic-specific physical examination should assess body hair distribution, abdominal obesity, peripheral pulses, inguinal hernia, phallus size, penile plaques, position of meatus, retractile foreskin, testis size and location, presence of vas deferens, spermatocoele, cremasteric reflex, presence of hydrocele, presence of suprapubic fat, bulbocavernosus reflex, prostate size, tenderness, and presence of seminal vesicles.

Laboratory work should include serum testosterone (total, free, and percent free; prolactin is optional), serum glucose (either fasting or postprandial), a lipid profile (fasting), and a prostate-specific antigen (PSA) (per practice guidelines).

C One or two visits may be needed to fully elucidate the problem. The problem may be either ED, ejaculatory dysfunction, depression, or hypogonadism. These may be present unilaterally or in combination. The blood screening may reveal diabetes, hyperlipidemia, low testosterone, or high glucose state. We consider diabetes to be a significant risk factor for ED if the HbA1c is above 8. About 10% of men with ED will have undiagnosed diabetes, and about 30% will have undiagnosed hyperlipidemia. Many men with ED will have concomitant hypertension.

D Detect hypogonadism with a serum testosterone level. Collect a serum prolactin to rule out hyperprolactinemia, if not attributable to medicines or other medical issues. Low libido may not be synonymous with hypogonadism. The ADAM questionnaire is promoted as sensitive for low libido.
Patient with COMPLAINT OF ERECTILE DYSFUNCTION

A  SHIM, CESD, ADAM, History

B  Physical examination, laboratory tests

C  Identify problem

D  Hypogonadism
   Low libido, hypoactive sexual desire

E  Depression

F  Erectile dysfunction

G  Ejaculatory disorder
Independently, Feldman and colleagues and Shabsigh and colleagues have shown strong associations between depression and ED. In Shabsigh’s study, patients were screened for depressive symptoms using the Primary Care Evaluation of Mental Disorders and the BDI. Of men, 54% reported depressive symptoms with ED alone, 56% of 18 men with ED and BPH, and 21% with BPH alone. Patients with ED were 2.6 times more likely to report depressive symptoms than were men with BPH alone (p < .005). In another study, Araujo and colleagues sought to determine whether ED was associated with depressive symptoms and whether this association was independent of aging or para-aging phenomena. Data were obtained from the Massachusetts Male Aging Study (MMAS), wherein they found that ED was associated with depressive symptoms after controlling for potential confounders (odds ratio 1.82; 95% confidence interval 1.21 to 2.73) and concluded that the relation between depressive symptoms and ED in middle-aged men was robust and independent of important aging and para-aging confounders, such as demographic, anthropometric, and lifestyle factors; health status; medication use; and hormones. We recommend the use of the validated instruments, the BDI and the CESD.

ED is defined as the inability to have satisfactory sexual activity. Sudden onset, association with a specific event, and variability in erectile function pattern all suggest psychogenic ED. A good morning erection, a good erection with a provocative movie or masturbation, and a poor erection with a partner are the hallmarks of psychogenic ED. Questions focused on the marriage, job, children, and other life issues should be offered to assist with formulating an opinion.

The gradual onset of ED, the lack of stressors, a good marriage, and an association with medical risk factors all point toward organic disease. Bear in mind, however, that even in cases of pure organic ED, patients and their partners will have a psychological response to the dysfunction.

The cardiovascular history should include questions about smoking, exercise tolerance, angina, myocardial infarction, hypertension, obesity, diabetes, hyperlipidemia, and previous cardiac surgery. In general, the goal is to assess for exercise tolerance. Six metabolic equivalents (METS) are required for sexual intercourse.

We assess ejaculatory disorders via direct questioning. The primary focus should be to determine primary rapid ejaculation—a lifelong state, wherein the man ejaculates within 1 minute of achieving an erection or within 1 minute of vaginal penetration. Stress accompanies this state, owing to the lack of voluntary ejaculatory control. We lack questionnaires in this area. Secondary rapid ejaculation is rapid ejaculation that accompanies ED; it is usually of short duration.

**Essential Criteria Required for the Diagnosis of Rapid Ejaculation**

Rapid ejaculation, the generally accepted diagnostic label for this disorder, has been known by other names, including ejaculation praecox and early, premature, or uncontrolled ejaculation. Not only are the names confusing; accurate and scientific diagnostic criterion sets are equally elusive. By combining the criterion sets of ICD-10 with DSM-IV, rapid ejaculation is diagnosed along four dimensions: (1) ejaculatory latency, (2) voluntary control, (3) presence of marked distress or interpersonal disturbance, and (4) the exclusionary criterion that the symptoms are not due to another mental, behavioral, or physical disorder. According to ICD-10, ejaculation must occur “within 15 seconds of the beginning of intercourse.” DSM-IV is equivocal on duration, stating that “ejaculation occurs with minimal sexual stimulation before, on, or shortly after penetration.” ICD-10 makes no mention of voluntary control, whereas DSM-IV notes that ejaculation occurs “before the person wishes.” Both nosologies require the man to be distressed (ICD-10 offers a time frame of 6 months; no specific time frame is defined in DSM-IV). Finally, both ICD-10 and DSM-IV require the clinician to make a judgment with respect to the independence of this condition from other mental, behavioral, or physiologic disorders.

Additionally, DSM-IV requires the clinician to make three additional judgments: whether the dysfunction is lifelong or acquired, whether it is of a generalized or specific type, and whether it is due to psychological or combined biologic and psychological factors. The distinction between the lifelong and acquired may ultimately prove to help most in clarifying the etiology of the dysfunction.

**References**


With respect to treatment, the new paradigm in the office diagnosis and treatment of male sexual function extends beyond pure erectile function and erectile dysfunction (ED). The evaluation now includes determining disorders of ejaculation, libido, erectile function (including any cardiac risk factors, as well as cardiovascular suitability for sexual activity), and depression.

A. Take the patient’s history.

B. Conduct a physical examination.

C. Identify and treat the problem.

D. The treatment of hypogonadism (low libido) and hypoactive sexual disorder (ICD-9 code 257.2) may be combined with the treatment of ED or may begin independently of the treatment of ED. Low libido that does not improve with testosterone replacement may be best treated by a referral to a mental health professional.

E. Treatment of depression is usually beyond the scope of the urology practice. It is best treated with a combination of antidepressant medication and psychotherapy. Although one study demonstrated that depressive symptoms in the face of ED responded to treatment of the ED with sildenafil, this would be considered an unconventional intervention.

F. The current treatment for men with ED centers on their suitability to take oral type 5 phosphodiesterase therapy. The only FDA-approved drug in the United States is sildenafil (Viagra [Pfizer, NY]). The two issues that clinicians must face while considering the patient a candidate for this oral therapy are cardiac suitability and the concomitant use of oral or topical nitrates. A man who uses nitrates, in any form, is not a candidate for sildenafil therapy. The cardiac suitability is detailed under “J.”

G. Ejaculatory disorders are assessed via direct questioning. Questionnaires in this area are lacking. Secondary or acquired rapid ejaculation is diagnosed if the patient reports a period of normal functioning. An example of secondary rapid ejaculation is the development of this problem after the onset of ED.

H. There is some controversy about the type of therapy. There are oral preparations, intramuscular injections, topical gels, and transdermal preparations. Side effects include elevations in the serum hematocrit, in the lipid profile, and in the liver function enzymes.

I. The treatment of depression usually falls under the domain of the mental health professional. Mild depressive symptoms may improve after treatments with a type 5 phosphodiesterase (PDE) inhibitor, such as sildenafil.

J. The cardiovascular history should include questions about smoking, exercise tolerance, angina, myocardial infarction, hypertension, obesity, diabetes, hyperlipidemia, and previous cardiac surgery. In general, the goal is to assess for exercise tolerance. An assessment of six metabolic energy equivalents is required for sexual intercourse.

Guidelines are available for the clinician to rapidly assess the cardiac status of the patient (Table 96-1).

K. In general, men with low risk can go directly to oral type 5 phosphodiesterase therapy. At this time, the only FDA-approved drug for male ED is sildenafil (Pfizer). Other oral agents under review include vardenafil (Bayer, GlaxoSmithKline) and tadalfil (Lilly-ICOS). Sildenafil is contraindicated if the patient takes nitroglycerin in any form. It is anticipated that all type 5 phosphodiesterase inhibitors will have the same nitrate contraindication. Men in the intermediate range need further cardiac assessment, which will then stratify them into either a low- or high-risk group. The testing that is most commonly employed is either a standard Bruce protocol exercise stress test or a nuclear stress test if the patient had difficulty with ambulation or another contraindication. Men in the high-risk group will need careful monitoring if deemed appropriate candidates for oral type 5 PDE inhibitor therapy. Men with psychogenic ED do well with oral type 5 PDE therapy. Some men will combine oral type 5 PDE therapy with either the vacuum device or intracavernosal injections to augment erectile response. Adjunctive therapy for men with ED and cardiovascular risk factors includes assessing and treating the following.
Patient with COMPLAINT OF SEXUAL DYSFUNCTION

A. History, sexual health inventory for men (SHIM)
   - Centers for Epidemiologic Studies Depression inventory
   - Androgen deficiency in the aging male questionnaire

B. Physical examination, testosterone level

C. Identify and treat problem

D. Hypogonadism,
   - low libido
   - hypoactive sexual disorder

E. Depression

F. Erectile dysfunction

G. Ejaculatory disorder

H. Testosterone replacement

I. Antidepressant,
   - sildenafil, mental health clinician

J. Brief cardiac assessment

K. Sildenafil or other type 5 PDE inhibitor

L. Injections,
   - vacuum,
   - prosthesis

M. Selective serotonin reuptake inhibitor
   - with/without psychosexual therapy
Table 96-1 Cardiovascular Disease—Princeton Guidelines: Categories of Cardiovascular Risk

<table>
<thead>
<tr>
<th>Low Risk</th>
<th>Intermediate Risk</th>
<th>High Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymptomatic, &lt; 3 risk factors for CAD</td>
<td>Asymptomatic, &gt; 3 major risk factors for CAD, excluding gender</td>
<td>Unstable refractory angina</td>
</tr>
<tr>
<td>Controlled hypertension</td>
<td>Moderate, stable angina</td>
<td>Uncontrolled hypertension</td>
</tr>
<tr>
<td>Mild, stable angina</td>
<td>Recent MI (&gt; 2, &lt; 6 wk)</td>
<td>LVD/CHF (NYHA class III/IV)</td>
</tr>
<tr>
<td>Post–successful coronary revascularization</td>
<td>LVD/CHF (NYHA class II)</td>
<td>Recent MI (&lt; 2 wk), CVA</td>
</tr>
<tr>
<td>Uncomplicated past MI (&gt; 6–8 wk)</td>
<td>Noncardiac sequelae of atherosclerotic disease (eg, CVA, PVD)</td>
<td>High-risk arrhythmias</td>
</tr>
<tr>
<td>Mild valvular disease</td>
<td></td>
<td>Hypertrophic obstructive and other cardiomyopathies</td>
</tr>
<tr>
<td>LVD/CHF (NYHA class I)</td>
<td></td>
<td>Moderate/severe valvular disease</td>
</tr>
</tbody>
</table>

CAD = coronary artery disease; CHF = congestive heart failure; CVA = cardiovascular accident; LVD = left ventricular dysfunction; MI = myocardial infarction; NYHA = New York Heart Association; PVD = peripheral vascular disease.


areas: smoking cessation, weight loss, exercise, attitude, and diet. Finally, inclusion of the partner in the discussion and treatment plan is often quite helpful.

L If a man fails sildenafil or cannot take sildenafil because of nitrate use or untoward side effects (most commonly headache, dyspepsia, and flushing), then suitable alternatives would include the use of the vacuum erection device, injection of vasoactive agents intracavernosally, such as prostaglandin E1, or implantation of a penile prosthesis. Specific areas that deserve mention include treating ED after radical prostatectomy, after spinal cord injury or other neurologic disorders, and with chronic renal failure or dialysis. These men may do well with oral type PDE 5 therapy. Men who have undergone non–nerve-sparing radical prostatectomy do not fare as well with oral type 5 PDE therapy. Some men on injection prefer to switch to oral type 5 PDE therapy. Interestingly, some men who have tried both injections and oral type 5 PDE therapy prefer the intracavernosal injections.

M Secondary or acquired rapid ejaculation is included in the treatment of male ED. Improvement in erectile function usually leads to improvement in ejaculation as well; the ejaculatory problems are usually corrected as the ED is corrected.

Pharmacologic Treatment of Primary Premature Ejaculation

The treatment of primary rapid ejaculation is evolving. Oral therapy with a selective serotonin reuptake inhibitor (SSRI) has become standard therapy for this disease, though the best drug and the dosing schedules remain discretionary. Clinicians are aware that several classes of drugs impede or eliminate orgasm. These include monoamine oxidase (MAO) inhibitors, tricyclic and serotonergic antidepressants, and a newly developed compound referred to as SS-cream. Double-blind, placebo-controlled studies with clomipramine and the major SSRIs, using strict dosages in carefully selected populations, have repeatedly demonstrated that these agents are effective in delaying ejaculation. When subjects discontinue the medication, however, improvements are lost, and, generally, ejaculation latencies return to baseline. Side effects of these medications are generally mild, are dose related, and do tend to diminish with time; dry mouth, headache, drowsiness, and gastrointestinal upset are most frequently observed.

To determine which of the major SSRIs were most effective in delaying orgasm, Waldinger and colleagues performed a head-to-head study between fluoxetine, fluvoxamine, paroxetine, and sertraline in treating rapid ejaculation. They found that paroxetine induced the longest delay in ejaculation, followed by fluoxetine and sertraline. No clinically significant delay in ejaculation was noted with fluvoxamine.

SS-cream is a newly developed topical agent made from the extracts of nine natural products. It is applied to the glans penis 1 hour before sexual intercourse. In placebo controlled, double-blind studies, this compound significantly improved ejaculator latency and sexual satisfaction. SS-cream increases the penile sensory threshold in a dose-dependent manner and has side effects that include mild local burning and mild pain.

Psychological Intervention for Primary Rapid Ejaculation

Since the early 1970s, an array of individual, conjoint, and group therapy approaches employing behavioral strategies such as stop–start, the squeeze technique, progressive senate focus exercises, masturbatory exercises, and “quiet vagina,” with the female astride, have evolved as the treatments of choice for rapid ejaculation. These therapies are usually the domain of the mental health professional.

Our practice is to use clomipramine 25 to 50 mg daily for 1 month, then twice weekly, with an additional dose just prior to anticipated intercourse. It may be best to combine psychological intervention and oral SSRI therapy for optimal long-term outcome.
Additional Readings


To impregnate successfully, a man must be able to ejaculate his semen. That act necessitates two separate processes: emission and ejaculation. The transfer of spermatozoa and secretions from the testicle, epididymis, vas deferens, seminal vesicles, and prostate to the posterior urethra constitutes emission. Ejaculation involves the propulsion of those contents through the urethral meatus by a sequence of rhythmic contractions of the bulbospongious and ischiocavernous muscles. Any interruption in that cascade of events can contribute to ejaculatory dysfunction and infertility. Ejaculatory dysfunction can be classified as follows: ejaculatory failure, ejaculatory duct obstruction, premature ejaculation, and retrograde ejaculation (RE). RE is defined as the backward flow of semen into the bladder that can be attributed to various anatomic, neurogenic, pharmacologic, and idiopathic factors.

**Pathophysiology**

Although RE is not a common cause of infertility, it is prevalent following transurethral and open prostatectomy, as well as any bladder neck surgery. The incidence of RE can be as high as 90% following such operations, secondary to incompetence of the bladder neck. Closure of the bladder neck during ejaculation is imperative for the normal antegrade flow of semen. Electromyographic study of the bladder neck and external sphincter reveals increased activity during emission, with subsequent increased pressure within the posterior urethra. Y-V plasty of the bladder neck, a procedure historically performed to remedy vesicoureteral reflux in children, can alter the integrity of the bladder neck with subsequent RE in adulthood. Likewise, ectopic ureterocele, urethral trauma, urethral stricture, and congenital valves can generate RE via disruption of the anatomic integrity of the bladder neck and urethra. Patients with congenital anomalies such as cloacal exstrophy and imperforate anus who undergo exstrophy repair or bladder neck reconstruction may also be afflicted with RE.

Emission and ejaculation are separate processes that can occur independently of each other. Emission is mediated by the sympathetic nervous system through T10–L2 level preganglionic fibers, whereas ejaculation is controlled by the S2–S4 parasympathetic and somatic efferents fibers. Sympathetic stimulation results in bladder neck closure and contraction of the vas deferens, seminal vesicle, and prostate. The motor efferents that innervate the periurethral and pelvic musculature are responsible for the rhythmic contraction of these muscles and expulsion of the ejaculate. Thus, spinal cord injury that results from trauma, congenital neurologic or vascular defects, retroperitoneal or spinal surgery, infection, or malignancy may interfere with the ejaculatory process. Diabetic patients are more prone to RE, with a reported incidence of 32%. RE in diabetics can be attributed to neuropathies affecting the sympathetic nervous system with a reduction in alpha stimulation and resultant bladder neck incompetence.

Various pharmacologic agents that exert a sympatholytic effect promote inhibition of emission and reduction of bladder neck closure during ejaculation. Antihypertensives, antidepressants, and antipsychotics are commonly associated with ejaculatory dysfunction but for different pharmacologic reasons. Tamsulosin and phenoxybenzamine, α-blockers commonly used to treat lower urinary tract symptoms secondary to benign prostate hyperplasia (BPH), may result in incomplete bladder neck closure and thus RE. Antidepressants that may contribute to ejaculatory dysfunction and RE include tricyclic antidepressants, monoamine oxidase inhibitors, and selective serotonin reuptake inhibitors. Patients on neuroleptics, such as haloperidol and risperidone, also frequently complain of erectile and ejaculatory disturbances. The effect of those agents is mediated through the serotonergic receptors of the central nervous system (CNS) and is inhibitory in nature. Risperidone induces RE by interfering with the sympathetic modulation of the bladder neck and urethral sphincter. Finally, men in whom no etiologic factors can be found are invariably classified as possessing idiopathic RE.

**A** Patients with RE typically present with orgasm without semen ejaculation (dry orgasm) or low-volume semen ejaculation. However, most men who pursue medical evaluation usually complain of infertility as the first sign of ejaculatory dysfunction. Undoubtedly, a detailed history and physical examination are imperative in the initial evaluation of any patients presenting with ejaculatory dysfunction. A careful history of previous urologic or retroperitoneal operations, congenital anomalies, trauma, spinal cord injury, neurologic disease (eg, multiple sclerosis), diabetes mellitus, and medications can frequently elucidate the underlying cause of RE. Physical examination includes a meticulous assessment of the testicles, the epididymis, and the vas deferens. If anatomic abnormalities are suspected, perform transrectal ultrasonography or vasography to evaluate the prostate, the seminal vesicles, and the ejaculatory ducts.

**B** Confirming RE is fairly straightforward because the presence of sperm in the postcoital urine specimen is
Retrograde Ejaculation

Patient with DRY ORGASM OR LOW-VOLUME EJACULATE

A. History
   Physical examination

B. Postejaculation urinalysis
   - No sperm
   - Sperm

   - Urinary fructose test
     - Seminal fluid without sperm present in the urine
       - Azoospermia
       - Evaluation and work-up for azoospermia
     - No seminal fluid in the urine
       - Lack of ejaculation

   - Retrograde ejaculation
     - Conservative approach or medical therapy
       - Treatment failure
         - Antegrade ejaculation
         - Failure
           - Hotchkiss, bladder neck reconstruction
       - Urine pH adjustment and alkalinization with sperm retrieval
         - Success
diagnostic. In the absence of sperm on urinalysis, clinicians can perform a fructose test to assess for any seminal emission.

C Tailor therapeutic options for RE toward the causative factors and the couple’s desire for fertility. Withdraw or change any suspected offending medications if not medically contraindicated. Neurologic and minor anatomic defects may be rectified by medical therapy. Sympathomimetic agents such as imipramine and ephedrine may be tried to increase the bladder neck tone, and Table 97-1 lists the dosages.

When conservative medical therapy fails, clinicians can aim efforts at harvesting sperm, in conjunction with intrauterine insemination. Various techniques of sperm retrieval may be employed to optimize sperm quality. Because of urine toxicity on sperm, adjust the urinary pH and osmolarity to allow for optimal sperm survival; acidity causes immobilization, whereas hyperosmolarity results in cellular membrane disruption. A relatively simple and non-invasive method involves increased fluid ingestion to dilute the urine (specific gravity of 1.010) and urine alkalization (pH of 7.0 or above) through sodium bicarbonate administration approximately 2 hours before intercourse. After ejaculation, sperm from the postcoital urine specimen is then isolated and examined. If the sperm is deemed good quality, use it for intrauterine insemination, in vitro fertilization with embryo transfer, or intracytoplasmic sperm injection (ICSI). The couple can perform intravaginal insemination with less inconvenience or discomfort. If these methods of sperm procurement fail to yield optimal sperm for insemination, the patient can then be catheterized, followed by instillation of a buffer solution into the bladder.

After emptying the bladder via catheterization, various buffer solutions can be instilled into the bladder to approximate the urinary pH and osmolarity to those of fresh ejaculate; examples include Hanks or Earle’s balanced salt solution, Ham’s modified F-10 medium, low-electrolyte glucose solution, or BWW (Biggers, Whitten, and Wittingham) buffered medium. The patient is then asked to masturbate and subsequently void into a container, which may contain another buffer medium to further enhance sperm motility. The specimen is then centrifuged and the sperm pellet isolated. In 1955, Hotchkiss and colleagues described this method of administering buffer medium to minimize the detrimental effect of urine on sperm quality, which is currently employed in various modified versions.

Other techniques, such as postcoital vaginal voiding, cryopreservation of retrograde ejaculate, and ejaculation with a distended bladder to promote antegrade flow of ejaculate, have also been reported.

If conservative medical therapy and sperm retrieval with insemination fail to lead to successful pregnancies, one may resort to surgical intervention to correct RE. The Abrahms procedure, originally described in 1975, has been performed with some success. This transvesical operation involves reconstruction of the internal sphincter through excision of the mucosa around the bladder neck with subsequent plication of the bladder neck muscle to reduce its caliber. An alternative with reported success is the Young-Dees approach. This procedure aims to alleviate bladder neck incompetence via bladder neck reduction, lengthening of the deep urethra proximally, and reinforcement of the bladder neck with trigonal muscle.

Another option that we have employed with good outcome is to inject a partially competent bladder neck with a bulking agent. In one such case, the bladder neck of a 26-year-old infertile man was reconstructed with the injection of Teflon paste. The resultant bulking obstruction of the bladder neck permitted antegrade propulsion of semen and allowed him to father two children. Any commonly available injectable agents would be similarly suitable.

### Conclusion

The current technological advances of assisted reproduction can provide men who suffer from RE with a much better chance of securing a successful pregnancy with their partners. When procreation is not a priority or a necessity, RE patients may not require any treatment. If treatment is desired, attempt a conservative approach prior to resorting to invasive or surgical interventions. Nonetheless, formulate the therapeutic strategy based on the etiologic factors and needs of the patient and partner.

### References


### Table 97-1 Medical Therapy for Retrograde Ejaculation

<table>
<thead>
<tr>
<th>Pharmacologic agent</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ephedrine</td>
<td>25–50 mg 2 hours before coitus</td>
</tr>
<tr>
<td>Imipramine</td>
<td>25 mg bid</td>
</tr>
<tr>
<td>Phenylpropanolamine</td>
<td>75 mg bid</td>
</tr>
<tr>
<td>Pseudoephedrine</td>
<td>60–120 mg before coitus</td>
</tr>
</tbody>
</table>


Priapism

Allen D. Seftel, MD

A Priapism is a prolonged, nonvoluntary erection lasting > 4 to 6 hours. A recent American Foundation for Urologic Disease Consensus Panel Conference defined priapism as “unwanted penile erection that persists beyond or is unrelated to sexual stimulation” (Table 98-1 and Table 98-2).

B The initial management depends on the type of priapism. Priapism generally falls under urologic care, although oncologists and pediatricians do treat this entity as well. Clinicians must inform all patients that this disease can render them permanently impotent.

The initial management is as follows:

• History (medical, medications, and sexual)
• Physical examination and vital signs, urology consultation

Laboratory tests to consider:

• Complete blood count (CBC), differential white blood count (WBC), and platelet count
• Urine toxicology/drug of abuse screen
• Urine analysis, and reticulocyte count

C Priapism that is painful, irrespective of trauma, is considered low-flow or ischemic priapism. The diagnosis is usually clinical: a prolonged, painful, unwanted erection. “B” in the algorithm includes early urologic management, with the addition of the following:

Assess corporal blood flow. This can readily be done by aspiration of the corpora with a small-bore syringe. Further, obtain a blood gas. Dark, crank-case blood, or a very low penile blood gas PO2 on aspiration is consistent with ischemic priapism. Duplex Doppler ultrasonography helps to assess corporal blood flow. If the patient is a young, African American male, then a hemoglobin electrophoresis is indicated to assess for sickle cell disease. A serum prostate-specific antigen (PSA) is optional in the older male to rule out prostate cancer. Clinicians can diagnose ischemic priapism by obtaining a history, a physical examination, and dark blood on corporal aspiration.

D The initial treatment (< 4 hours) for ischemic, sickle cell priapism centers on opioid analgesia, intravenous hydration, and nasal oxygen supplementation. Characteristically, the priapistic erections are an aftermath of the morning erection. If these conserva-

tive measures fail, then more invasive treatment is necessary.

E If the sickle cell priapism does not respond to conservative measures, or in the case of ischemic, nonsickle cell priapism, then institute an aspiration of the penis with a dilute α-adrenergic agent, such as phenylephrine. Give the patient 300 to 400 µg intracavernosally, at 5-minute intervals, for a maximal total dose of 1,000 µg. Monitor blood pressure because the α-adrenergic drugs can induce a severe hypertension; however, sublingual nifedipine can offset the hypertension. Irrigating the cavernosa with sterile saline should accompany instilling the α-adrenergic drug. Local penile anesthesia, such as a penile ring block, is warranted to reduce pain and help with detumescence. Oral or intravenous sedation is indicated as well. If the patient has sickle cell disease and the hematocrit < 30%, a blood transfusion is indicated. Likewise, an exchange transfusion is indicated for a high sickle hemoglobin (hemoglobin S).

F If detumescence is achieved, then observe the patient for a few hours to ensure that there is no recurrence of the priapism.

G If complete detumescence occurs, then arrange follow-up with the patient in the office to assess the cause of

Table 98-1 Etiology—as per American Foundation for Urologic Disease Classification

<table>
<thead>
<tr>
<th>Drug induced</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hematologic</td>
</tr>
<tr>
<td>Sickle cell disease and other hemoglobinopathies</td>
</tr>
<tr>
<td>Thrombophilia states (protein C and other thrombophilias, lupus)</td>
</tr>
<tr>
<td>Hyperviscosity states (hyperleukocytosis, polycythemia)</td>
</tr>
<tr>
<td>Idiopathic</td>
</tr>
<tr>
<td>Central nervous system mediated</td>
</tr>
<tr>
<td>Other</td>
</tr>
</tbody>
</table>

Table 98-2 High-Flow States (Arterial or Nonischemic Type)

<table>
<thead>
<tr>
<th>Penile/perineal trauma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Straddle injury</td>
</tr>
<tr>
<td>Cavernosal artery injury</td>
</tr>
<tr>
<td>Arteriosinusoidal fistula</td>
</tr>
<tr>
<td>Cocaine</td>
</tr>
<tr>
<td>Metastatic malignancy</td>
</tr>
<tr>
<td>Fabry’s disease</td>
</tr>
<tr>
<td>Iatrogenic (following deep dorsal vein arterialization)</td>
</tr>
</tbody>
</table>
Patient with PRIAPISM

**Initial management**
- History (medical, medications, and sexual)
- Physical examination and vital signs
- Consult urology
- Laboratory tests to consider:
  - CBC, differential WBC, and platelet count
  - Urine toxicology/drug of abuse screen
  - Urine analysis, reticulocyte count

**Urologic management**

**Nonischemic**
- Observation
- Patient education
- Duplex Doppler ultrasonography

**K**
- Selective pudendal embolization
  - clot vs foam, possibly coils
  - Surgical ligation of artery

**Ischemic**

**E**
- Non–sickle cell
  - Penile vs systemic anesthesia:
    - Local penile shaft block
    - Dorsal or circumferential nerve block
    - Oral vs intravenous conscious sedation
    - Aspiration with/without irrigation with dilute adrenergic agent

- If still tumescent after 4 hours

**Sickle cell**
- Opioid analgesia
- Hydration: intravenous vs oral
- Oxygen if hypoxic
- Transfusion: simple or exchange
- No detumescence; sickle cell only

**F**
- Detumescence

**G**
- Complete
  - Patient education
  - Scheduled follow-up
  - Pain management

**H**
- Partial
  - Inpatient observation and serial examination
  - Pain management
  - Interval assessment of corporal blood flow:
    - inspection, blood gas, duplex Doppler ultrasonography
    - α-agonist (oral vs intracavernosal)

**I**
- None
  - Percutaneous vs surgical shunt
  - Distal first
  - Proximal if absent cavernosal artery
  - flow by duplex Doppler ultrasonography
the priapism. The patient with recurrent, ischemic priapism can be taught self-injection with the \( \alpha \)-adrenergic agent to self-treat this entity. Alternatively, one could try an oral \( \alpha \)-agonist on a daily basis. If a urine toxicology study is positive, refer the patient for counseling. If the priapism is due to a neoplasm, then address this oncologic process. For drug-induced priapism, remove the offensive agent. Appropriately treat hematologic causes, such as the hypercoagulable state, or hyperviscosity states, or neurologic causes (see Table 98-1).

**H** Re-treat partial detumescence with the intracavernosal \( \alpha \)-adrenergic drugs. Observe the patient and obtain a Doppler sonogram to assess corporal blood flow. If the partial erection resolves, then the patient can be followed as outlined under “F.” Good blood flow and well-oxygenated blood on the aspirate allow for an observational course. If the detumescence is not full and there is poor blood flow, then think about a shunt for the patient. Partial erection that remains with good blood flow over 24 hours indicates that the patient has a high flow variant; therefore, consider an arterial embolization.

**I** Refractory, low-flow priapism is a surgical emergency. Initially, the clinician places a distal, Winter shunt; however, if this is unsuccessful in achieving detumescence, then use a distal cavernosal-spongiosal shunt (El-Ghorab). However, employ the proximal cavernosal-spongiosal shunt as a last resort.

**J** Nonischemic priapism is usually the result of blunt perineal trauma (see Table 98-2). The partially erect penis is usually nonpainful, with the aspirate red and the blood gas consistent with arterial blood. Doppler ultrasonography reveals cavernosal arterial flows > 20 cm/s. The patient can go untreated without untoward effects.

**K** Treatment is usually via percutaneous fluoroscopic approach, wherein a clot, artificial material, or a coil is placed near the fistulous artery via the Seldinger technique.

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### Additional Readings

SECTION 14
STERILITY AND INFERTILITY
The male scrotal varicocele occurs in 15% of the male population and 40% of men presenting for an infertility evaluation. The male scrotal varicocele is usually left-sided (about 80 to 90%). However, a few men have bilateral disease. The new onset of a varicocele mandates evaluating the upper urinary tracts because a presenting symptom of a renal tumor may be a varicocele of new or recent onset.

The scrotal varicocele has three potential sources: the internal spermatic veins (which drain into the aorta on the right and the renal vein on the left), the gubernacular veins, and the external spermatic veins. Varicoceles generally arise in the postpubescent and the young adult male. The etiology of the varicocele is due to the acute angulation of the left internal spermatic vein as it enters the left renal vein. Incompetent venous valves, increased pressure, and collateral venous drainage are the three dominant theories in the etiology of the varicocele. The effect on the testis is an adverse effect on spermatogenesis. Theories include local hyperthermia, hypoxia, oxidative stress, and hyperperfusion injury. The resultant effects include a decrease in testicular size and a negative effect on the sperm count and motility. The effect on the sperm morphology is controversial.

**Clinical Presentation**

The clinical presentation often takes place as part of evaluating chronic scrotal pain (for acute pain, rule out testicular torsion) or as part of the evaluation of male factor infertility in the adult. The young adolescent will have this entity diagnosed on routine physical examination.

Because a Grade III varicocele is large, the clinician can easily detect it when the patient is standing. However, a Grade II varicocele is detected on routine physical examination, whereas a Grade I varicocele is viewed better with a Valsalva maneuver. A subclinical varicocele is not detected on examination but appreciated with the office Doppler after Valsalva. Controversy exists with respect to the need for treating the Grade I and subclinical varicocele.

For the subfertile male, the evaluation will generally comprise a semen analysis and possibly a hormonal (blood) profile. The varicocele will generally affect the sperm count and motility, with controversial effects on the sperm morphology. A scrotal sonogram is indicated if the varicocele is large and the testicle cannot be detected on examination. Controversy exists about the need for identifying the subclinical varicocele. Advocates of this entity would recommend an ultrasound examination if the varicocele were nonpalpable in the subfertile male. For the man with scrotal pain, a scrotal ultrasound examination may help to delineate scrotal or testicular anatomy and to rule out other potential causes of the scrotal pain.

Surgical repair is indicated for a subnormal count or motility in men with a Grade II or III varicocele. Surgical repair of a Grade I, or a subclinical varicocele, is controversial. Scrotal or testicular pain that attributes to the varicocele indicates surgical intervention. Treating the varicocele in the adolescent male is based on loss of testicular volume. A > 10 to 20% disparity between the affected left testis and the unaffected right testis indicates surgical correction.

**Treatment**

In the adult, testicular pain, other symptoms related to the varicocele, or subfertility requires surgical correction. Repair is indicated for a low sperm count or a low sperm motility. Controversy exists about the benefit of a varicocele repair with low sperm morphology. There is also debate with respect to the correction of the varicocele in the face of azospermia. Further discussion exists about the role of varicocele repair in the face of artificial insemination (intrauterine insemination) or in vitro fertilization. It is prudent to correct the varicocele in the presence of an abnormal sperm count or motility prior to intrauterine insemination, while varicocele correction assumes a lesser role when the couple is contemplating in vitro fertilization (IVF).

Perform surgical repair using the subinguinal approach, with either magnification loupes or an operating microscope; inguinal approach; and retroperitoneal approach or laparoscopic approach. Specific surgical complications include recurrence in 3 to 5% of cases, hydrocele formation in <5% of cases, and injury to the testicular artery in <5% of cases. We should see successful varicocele repair in over 95% of cases, resulting in improved sperm count and motility by about 50%.

Alternatives to surgical repair include angiographic embolization of the vessels via a percutaneous transvenous approach or via injection of the veins subcutaneously. These approaches are not first-line therapy in the United States.
### Additional Readings


Oligospermia is < 20 million sperm/cc of ejaculate, whereas a normal ejaculate volume is assessed as follows:

**A** Perform a physical examination and determine serum follicle-stimulating hormone (FSH).

**B** If a varicocele exists, consider a varicocele repair or embolization. The varicocele treatment scheme should be adhered to.

**C** If there is no varicocele and the FSH is high (> 1.5 to 2 × normal), then there is a degree of testicular failure. Arrange for a testis biopsy if there is oligospermia with poor or absent motility, which might preclude in vitro fertilization. Other alternatives include donor insemination or adoption.

If the ejaculate volume is low, think of retrograde ejaculation or an ejaculatory duct obstruction.

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**Additional Readings**


Patient with OLIGOSPERMIA

Oligospermia < 20 million sperm/cc
Normal ejaculate volume

A. Physical examination, serum FSH, normal FSH

B. Check for varicocele

C. High FSH

Intrauterine insemination, testis biopsy
with in vitro fertilization/intracytoplasmic sperm injection or donor sperm/adoption

Surgical repair vs embolization
Azoospermia is the absence of sperm in the normal volume ejaculate. Low ejaculate volume with either azoospermia or oligospermia might suggest an ejaculatory duct obstruction or retrograde ejaculation.

The major issues are the identification of the vas deferens, testicular size, and serum follicle-stimulating hormone (FSH).

A, B, C If the physical examination verifies the presence of the vasa, determine the testicular size and serum FSH. If the testicular size is small and the serum FSH is > 2 times normal, chances are high that the patient has primary testicular failure. A testis biopsy helps determine causes such as Klinefelter’s syndrome or Y chromosome microdeletions and, in rare cases, may yield an occasional sperm suitable for intracytoplasmic sperm injection (ICSI). Usually, these tests are devoid of any sperm. If the FSH is > 2 times normal and the testicular size is normal, then a biopsy may be helpful to distinguish Sertoli cell–only syndrome (germ cell aplasia) from maturation arrest. Rarely, one can find viable sperm in the face of maturation arrest. If a rare sperm is found, ICSI can be attempted. Other options include donor insemination or adoption.

D If the FSH is low, assess serum prolactin, luteinizing hormone, and testosterone levels. All of these will be abnormally low in the face of hypogonadotropic hypogonadism. Treat this condition with intramuscular human chorionic gonadotropin and pergonal. A high prolactin level is more often associated with erectile dysfunction and is often caused by a pituitary tumor or may be the side effect of medication.

E If the FSH is normal, the testis size is normal, and the vasa are present and somewhat full to palpation, then a testis biopsy followed by a vasoepididymostomy is indicated. Usually, sperm are present in this obstructed condition. Sperm banking may be useful if the vasoepididymostomy does not remain patent or in the face of an abnormal postreconstruction semen analysis not suitable for intrauterine insemination.

F Absent vasa at the testicular level are found in men with cystic fibrosis or congenital bilateral absence of the vas deferens (CBAVD). On rare occasions, men who have undergone bilateral herniorrhaphies as a child (or even as an adult) may have a large, atrophic, or absent segment of the vas deferens as the result of compromise. The men with cystic fibrosis or CBAVD and their partners will need an evaluation for deletions of the various cystic fibrosis genes and genetic counseling to discuss the ramifications of passing these genes onto their offspring. Sperm is extracted via microepididymal sperm aspiration (MESA), testicular sperm extraction (TESE), or testis biopsy with sperm banking indicated. In vitro fertilization is mandatory in these cases. Alternatives include adoption or donor insemination.

Additional Readings
Patient with Azoospermia, Normal Ejaculate Volume

A. Physical examination, serum FSH

Vasa present

B. Assess FSH and testicular size

C. Elevated FSH (>2× normal), small testis size
   - Testis biopsy, sperm banking, IVF/ICSI, or donor sperm/adoption

D. Elevated FSH (>2× normal), normal testis size
   - Hypogonadotropic hypogonadism

E. Low FSH
   - Normal testis size
   - Epididymis full to palpation
   - Consider testis biopsy
   - Genetic testing
   - CBAVD
   - Cystic fibrosis or variant
   - Consider renal ultrasonography

F. FSH usually normal

Vasa absent

F. FSH usually normal

E. Normal FSH
   - Normal testis size
   - Epididymis full to palpation
   - Consider testis biopsy
   - Genetic testing
   - MESA, TESE, testis biopsy, sperm banking, IVF/ICSI, or donor sperm/adoption

E. Normal FSH
   - Normal testis size
   - Epididymis full to palpation
   - Consider testis biopsy
   - Genetic testing
   - MESA, TESE, testis biopsy, sperm banking, IVF/ICSI, or donor sperm/adoption

D. Low FSH
   - Normal testis size
   - Epididymis full to palpation
   - Consider testis biopsy
   - Genetic testing
   - MESA, TESE, testis biopsy, sperm banking, IVF/ICSI, or donor sperm/adoption

C. Elevated FSH (>2× normal), small testis size
   - Testis biopsy, sperm banking, IVF/ICSI, or donor sperm/adoption

B. Assess FSH and testicular size

A. Physical examination, serum FSH
SECTION 15
ADRENAL DISORDERS
Cushing’s Syndrome
Alireza Moinzadeh, MD, and John A. Libertino, MD

The normal physiology of the adrenal gland includes secretion of cortisol from the zona fasciculata. This adrenocortical steroid secretion is stimulated by a peptide hormone from the anterior pituitary called adrenocorticotropic hormone (ACTH). ACTH secretion is in turn positively regulated from the hypothalamic corticotropin-releasing hormone (CRH). CRH release is under negative feedback control by cortisol (Figure 102-1A).

Cushing’s syndrome is a term that encompasses a variety of pathophysiologic states leading to hypercortisolism. It is a rare syndrome with an estimated annual incidence of 0.1 to 1 new case per 100,000. Simple classification of this syndrome is either ACTH dependent or ACTH independent (Table 102-1). The most common etiology of Cushing’s syndrome (~70% of the time) is Cushing’s disease.

Cushing’s disease is defined as hypercortisol production secondary to increased ACTH from the pituitary gland (Figure 102-1B). Other etiologies that must be differentiated include adrenal adenoma or carcinoma (Figure 102-1C), ectopic ACTH secretion (Figure 102-1D), and the more rare entity known as pseudo-Cushing’s syndrome (Figure 102-1E). Exogenous administration of cortisol may also lead to Cushing’s syndrome. The following algorithm guides in the screening for Cushing’s syndrome, ruling out pseudo-Cushing’s, and differentiating and treating the various etiologies of ACTH-dependent versus ACTH-independent Cushing’s syndrome.

A The impetus for work-up of Cushing’s syndrome rests on clinical suspicion for the disease. Clinical features include hypertension, diabetes, truncal obesity, moon face, red cheeks, proximal muscle weakness, thin skin, easy bruising, increased supraclavicular and infrascapular fat pads (buffalo hump), pendulous abdomen with striae, poor wound healing, and psychiatric illness (Figure 102-2). These clinical features vary widely from one series to the next and are dependent on many factors, such as duration and degree of the disease.

B When Cushing’s syndrome is suspected, a variety of screening tests are available for initial testing, such as the 24-hour urinary free cortisol assay and the overnight 1 mg dexamethasone suppression test. The most sensitive test is the 24-hour urinary free cortisol level. This test bypasses the endogenous diurnal variation in cortisol secretion in that it measures the amount of cortisol integrated over a 24-hour period. Similar to the metabolic work-up for kidney stones, a 24-hour urine creatinine should be ordered to ensure a complete collection. When two to three collections are obtained, the test has a sensitivity of 95 to 100% and a specificity of 94 to 98%.

<table>
<thead>
<tr>
<th>Etiology and Classification of Cushing’s Syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACTH dependent</td>
</tr>
<tr>
<td>(70%) Cushing’s disease</td>
</tr>
<tr>
<td>(10%) Ectopic ACTH or CRH production</td>
</tr>
<tr>
<td>ACTH independent</td>
</tr>
<tr>
<td>(10%) Adrenal adenoma</td>
</tr>
<tr>
<td>(8%) Adrenal carcinoma</td>
</tr>
<tr>
<td>Other rare etiology</td>
</tr>
<tr>
<td>Exogenous (medication)</td>
</tr>
<tr>
<td>Pseudo-Cushing’s syndrome (major depression or alcoholism)</td>
</tr>
</tbody>
</table>

Value is approximate percentage of etiology based on large reported studies.
Cushing's Syndrome

Patient with SUSPECTED CUSHING'S SYNDROME

A Impetus for work-up

B 24-hour urine collection (times 3) for cortisol

- Negative
  - No Cushing's syndrome
- Positive
  - Cushing's syndrome
- Equivocal
  - Low-dose dexamethasone Test

C Equivocal

D Plasma ACTH

- Plasma ACTH > 15 pg/mL
  - ACTH-dependent Cushing's syndrome
  - High-dose dexamethasone test
    - Relative decrease in plasma or urine cortisol
      - Pituitary tumor (Cushing's disease)
    - No decrease in plasma or urine cortisol
      - Ectopic ACTH production

- Plasma ACTH 5–15 pg/mL is equivocal but usually indicates ACTH dependence
  - ACTH-independent Cushing's syndrome

- Plasma ACTH < 15 pg/mL or undetectable
  - Suspect adrenal tumor or hyperplasia

E High-dose dexamethasone test

F Adrenal tumor confirmed

G Pseudo-Cushing's or no Cushing's syndrome

H Pituitary imaging

- Transsphenoidal surgery

I Treat primary lesion appropriately

J MRI or CT scan of adrenal glands

K Surgical removal
C Dexamethasone serves as a substitute for endogenous cortisol in suppressing secretion of ACTH. Although this test may be used for the initial screening of Cushing’s syndrome, it plays a more important role in ruling out pseudo-Cushing’s syndrome in patients with marginally elevated urinary cortisol. Cushing’s syndrome may be mistakenly diagnosed in patients with obesity, severe depression, or alcoholism. Usually 1 mg of dexamethasone is given at 11:00 pm or midnight and the plasma cortisol is measured the following morning at 8:00.

D To differentiate ACTH-dependent and -independent Cushing’s syndrome, measure the plasma ACTH by the very sensitive radioimmunoassay at 9:00 am on two separate occasions. If the ACTH is undetectable, the result is ACTH independent; if the ACTH is detectable, the etiology is ACTH dependent.

E The high-dose dexamethasone suppression test (2 days of 2 mg every 6 hours for a total of eight doses) allows for the differentiation of Cushing’s disease from that of ectopic ACTH production. With Cushing’s disease, a relative decrease in plasma and urinary cortisol is seen after the high-dose dexamethasone suppression test. Conversely, with ectopic ACTH production, complete resistance to such a decrease in plasma and urinary cortisol is usually seen. When the suppression of the urinary free cortisol is less than 10% of baseline, the test has a sensitivity of 70% and a specificity of 100%. Where such differentiation is still not clear, one can perform the metyrapone stimulation test or the more invasive/direct petrosal venous sinus catheterization measurement of ACTH.

F When ACTH-independent Cushing’s syndrome is suspected, the adrenal mass should be seen on computed tomography (CT) or magnetic resonance imaging (MRI). The discovery of an adrenal tumor usually leads to surgical removal. This is unilateral in the case of adrenal adenoma or carcinoma and bilateral in the case of micronodular or macronodular hyperplasia. At major medical centers, laparoscopic adrenalectomy is now the treatment of choice.

G When Cushing’s disease is suspected, obtain a CT or MRI of the pituitary gland. Given the small size of pituitary ACTH-secreting tumors, approximately 50% of pituitary tumors are identified by such imaging. This highlights the significance of hormonal diagnosis. MRI is more sensitive for pituitary imaging, whereas CT scan allows better visualization of the bony structures. An approximately 85% cure rate is achieved with transsphenoidal surgery. For transsphenoidal surgery failures, irradiation provides cure in most patients.

H When ectopic ACTH production is suspected, obtain a CT or MRI of the chest/abdomen/pelvis. Future radio-labeled scintigraphy studies will allow for improved localization. The differential diagnosis includes carcinoid, thymoma, oat cell carcinoma of the lung, medullary carcinoma of the thyroid, pheochromocytoma, islet cell tumor, and carcinoma of the prostate. Surgical treatment should be directed at the primary tumor. Consider bilateral adrenalectomy in patients...
whose primary tumor cannot be located or in whom carcinoma cannot be cured.

Additional Readings


The normal physiology of the adrenal gland includes the secretion of aldosterone, the principal mineralocorticoid, from the zona glomerulosa. The secretion of aldosterone is primarily regulated by the renin-angiotensin-aldosterone axis. In situations of decreased renal perfusion, renin secretion is increased, which in turn increases the conversion of angiotensinogen to angiotensin I. Angiotensin I is in turn converted to angiotensin II by the angiotensin-converting enzyme (ACE). Angiotensin II acts on the zona glomerulosa cells to increase the production of aldosterone. Ultimately, aldosterone increases renal Na+ reabsorption, leading to an increased extracellular fluid and blood volume (Figure 103-1).

Of unselected patients with hypertension, only 1 to 2% will have primary aldosteronism. However, this is one of the few forms of hypertension that may be curable by surgical correction. First described by Jerome Conn in 1954, aldosterone-producing adrenocortical adenomas (aldosteronomas) tend to be the most common cause of primary aldosteronism. The other major etiology is bilateral hyperplasia (idiopathic hyperplasia) of the zona glomerulosa leading to increased aldosterone production. Primary aldosteronism tends to be more common in women (2.5 times) compared with men and is rare in children. The peak incidence is in the fourth to sixth decade of life. The aldosteronoma itself is benign and usually small (< 3 cm in diameter). Eighty-five percent weigh less than 10 g. Unilateral tumors are more common on the left side.

Although not the focus of this chapter, an understanding of the term “secondary aldosteronism” is important. This term applies where increased renin secretion occurs. The most common cause is renovascular hypertension.
Patient with SUSPECTED PRIMARY ALDOSTERONISM

A. Assess symptoms

B. Serum and urine biochemical analysis

C. Hypokalemia (<3.5 mEq/L)
Kaliuresis (24 hr, >30 mEq/L)
Low plasma renin activity (<1 ng/mL/h)

D. Increased aldosterone/decreased renin ratio > 30

E. Salt loading

F. Localization of tumor with CT or MRI

G. Adrenal vein sampling urinary 18-hydroxycortisol and plasma 18-hydroxycorticosterone

H. Medical treatment

I. Surgical removal of tumor (unilateral adrenalectomy)

Consider other causes:
- Renovascular
- Pheochromocytoma
- Cushing's syndrome
A Clinical features of primary aldosteronism are nonspecific. Although some patients have symptoms related to their hypertension such as headache or blurry vision, others have complaints such as weakness of proximal muscle groups, polyuria, nocturia, polydipsia, and tachycardia. Patients with hypertension should be studied for the presence of primary aldosteronism when spontaneous hypokalemia is present and it is difficult to maintain a normal serum potassium level despite administration of potassium supplementation.

B The biochemical hallmarks of primary aldosteronism include decreased serum K⁺, alkalosis, increased plasma aldosterone, increased urinary aldosterone, and increased urine K⁺. In this regard, 24-hour urine collection and serum biochemical analysis are the screening tests of choice. Prior to performing the above tests, it is important to make sure that patients are off antihypertensive medications that may falsely lead to diagnosis of hypokalemia.

C Hypokalemia, spontaneous or provoked (with salt load), in the setting of metabolic alkalosis provides an important clue. Although normokalemic hyperaldosteronism occurs in about 20%, most patients have a decreased serum level of potassium. Increased urinary excretion of potassium > 30 mEq/L per 24-hour period in the presence of hypokalemia suggests aldosteronism. Plasma renin activity tends to be suppressed in most patients. However, the sodium intake, postural changes, medications used (ACE inhibitors), and water depletion may all affect renin values. The large number of false-positive and false-negative results limits the value of renin activity by itself in screening for primary hyperaldosteronism.

D As neither plasma aldosterone measurements nor plasma renin activity is reliable in defining primary aldosteronism individually, the proposed ratio of aldosterone to renin offers a more sensitive screening test. Ratios > 30 correlate with primary aldosteronism.

E In equivocal cases, the saline infusion test (salt load test) is used. This test consists of intravenous infusion of 2 L of normal saline over 4 hours with the patient in the supine position. It is based on the premise that the patient with primary hyperaldosteronism is in a state of increased Na⁺ retention. Hence, with infusion of additional Na⁺, no suppression of aldosterone should occur. Suppression of serum aldosterone values to < 10 ng/dL is considered a normal response. Non-suppressible production of aldosterone is compatible with the diagnosis of primary aldosteronism (urinary aldosterone > 14 µg/24 h with urinary Na⁺ of at least 250 mEq/24 h).

F Computed tomography scanning with thin sections of 3 mm can detect most aldosteronomas that measure greater than 10 mm. Perform this test only after biochemical confirmation so as to minimize false-positives with incidentally discovered masses. Some cases of bilateral hyperplasia also have macronodular hyperplasia, which could also lead to the false diagnosis of aldosteronoma.

Large adrenal masses (> 3 cm) in a biochemically active proven patient should make one suspicious of adrenal cancer. Magnetic resonance imaging (MRI) currently provides no advantages over CT scanning. MRI may be considered in patients with contrast allergies.

G Adrenal vein sampling is performed in the event of doubt over the laterality of an aldosterone-producing adenoma versus bilateral hyperplasia. Great interventional radiologic expertise is required to sample venous return from the very short adrenal veins. The plasma cortisol concentration is simultaneously measured to ensure an index of success prior to the interpretation of results. In general, the side with an aldosterone-secreting adenoma has four times the aldosterone-to-cortisol ratio compared with the suppressed side. A current adjunctive test to help differentiate between adrenal adenoma and hyperplasia is the measurement of urinary 18-hydroxycortisol and plasma 18-hydroxycorticosterone. Bedside testing shows that elevated values of these two steroids are associated with aldosterone-producing adenoma rather than bilateral hyperplasia.

H Medical management of bilateral hyperplasia primarily consists of treatment with spironolactone, a competitive antagonist of the aldosterone receptor.

I Unilateral aldosterone-producing adenoma requires surgery. More than 90% of patients undergoing surgery will have cure of hypertension or significant improvement. Before surgical intervention, correction of hypokalemia and control of blood pressure are required. Retroperitoneal or transperitoneal laparoscopic adrenalectomy is the current gold standard procedure.
### Additional Readings


The normal physiology of the adrenal gland includes secretion of catecholamines from the adrenal medulla. Preganglionic fibers from the autonomic nervous system synapse directly on chromaffin cells in the adrenal medulla and signal the secretion of epinephrine (80%) and norepinephrine (20%) into the circulation. Pheochromocytomas are tumors that arise from these chromaffin cells. If they are derived from extra-adrenal chromaffin cells, then the term paraganglioma is applied. These tumors can be found from the neck to the base of the pelvis (Figure 104-1).

Pheochromocytoma has been described in all age groups with peak incidence in individuals between the ages of 30 and 50 years. Nearly 90% of these tumors are benign. Ten percent of tumors are bilateral and 10% are diagnosed in children. Ten percent of these tumors are familial, seen in association with multiple endocrine neoplasia (MEN), von Hippel-Lindau disease, and neurofibromatosis. The tumor accounts for 0.1 to 0.5% of patients with hypertension in the United States. Even though it is a rare tumor, missed diagnosis may have dire consequences and can even be fatal. The first successful removals were performed in 1926 by Roux in France and Charles Mayo in the United States.

A Signs and symptoms include hypertension, frontal headache, diaphoresis, palpitation, facial pallor, apprehension, and hyperglycemia. Hypertension, the hallmark clinical finding, is sustained in 50% of patients and paroxysmal in the remainder. Along with hypertension, the triad of headache, tachycardia (palpitations), and diaphoresis is most predictive in the diagnosis of pheochromocytoma. The associated syndrome complexes previously mentioned should be kept in mind. MEN IIA includes medullary thyroid carcinoma, bilateral familial pheochromocytoma, and hyperparathy-
Patient with SUSPECTED PHEOCHROMOCYTOMA

A  Assess symptoms

B  Biochemical diagnosis

C  Provocative test: Glucagon stimulation Clonidine suppression

D  Localization: CT MRI MIBG

E  Surgical removal of tumor

Normal
Equivocal biochemical studies

Normal
Elevated biochemical studies

Seek other causes
Biochemical analysis is currently extremely accurate in diagnosing pheochromocytomas. Most clinicians favor measurement of total urinary catecholamines and metanephrines, along with urinary vanillylmandelic acid (VMA) in 24-hour urine collected samples as the initial screening test. For confirmation, levels of plasma catecholamines (norepinephrine, epinephrine, and dopamine) are obtained (Table 104-1). With the combination of plasma and urine tests, the sensitivity and specificity approach 100%. When these levels are elevated, perform localization studies. It is imperative that the conditions of testing be standardized. This includes but is not limited to time when blood is collected, interference of medications the patient is taking, overnight fasting, and patient position.

Provocative tests currently are rarely required given the accuracy of biochemical tests previously mentioned. In patients with hypertension and borderline elevated values of plasma or urinary catecholamines, provocative testing may be necessary. The glucagon stimulation test (0.5 to 1.0 mg intravenously) causes a pressor response, which may be hazardous in patients with a high basal blood pressure. A threefold increase in plasma catecholamine is diagnostic of pheochromocytoma. With the clonidine suppression test, a 300 μg oral dose of clonidine is given, and blood pressure, plasma epinephrine, and norepinephrine levels are measured. Clonidine, a centrally acting α-agonist, reduces neurogenically mediated catecholamine release (which occurs in neurogenic or essential hypertension). In patients with a pheochromocytoma, the blood pressure is lowered, but the levels of plasma catecholamines are unaltered. In patients with essential hypertension, clonidine will suppress catecholamine release.

Because of the appreciable incidence of bilateral and extra-adrenal tumors, localization studies are required. Computed tomography (CT) scanning is the most popular form of imaging owing to its availability (sensitivity ~95%, specificity ~70%). Magnetic resonance imaging (MRI) is the radiologic study of choice given its near 100% sensitivity (specificity ~70%). On T2-weighted images, the adrenal gland is bright (“light bulb”). Unlike a CT scan, MRI does not require radiation or the administration of intravenous contrast agents. Finally, whole-body iodine-131 (131I)-labeled metaiodobenzylguanidine (MIBG) scans aid in diagnosing adrenal and extra-adrenal and recurrent or metastatic pheochromocytomas (sensitivity ~85%, specificity ~100%).

Optimal preoperative management is critical for surgery. Preoperative management includes medication to normalize blood pressure and expansion of blood volume. Classically, phenoxybenzamine (a nonselective α-adrenergic agent) was given as first-line treatment. More recently, specific α-adrenergic (prazosin) and calcium channel blockers have been used with good result. To avoid the profound hypertension that may result as a consequence of increased peripheral vascular resistance, β-blockers are never used as first-line treatment. As the disease may particularly affect the cardiovascular system, a preoperative cardiology consultation is warranted. Whether open or laparoscopic surgery is performed, the surgeon must try to minimize manipulation of the adrenal gland and attempt to ligate the adrenal vein early during the surgery to reduce catecholamine surges.

Table 104-1 Resting Plasma Catecholamine Levels

<table>
<thead>
<tr>
<th>Plasma Level</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 2,000 pg/dL</td>
<td>Abnormal; confirms pheochromocytoma</td>
</tr>
<tr>
<td>500–2,000 pg/dL</td>
<td>Equivocal; repeat test, measure urinary metabolites, move to pharmacologic testing (glucagon stimulation, clonidine suppression)</td>
</tr>
<tr>
<td>&lt; 500 pg/dL</td>
<td>Normal; rules out pheochromocytoma</td>
</tr>
</tbody>
</table>

Additional Readings


Given the increased use of computed tomography (CT) and magnetic resonance imaging (MRI), incidental adrenal masses are found during nonadrenal abdominal imaging in 0.6 to 5% of patients. In autopsy series, this figure ranges from 1.4 to 5.7%. Most of these “incidentalomas” are non-hypersecreting adrenocortical adenomas and range from 0.5 to 6 cm in size. Even in patients with a predisposition to metastatic disease, such as patients with primary lung carcinoma, the most likely cause of an incidentaloma is an adrenal adenoma. Thus, exploratory operation cannot be advised routinely even in this setting. Although most adenomas are isointense on MRI, and CT scan demonstrates smooth margins, in this size range it is difficult to differentiate adenomas from metastatic lesions because of appreciable overlap. These factors contribute to the high incidence of indeterminate masses. The physician’s major focus is to distinguish benign, malignant, and hypersecreting masses.

A Obtain a detailed history and physical examination. As it is most important to rule out an active hypersecreting adrenal mass, one should focus the history on questions dealing with cortisol hypersecretion, aldosterone hypersecretion, and catecholamine hypersecretion (see Chapters 102, 103, and 104).

B Conduct a screening biochemical work-up. This may include serum potassium, 24-hour urine metanephrines, catecholamines, and free cortisol. Positive results from any of the screening tests or high clinical suspicion based on history and examination requires full evaluation. This style of tailored biochemical evaluation as reviewed by Ross and Aron limits cost without decreasing accuracy.

C Biochemically inactive adrenal tumors may represent adenoma (51%), metastatic cancer (31%), adrenal cancer (4%), cyst (4%), lipoma (2%), neonatal adrenal hemorrhage, idiopathic infections, fibroma, myoma, myelolipoma, hemangioma, lymphangioma, or hamartoma.

D The size of the mass is assessed using CT or MRI. Most accurate estimates are seen with thin cuts of the adrenal gland between 3 and 5 mm. In addition to size, CT scan imaging can yield some information on the etiology of the mass. Usually, adenomas have a noncontrast Hounsfield unit (HU) of < 10 (specificity ~100%). Sophisticated analysis on MRI, called “chemical shift,” demonstrates that signal intensity loss is diagnostic of adrenal adenoma with 96 to 100% accuracy.

E Adrenocortical carcinomas tend to be > 6 cm 90% of the time. Because CT scan may underestimate the size of the lesion, solid lesions > 4 cm should be seriously considered for surgical removal.

F Nonhypersecreting adrenal lesions < 2 cm can be followed. Adrenal carcinoma of this size is exceedingly rare. Follow-up should note any change in size or function.

G The management of solid nonhypersecreting adrenal lesions between 2 and 4 cm is controversial. Because size is an inconsistent discriminator between benign and malignant masses, other factors such as the age of the patient (need for continued imaging/biochemical testing), imaging characteristics, and scintigraphic uptake should be considered. A summary of the literature yields the general information presented on the algorithm. If any doubt exists as to the benign nature of the mass, an adrenalectomy is warranted given the poor survival rate of patients with adrenal cancer. In the case of a known primary extra-adrenal cancer, metastasis may be ruled out by needle biopsy. Needle biopsy for diagnostic purposes for nonmetastatic work-up cannot be recommended at this time because of its high nondiagnostic rate.

Additional Readings
Asymptomatic Adrenal Mass

History
Physical examination

Screening functional studies

Positive:
Full functional evaluation
Work-up according to type of hypersecretion: cortisol, aldosterone, catecholamine
(see Chapters 102, 103, and 104)

Negative

Determine size and characteristics on CT or MRI

< 2 cm
Repeat CT or MRI at 3 mo, 6 mo, 12 mo

Increased size
Repeat functional tests

Stable size
Follow

2–4 cm
Treatment controversial:
Age of patient < 50 yr
Suspicious CT/MRI characteristics
Any increase in size
Discordant/no uptake on scintigraphy

Age of patient > 50 yr
No suspicious CT/MRI characteristics
Concordant/symmetric uptake on scintigraphy

> 4 cm and solid
Surgical removal

Patient with INCIDENTALLY DISCOVERED ADRENAL MASS
The importance of neuroblastoma in the realm of urologic practice derives from its common primary location in the retroperitoneum and adrenal medulla. Neuroblastoma is the most common extracranial solid tumor of childhood, with an incidence rate between 1 in 7,000 and 10,000 in screened populations.\(^1,2\) Accounting for 6 to 10% of all childhood cancers, neuroblastoma generally has poor survival—it accounts for 15% of all childhood cancer deaths.\(^3\) This tumor arises from neuroectodermal cells of the neural crest that ultimately migrate to the adrenal medulla and the sympathetic nervous system.\(^4\) Most (75 to 80%) neuroblastoma tumors are found in the abdomen or pelvis, with the adrenal medulla the most common site of origin. Generally, neuroblastoma is a disease of young children, with the median age of presentation being 22 months. Most of these tumors arise prior to age 4 years because 30% present during the first year of life, and another 50% occur between 1 and 4 years.\(^4,5\)

The natural history of neuroblastoma is variable, with spontaneous regression in some children and rapid growth and metastasis in others. Beckwith and Perrin, who first suggested the pattern of spontaneous regression, found small foci of neuroblastoma cells in the adrenal glands of infants under age 3 months who died of other causes. They estimated that these foci occurred much more frequently than did the incidence of clinically significant neuroblastoma and that spontaneous regression likely occurred in this population.\(^6\) Additional data from a Japanese neuroblastoma screening program also indicate that regression is a significant aspect of the natural history of these tumors in the infant population.\(^7\) Indeed, a later study of the Japanese screening program illustrated that many tumors discovered at a screening program in Japan spontaneously regressed.\(^8\)

Although the Japanese screening program further elucidated the natural history of neuroblastoma, other screening programs have not been as effective clinically. Recent studies from Quebec and Germany have illustrated that routine infant screening for neuroblastoma neither reduced mortality nor reduced the incidence of disseminated disease.\(^9,10\) Support for spontaneous regression of early tumors and for discontinuation of screening programs occurred when Brodeur and colleagues found that tumors detected at screening programs had more favorable biologic characteristics than those found clinically.\(^11\) It is apparent that screening programs do not detect tumors that are likely to become clinically significant later.

The most common sites of primary tumor are in the abdomen; thus, it makes intuitive sense that the most common presentation is that of a hard, lobular, and fixed abdominal mass. These often originate in the flank and extend toward the midline. Other presentations are often secondary to primary tumor location, which can be anywhere along the sympathetic trunk. For example, Horner’s syndrome can be seen with thoracic tumors, whereas a pelvic tumor may cause bowel or bladder dysfunction.\(^1,5\) A high percentage of patients have metastatic disease on presentation, so it is not uncommon for presenting symptoms to relate to these metastatic sites, such as bone or joint pain or skin lesions.

Hypertension is not an unusual presentation for neuroblastoma and is often secondary to catecholamine secretion by the tumor or compression of a renal artery. Other less common presentations include neck masses or spinal cord compression symptoms from a paraspinal tumor extending into the spinal canal. Opsomyoclonus syndrome is a presentation for neuroblastoma in approximately 2% of cases. This syndrome is characterized by rapid, involuntary movements of both the eyes and limbs.\(^1,5\) Another less common presenting symptom is intractable, watery diarrhea, secondary to secretion of vasoactive intestinal polypeptide by the tumor.\(^5,12\)
Neuroblastoma

Patient with SUSPECTED NEUROBLASTOMA

A Incidence, natural history, screening

B Historical or physical findings suggestive of neuroblastoma

C CT/MRI
MIBG scan (where available) and/or Tc bone scan
Urinary VMA/HVA
Bone marrow biopsy/aspiration
Surgical biopsy/excision

D Histologic confirmation of neuroblastoma
Shimada classification
Determination of genetic/biologic markers

E Stage 1
Excision

Stage 2
Excision

Stage 3
Excision

Stage 4
Excision/biopsy

Stage 4 S
Excision/biopsy

F Stage 1
Chemotherapy

Stage 2
Chemotherapy with/without radiation

Stage 3
Chemotherapy with/without radiation

Stage 4
Chemotherapy

G Additional chemotherapy
Bone marrow transplantation
Several staging systems have been proposed for neuroblastoma in the past. A consensus staging system, however, was created in 1986 at an international conference for neuroblastoma. The International Neuroblastoma Staging System (INSS) incorporated aspects of previous staging systems. This system has been updated, and Table 106-1 provides the most recent INSS definitions.

The 1991 International Neuroblastoma Staging System Conference also suggested appropriate patient evaluation. The primary tumor should be evaluated with a computed tomography (CT) or magnetic resonance imaging (MRI) with three-dimensional measurements. In addition, participants at this conference suggested performing metaiodobenzylguanidine (MIBG) scintigraphy with iodine 131 or iodine 123, where available; it is useful in differentiating active residual tumor from scar tissue and may be useful in evaluating for cortical bone involvement. If the MIBG scan is negative for cortical bone involvement, then the clinician should carry out a technetium (Tc) bone scan.

To evaluate bone marrow involvement, marrow aspiration is performed at the posterior iliac crests bilaterally. A single positive aspirate is required to confirm marrow involvement; however, bilateral aspirates should be performed. CT or MRI initially evaluates lymph node involvement. Representative ipsilateral and contralateral (if identifiable) nodes are sampled at the time of surgery. The surgeon should carry out biopsy for any enlarged nodes or presume a positive result if biopsy cannot be performed.

Finally, evaluate tumor markers. Neuroblastomas typically will illustrate elevation of the urinary catecholamine metabolites, vanillylmandelic acid (VMA) and homovanillic acid (HVA). Following surgical resection, these levels should fall to baseline and are therefore useful in tracking tumor recurrence or progression. Other markers include serum ferritin > 143 ng/mL, serum neuron-specific enolase > 200 ng/mL, and lactate dehydrogenase (LDH) > 1,500 U/L, which all indicate a poorer overall prognosis.

Histologically, neuroblastoma tumors illustrate neuroblastic cells, with or without schwannian stromal development. The Shimada classification is a method of determining favorable or unfavorable histology that is based on stromal proliferation, differentiation of the neuroblastic cells, and mitosis-karyorrhexis index in light of the patient’s age.

Several genetic indices illustrate an impact on overall prognosis of a neuroblastoma tumor. Apart from the age of the patient, the INSS stage of the disease, and the histology of the tumor (as determined through the Shimada classification), other genetic factors include the ploidy of the tumor, degree of amplification of the N-myc oncogene, gains of region 17q, and loss of heterozygosity at several loci, including 1p, 11q, and 14q. The relation between these biologic factors and prognosis is summarized in Table 106-2.

The role of surgery in neuroblastoma is both diagnostic and therapeutic. Clearly, surgery is important for proper staging of neuroblastoma tumors in the INSS. Surgical resection may be curative for stage 1 or 2 tumors. Disease-free survival in children with stage 1 tumors is approximately 90% with surgical resection alone. Patients with stage 2A or 2B disease usually require chemotherapy after surgical resection.

In patients with stage 3 disease, surgical resection of the tumor appears to improve overall survival. Several studies have illustrated significant improvement in survival with resection. The role of surgery in stage 4 disease, however, is less clear. It appears that gross total
Resection is associated with survival in these patients, but is not statistically correlated. Yet other studies have indicated that resection does not seem to impact survival in stage 4 disease. Shorter and colleagues illustrated that the survival rate for patients with stage 4 disease who underwent biopsy or complete resection was similar (15% with a 4-year survival), whereas those who underwent incomplete resection had higher survival rates (45% with a 4-year survival). Further study of the cohort found that those in the incomplete resection group had a higher percentage of favorable biologic indices, thereby suggesting that these indices are actually more important than the extent of surgical resection in stage 4 tumors. One study found that induction chemotherapy with cyclophosphamide, doxorubicin, vincristine, VP-16 (etoposide), and cisplatin, plus surgical resection of bulk disease, had good clinical results in patients with stage 4 tumors compared with previous findings.

Surgical complications occur when resecting neuroblastomas, and surgeons must take great care as these tumors often encapsulate important vessels and structures. Major complications have been reported when tumors are closely associated with or invade major structures. Postoperative deaths have been reported from major vascular disruption and hypoglycemia. Similarly, renal failure has been reported after the need for a unilateral nephrectomy secondary to tumor encapsulation. The most frequent complication in the postoperative period is diarrhea, which is thought to be secondary to denervation of the gut after surgery. The difficult nature of neuroblastoma resection, as well as the potential complications secondary to surgery, emphasizes the importance that resection be performed by experienced surgeons.

F Most chemotherapy regimens use cisplatin, doxorubicin, etoposide, and cyclophosphamide. Several studies illustrate that the timing of tumor resection in relation to chemotherapy does not seem to affect survival. One study illustrated, however, that surgical complication rates were significantly higher for prechemotherapy resection in stage 4 patients and higher, albeit not significantly, for prechemotherapy resection in stage 3 patients.

Clinicians have used radiation therapy in intermediate- to high-risk patients. In intermediate-risk patients, radiation therapy, combined with chemotherapy, did show a significant advantage in overall survival (73 vs 41%). Radiotherapy has been used for consolidation in patients with an unresectable tumor. Finally, total body radiation is occasionally used as a precursor to bone marrow transplantation (BMT) in patients with stage 4 disease.

G The use of BMT has recently shown some promise in advanced neuroblastoma. Historically, the long-term survival for patients with stage 4 neuroblastoma was less than 15%. Several initial studies illustrated an increase in survival in individuals with stage 4 tumors after BMT, with 2- to 5-year survival rates between 30 and 50%. A more recent study, however, showed that survival differed significantly among children who underwent BMT and those who had further chemotherapy. After an initial round of intensive chemotherapy, children were randomized into a group undergoing BMT or a group undergoing additional chemotherapy. The BMT group had a 3-year, event-free survival (EFS) of 34%, whereas the chemotherapy group had a 22% 3-year EFS. This study indicates that BMT should be part of the typical regimen for advanced neuroblastoma treatment, although this is not routine treatment everywhere. It should be noted that BMT is not a benign procedure; one study illustrated a 9% mortality rate secondary to BMT in children with advanced neuroblastoma.

Table 106-2 Biological Characteristics and Prognosis

<table>
<thead>
<tr>
<th>Biologic Characteristic</th>
<th>Prognostic Implications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ploidy</td>
<td>Diploid/tetraploid tumors – unfavorable clinical course and decreased survival</td>
</tr>
<tr>
<td></td>
<td>Hyperdiploid/aneuploid tumors – lower-stage tumors with favorable clinical courses</td>
</tr>
<tr>
<td>N-myc oncogene</td>
<td>Amplification – unfavorable prognostic indicator</td>
</tr>
<tr>
<td>17q gain</td>
<td>Increased aggressiveness of tumor, advanced stages, unfavorable clinical course</td>
</tr>
<tr>
<td>LOH 11q</td>
<td>Occurs in approximately 22% – no association with prognosis</td>
</tr>
<tr>
<td>LOH 1p</td>
<td>Advanced stage, decreased survival</td>
</tr>
<tr>
<td>LOH 14q</td>
<td>Occurs in approximately 30% – no association with prognosis</td>
</tr>
<tr>
<td>X chromosome</td>
<td>Deletion (XO) – favors onset of neuroblastic tumors</td>
</tr>
<tr>
<td></td>
<td>Supernumerary X (XXX, etc) – protects against neuroblastic tumors</td>
</tr>
<tr>
<td>Shimada classification</td>
<td>Favorable histology – better prognosis</td>
</tr>
<tr>
<td>Age</td>
<td>Unfavorable histology – worse prognosis</td>
</tr>
<tr>
<td></td>
<td>&lt; 1 year at diagnosis – better prognosis</td>
</tr>
<tr>
<td></td>
<td>&gt; 1 year at diagnosis – worse prognosis</td>
</tr>
</tbody>
</table>
References

The adrenal glands in a normal adult each weigh approximately 5 g. In the newborn, the adrenal glands are relatively large, and each weighs 5 to 10 g. The adrenals play an important role in fetal homeostasis. At birth, the adrenals regress rapidly during the first 6 weeks of life. The large size and vascularity of the neonatal adrenal place it at risk for hemorrhage.

Adrenal hemorrhage occurs most commonly in association with prolonged labor, sepsis, perinatal anoxia, bleeding disorders, hypoprothrombinemia, and bradycardia. Approximately 75% affect the right adrenal, probably because venous engorgement caused by temporary vena caval occlusion or compression is dampened by the renal vein on the left side, whereas the right adrenal vein drains directly into the vena cava. In approximately 10% of patients the condition is bilateral.

A triad of findings is usually present with adrenal hemorrhage: (1) flank mass (more than 85%), (2) jaundice (more than 80%), and (3) mild anemia (approximately 50%). Jaundice is secondary to reabsorption of blood from the retroperitoneum and depends on the degree of hemorrhage and rapidity of reabsorption. Most clinically significant cases become apparent by 1 week of age. Some male babies are diagnosed with a scrotal hematoma. If there is azotemia and gross hematuria, coexistent renal vein thrombosis also should be suspected.

Ultrasonography is the most useful modality for diagnosing adrenal hemorrhage. Typically, there is a well-defined, echo-free adrenal superior to an inferiorly displaced kidney. In some cases there may be internal echoes, depending on the state of liquefaction with the adrenal gland. If clots and necrotic tissue are present, a mixed pattern is encountered. Following complete liquefaction, the mass becomes completely echo free. If there is any question regarding the cause of the mass, a CT scan or MRI of the adrenal should be performed. MRI generally depicts blood within the adrenal gland. Ultrasonography is the best method of following these infants because it demonstrates the progressive decrease in size and resolution of the hemorrhagic area.

Measurement of the 24-hour urinary excretion of vanillylmandelic acid, homovanillic acid, and catecholamines is important because an increase in these substances is virtually diagnostic of neuroblastoma.

The degree of hemorrhage, its localization, and patient signs and symptoms determine the best management. In most cases the hemorrhage is unilateral, self-contained, and self-limited, especially if the hematoma is intracapsular. These babies can be followed by monitoring their blood counts and bilirubin levels. Follow-up ultrasonography is important to be certain that the hematoma regresses. A thin rim of calcification typically develops and often may be seen as early as 2 weeks of age. In contrast, the calcification associated with neuroblastoma typically is stippled throughout the mass.

Bilateral adrenal hemorrhage occurs in 8% of cases. Its management depends on the degree of hemorrhage. Adrenal insufficiency is likely to occur and can develop very early in the course of the disease.

Massive hemorrhage can result in intraperitoneal bleeding and adrenal insufficiency. Operative intervention with evacuation of the hematoma, ligation of bleeding vessels, or adrenalectomy may be necessary. Signs of adrenal insufficiency should be monitored. Massive right adrenal hemorrhage can lead to inferior vena caval occlusion.

**Additional Readings**

Patient with SUSPECTED ADRENAL HEMORRHAGE

A
History
Physical examination

B
Ultrasonography
CT scan

C
Unilateral, limited
Hematocrit, bilirubin
Observe
Follow-up sonogram

D
Bilateral
Limited
Adrenal insufficiency
Electrolyte therapy
Cortisone therapy

E
Unilateral, massive
Massive
Abdominal exploration
Cortisone therapy

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