Urologic Disorders in Infants and Children

PART XXII

Chapter 574

Congenital Anomalies and Dysgenesis of the Kidneys

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EMBRYONIC AND FETAL DEVELOPMENT

The kidney is derived from reciprocal interaction between the ureteral bud and the metanephric blastema. During the fifth week of gestation, the ureteral bud arises from the mesonephric (Wolffian) 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 the 20th week of gestation forms the entire collecting system, including the ureter, renal pelvis, calyces, papillary ducts, and collecting tubules. Signals from the mesenchymal cells induce ureteric bud formation from the Wolffian duct as well as ureteric bud branching. Reciprocal signals from the ureteric bud and, later, from its branching tips induce mesenchymal cells to condense, proliferate, and convert into epithelial cells. Under the inductive influence of the ureteral bud, nephron differentiation begins during the seventh week of gestation.

By the 20th week of gestation, when the collecting system is developed, approximately 30% of the nephrons are present. Nephrogenesis continues at a nearly exponential rate and is complete by the 36th week of gestation. During nephrogenesis, the kidneys ascend to a lumbar site just below the adrenal glands. At least 16 signaling agents have been identified that regulate renal development. Defects in any of the signaling activities could cause a kidney not to form **(renal agenesis)** or to differentiate abnormally **(renal dysgenesis)**. Dysgenesis of the kidney includes **aplasia, dysplasia, hypoplasia,** and certain forms of **renal cystic disease.**

The fetal kidneys play a minor role in the maintenance of fetal salt and water homeostasis. The rate of urine production increases throughout gestation; at term, volumes have been reported to be 50 mL/hr. The glomerular filtration rate is 25 mL/min/1.73 m^2 at term and triples by 3 months postpartum. The increase in the glomerular filtration rate is caused by a reduction in intrarenal vascular resistance and redistribution of intrarenal blood flow to the cortex, where more nephrons are located.

RENAL AGENESIS

Renal agenesis, or absent kidney development, can occur secondary to a defect of the Wolffian duct, ureteric bud, or metanephric blastema. Unilateral renal agenesis has an incidence of 1 in 450-1,000 births. Unilateral renal agenesis often is discovered during the course of an evaluation for other congenital anomalies such as VACTERL association (vertebral defects, anal atresia, congenital heart disease, tracheoesophageal fistula, renal and limb defects; see Chapter 100.1). Its incidence is increased in newborns with a single umbilical artery. In true agenesis, the ureter and the ipsilateral bladder hemitrigone are absent. The contralateral kidney undergoes compensatory hypertrophy to some degree prenatally, but primarily after birth. Approximately 15% of these children have contralateral vesicoureteral reflux, and most males have an ipsilateral absent vas deferens because the Wolffian duct is absent. Because the Wolffian and müllerian ducts are contiguous, müllerian abnormalities in females also are common.

The **Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome** (1 in 4,000 to 1 in 5,000 female births) is a group of associated findings that may include vaginal aplasia, uterine maldevelopment, and normal ovaries. Two types are described. In **type I**, only müllerian aplasia occurs, whereas in **type II**, there are associated anomalies, most commonly unilateral renal agenesis, or a horseshoe kidney, with skeletal anomalies present in 10% (see Chapter 591). **Zinner syndrome** is considered the male counterpart of MRKH syndrome (Fig. 574.1). In this condition, males with unilateral renal agenesis (or a regressed **multicystic dysplastic kidney** [MCDK]) have an ipsilateral seminal vesicle cyst and a possible epididymal cyst and dilated distal ureteral segment. These patients typically present in adolescence. Expectant management is usually followed with interim ultrasonography unless symptoms develop, including hematuria, hematospermia, or dysuria.

Renal agenesis is distinguished from aplasia, in which a nubbin of nonfunctioning tissue is seen capping a normal or abnormal ureter. This distinction may be difficult but usually is clinically insignificant. Unilateral renal agenesis is diagnosed in some patients based on the finding of an absent kidney on ultrasonography or renal scintigraphy (renal scan). Some of these patients were born with a hypoplastic kidney or a MCDK that underwent complete cyst regression. Although the specific diagnosis is not critical, if the finding of an absent kidney is based on an ultrasound, a functional imaging study such as a renal scan should be considered because some of these patients have an ectopic kidney in the pelvis. If there is a normal contralateral kidney, long-term renal function usually remains normal.

Bilateral renal agenesis is incompatible with extrauterine life and produces **Potter syndrome.** Death occurs shortly after birth from pulmonary hypoplasia. The newborn has a characteristic facial appearance, termed **Potter facies** (Fig. 574.2). The eyes are widely separated with epicanthal folds, the ears are low set, the nose is broad and compressed flat, the chin is receding, and there are limb anomalies. Bilateral renal agenesis should be suspected when maternal ultrasonography demonstrates **oligohydramnios,** nonvisualization of the bladder, and absent kidneys. The incidence of this

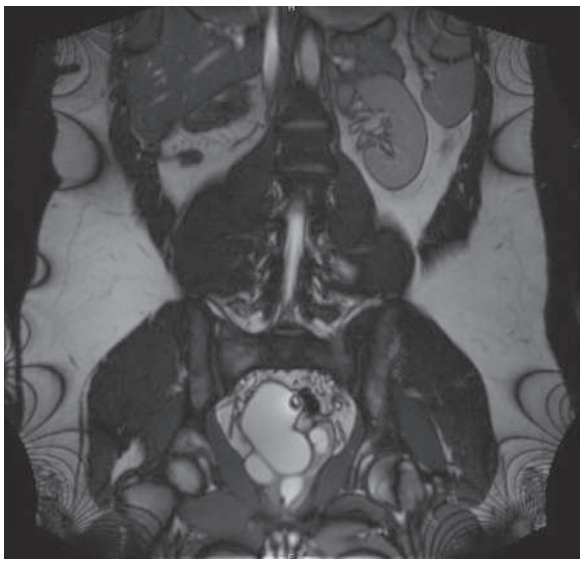

Fig. 574.1 Zinner syndrome. A 17-yr-old male with regressed right multicystic dysplastic kidney and dilated ectopic distal ureter draining into seminal vesicle cyst.

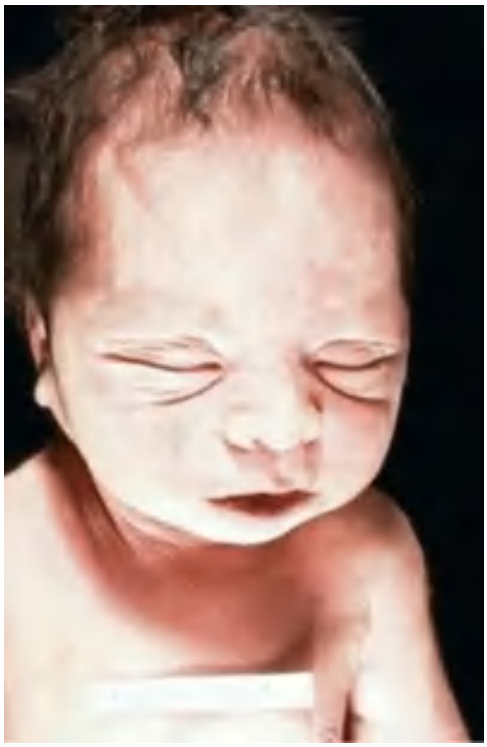

Fig. 574.2 Stillborn infant with renal agenesis exhibiting characteristic Potter facies.

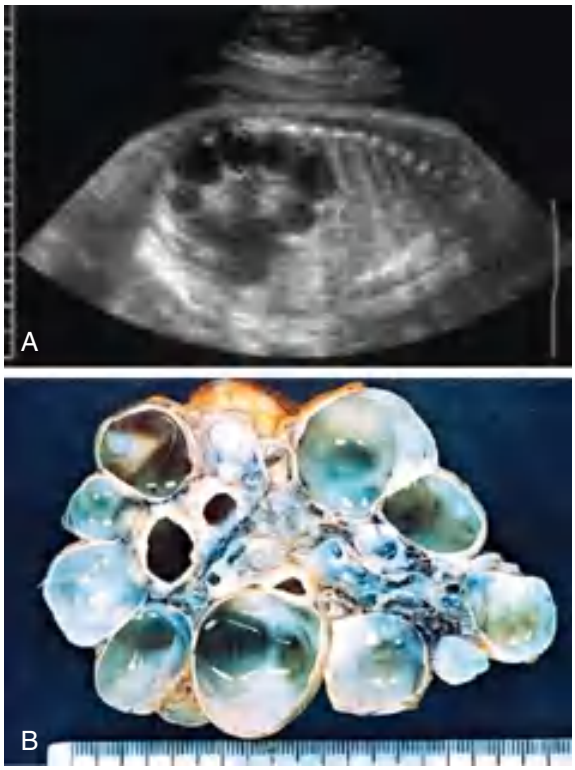

Fig. 574.3 A, Prenatal sonogram demonstrating multicystic dysplastic kidney. B, Surgical specimen.

disorder is 1 in 5,000 births, with a male predominance, and represents 20% of newborns with the Potter phenotype. Other common causes of neonatal renal failure associated with the Potter phenotype include cystic renal dysplasia and obstructive uropathy. Less common causes are autosomal recessive polycystic kidney disease (infantile), renal hypoplasia, and medullary dysplasia. Neonates with bilateral renal agenesis die of pulmonary insufficiency from pulmonary hypoplasia rather than renal failure (see Chapter 444).

The term **familial renal adysplasia** describes families in which renal agenesis, renal dysplasia, multicystic kidney (dysplasia), or a combination occurs in a single family. This disorder has an autosomal dominant inheritance pattern with a penetrance of 50–90% and variable expression. Because of this association, many clinicians advise screening first-degree relatives of persons who have renal agenesis or dysplasia.

The American Academy of Pediatrics recommends that children with a single kidney or single functioning kidney be allowed to play most sports. In fact, sports are less likely to cause kidney injury than motor vehicle crashes, horseback riding, or bicycle accidents. Children with one kidney are not at higher risk for renal injury during contact sports. Despite this, families should be made aware of the potential complications of injury to the patient's single kidney including potential need for dialysis or a renal transplant. Protective padding may be worn during sports, but there is no evidence that this prevents renal injury.

RENAL DYSGENESIS: DYSPLASIA, HYPOPLASIA, AND CYSTIC ANOMALIES

Renal dysgenesis refers to maldevelopment of the kidney that affects its size, shape, or structure. The three principal types of dysgeneses are dysplastic, hypoplastic, and cystic. Although dysplasia always is accompanied by a decreased number of nephrons (hypoplasia), the converse is not true: hypoplasia can occur in isolation. When both conditions are present, the term **hypodysplasia** is preferred. The term **dysplasia** is technically a histologic diagnosis and refers to focal, diffuse, or segmentally arranged primitive structures, specifically primitive ductal structures, resulting from abnormal metanephric differentiation. Nonrenal elements, such as cartilage, may also be present. The condition can affect all or only part of the kidney. If cysts are present, the condition is termed **cystic dysplasia.** If the entire kidney is dysplastic with a preponderance of cysts, the kidney is referred to as a **MCDK** (Fig. 574.3).

The pathogenesis of dysplasia is multifactorial. The "bud" theory proposes that if the ureteral bud arises in an abnormal location, such as an ectopic ureter, there is abnormal penetration and induction of the metanephric blastema, which causes abnormal kidney differentiation, resulting in dysplasia. Renal dysplasia also can occur with severe obstructive uropathy early in gestation, as with the most severe cases of posterior urethral valves or in a MCDK, in which a portion of the ureter is absent or atretic.

MCDK is a congenital condition in which the kidney is replaced by cysts and does not function; it can result from ureteral atresia. Kidney size is highly variable. The incidence is approximately 1 in 2,000. Some clinicians incorrectly use the terms *multicystic kidney* and *polycystic kidney* interchangeably. However, polycystic kidney disease is an inherited disorder that may be autosomal recessive or autosomal dominant and affects both kidneys (see Chapter 563). MCDK usually is unilateral and generally is not inherited. Bilateral MCDKs are incompatible with life.

MCDK is the most common cause of an abdominal mass in the newborn, but the vast majority are nonpalpable at birth. In most cases, it is discovered incidentally during prenatal ultrasound. In some patients, the cysts are identified prenatally, but the cysts regress in utero, and no kidney is identified on imaging at birth. Contralateral hydronephrosis is present in 5–10% of patients. Sonography shows the characteristic appearance of a kidney replaced by multiple cysts of varying sizes that do not communicate, and no identifiable parenchyma is present. In some patients, usually males, a small nonobstructing ureterocele is present in the bladder (see Chapter 577). Although 15% have contralateral vesicoureteral reflux, it is

usually low grade, and obtaining a voiding cystourethrogram is unnecessary unless there is significant contralateral hydronephrosis or the child develops an upper urinary tract infection. *Management is controversial.* Complete cyst regression occurs in nearly half of MCDKs by age 7 years. The risk of associated hypertension is 0.2–1.2%, and the risk of Wilms tumor arising from a MCDK is approximately 1 in 1,200. Because neoplasms arise from the stromal rather than the cystic component, even if the cysts regress completely, the likelihood that the kidney could develop a neoplasm is not altered.

Because of the occult nature of these potential problems, many clinicians advise follow-up with ultrasound and blood pressure measurement every 6 months to a year. The most important aspect of follow-up is being certain that the solitary kidney is functioning normally. *If there is an abdominal mass, the cysts enlarge, the stromal core increases in size, or hypertension develops, nephrectomy is recommended.* In lieu of follow-up screening, laparoscopic nephrectomy may be performed.

Renal hypoplasia refers to a small nondysplastic kidney that has fewer than the normal number of calyces and nephrons. The term encompasses a group of conditions with an abnormally small kidney and should be distinguished from aplasia, in which the kidney is rudimentary. If the condition is unilateral, the diagnosis usually is made incidentally during evaluation for another urinary tract problem or hypertension. Bilateral hypoplasia usually manifests with signs and symptoms of chronic renal failure and is a leading cause of end-stage renal disease during the first decade of life. A history of polyuria and polydipsia is common. Urinalysis results may be normal. In a rare form of bilateral hypoplasia called **oligomeganephronia,** the number of nephrons is markedly reduced, and those present are markedly hypertrophied.

The **Ask-Upmark kidney,** also termed **segmental hypoplasia,** refers to small kidneys, usually weighing less than 35 g, with one or more deep grooves on the lateral convexity, underneath which the parenchyma consists of tubules resembling those in the thyroid gland. It is unclear whether the lesion is congenital or acquired. Most patients are 10 years or older at diagnosis and have severe hypertension. *Nephrectomy usually controls the hypertension.*

Table 574.1 Cystic Diseases of the Kidney

INHERITABLE
Autosomal recessive (infantile) polycystic kidney disease (ARPKD)
Autosomal dominant (adult) polycystic kidney disease (ADPKD)
Juvenile nephronophthisis and medullary cystic disease complex
Juvenile nephronophthisis (autosomal recessive)
Medullary cystic disease (autosomal dominant)
Congenital nephrosis (familial nephrotic syndrome) (autosomal recessive)
Familial hypoplastic glomerulocystic disease (autosomal dominant)
Multiple malformation syndromes with renal cysts (e.g., tuberous sclerosis, von Hippel-Lindau disease)
Glomerulocystic kidney disease
Familial
Meckel-Gruber syndrome
Tuberous sclerosis
Zellweger syndrome
Trisomy 13
Jeune syndrome
Lissencephaly
Nephronophthisis
Orofacialdigital syndrome
NONHERITABLE
Multicystic kidney (multicystic dysplastic kidney)
Benign multilocular cyst (cystic nephroma)
Simple cysts
Medullary sponge kidney
Sporadic glomerulocystic kidney disease
Acquired renal cystic disease
Calyceal diverticulum (pyelogenic cyst)

Modified from Glassberg KI, Stephens FD, Lebowitz RL, et al. Renal dysgenesis and cystic disease of the kidney: a Report of the Committee on Terminology, Nomenclature and Classification, Section on Urology, American Academy of Pediatrics. *J Urol.* 1987;138:1085–1092. Table 2.

RENAL CYSTS IN CHILDREN

Although rare, there are many renal cystic disorders in children (Table 574.1). The most common is the **simple renal cyst** with a mean incidence of 0.22%. They are usually discovered incidentally during urinary tract imaging. Most are small and asymptomatic and do not require treatment, although follow-up imaging is recommended. If there are septations, irregular margins, calcifications, or a cluster of cysts, further evaluation may be indicated. The **Bosniak classification** of simple and complex renal cysts places various cystic lesions into four risk categories and helps guide a decision on whether removal of a lesion is necessary. A **calyceal diverticulum** is an outpouching of the collecting system into the corticomedullary region of the kidney, and it usually arises from the fornix of a calyx, usually in the upper or lower pole. Typically, the infundibulum between the diverticulum and renal pelvis is narrow. Occasionally, calculi form within the lesion, or it causes symptoms of flank pain, necessitating removal of the diverticulum.

A **multilocular cyst (multilocular cystic nephroma)** is a lesion in the kidney that falls in a spectrum of diseases, along with multilocular cyst with partially differentiated Wilms tumor, multilocular cyst with nodules of Wilms tumor, or cystic Wilms tumor. The multilocular cyst is considered benign and is unrelated to the MCDK. More than 95% occur in children <4 years, and most are discovered during evaluation for an abdominal or flank mass. The lesion should be removed.

ANOMALIES IN SHAPE AND POSITION

During renal development, the kidneys normally ascend from the pelvis into their normal position within the retroperitoneum. The normal process of ascent and rotation of the kidney may be incomplete,

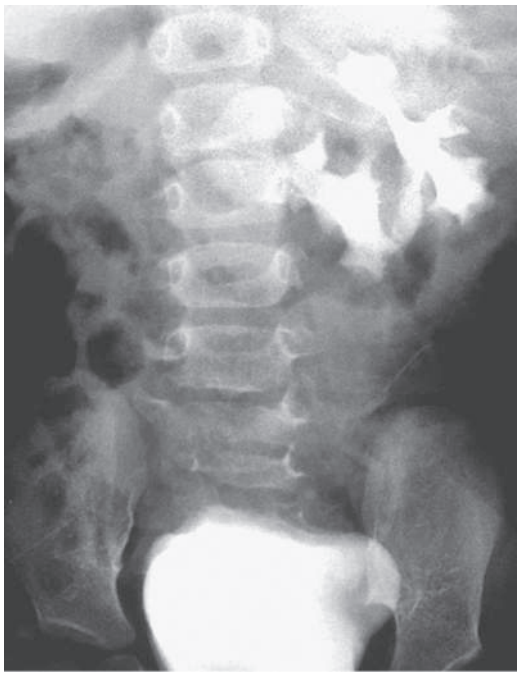

Fig. 574.4 Crossed renal ectopia. Intravenous urography shows both renal collecting systems to the left of the spine. Segmentation anomalies of the sacrum, which are subtle in this child, are one of the skeletal anomalies associated with renal ectopia. *(From Slovis T, ed. Caffey's Pediatric Diagnostic Imaging, 11th ed. Philadelphia: Elsevier; 2008. Fig. 145-23A, p. 2244.)*

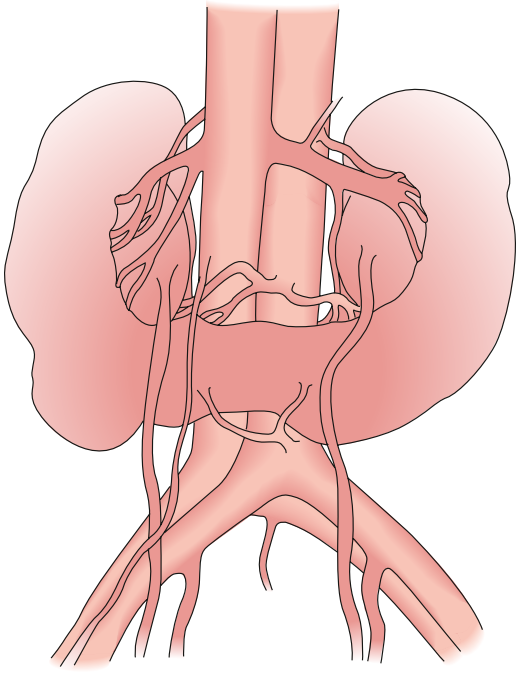

Fig. 574.5 Horseshoe kidney.

resulting in renal ectopia or malrotation. The ectopic kidney may be in a pelvic, iliac, thoracic, or contralateral position. Ectopia may be bilateral; the kidneys fuse in 90% of these cases. The incidence of renal ectopia is approximately 1 in 900 (Fig. 574.4).

Renal fusion anomalies are more common. The lower poles of the kidneys can fuse in the midline, resulting in a horseshoe kidney (Fig. 574.5); the fused portion is termed the *isthmus* and may be thick functioning parenchyma or a thin fibrous strand. Horseshoe kidneys occur in 1 in 400-500 births and are seen in 14–20% of patients with Turner syndrome (see Chapter 626); horseshoe kidneys are also associated with VACTERL and caudal regression syndromes, as well as trisomies 18 and 21. Wilms tumors are four times more common in children with horseshoe kidneys than in the general population. Stone disease, hydronephrosis secondary to ureteropelvic junction obstruction, and vesicoureteral reflux are other potential complications. The incidence of MCDK affecting one of the two sides of a horseshoe kidney also is increased. With crossed fused ectopia, one kidney crosses over to the other side, and the parenchyma of the two kidneys is fused. Renal function usually is normal. Most commonly, the left kidney crosses over and fuses with the lower pole of the right kidney. The insertion of the ureter to the bladder does not change, and the adrenal glands remain in their normal positions. The clinical significance of this anomaly is that if renal surgery is necessary, the blood supply is variable and can make partial nephrectomy more difficult.

ASSOCIATED PHYSICAL FINDINGS

Upper urinary tract anomalies are more common in children with certain physical findings. The incidence of renal anomalies is increased if there is a single umbilical artery and an abnormality of another organ system (e.g., congenital heart disease). External ear anomalies, imperforate anus, and scoliosis are also associated with renal anomalies. Infants with these physical findings should undergo a renal ultrasound.

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Chapter 575

Urinary Tract Infections

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PREVALENCE AND ETIOLOGY

Urinary tract infections (UTIs) commonly occur in children of all ages, though the prevalence varies with age. UTIs are most common in children under 1 year of age. The prevalence in *febrile* infants and children less than 24 months is 7%, and the prevalence in older children less than 19 years presenting with urinary symptoms and/or fever is 8%. During the first 3 months of life, UTIs are most common in uncircumcised febrile males with a prevalence of 20%, which is eight times higher than circumcised males and 2-3 times higher than females. After 6 months of age, UTIs are much more likely in females, with peaks during infancy, toilet training, and onset of sexual activity.

UTIs are caused primarily by colonic bacteria. *Escherichia coli* (see Chapter 246) causes the majority of UTIs, followed by *Klebsiella* spp. and *Proteus* spp., *Enterococcus,* and *Pseudomonas* (see Chapter 148). Other bacteria known to cause UTIs include *Staphylococcus saprophyticus,* group B streptococcus, and, less commonly, *Staphylococcus aureus, Candida* spp., and *Salmonella* spp.

CLINICAL MANIFESTATIONS AND CLASSIFICATION

The two basic forms of UTIs are **pyelonephritis** and **cystitis.** Focal pyelonephritis (lobar nephronia) and renal abscesses are less common.

Pyelonephritis

Pyelonephritis is characterized by any or all of the following: abdominal, back, or flank pain; fever; malaise; nausea; vomiting; and, occasionally, diarrhea. *Fever may be the only manifestation, especially in young children; particular consideration should occur for a temperature ≥39°C (102.2°F) without another source lasting more than 48 hours in infants*. Newborns can also show nonspecific symptoms, such as poor feeding, irritability, jaundice, or weight loss. Pyelonephritis is the most common bacterial infection in infants younger than 24 months of age who have fever without an obvious focus (see Chapters 220 and 221). Involvement of the renal parenchyma is termed acute pyelonephritis (Figs. 575.1 and 575.2), whereas if there is no parenchymal involvement, the condition may be termed **pyelitis**. Acute pyelonephritis can result in renal injury, termed **pyelonephritic scarring**.

Acute lobar nephronia (acute focal bacterial nephritis) is a localized renal parenchymal mass caused by acute focal infection without liquefaction; it more commonly occurs in older children. It may be an early stage in the development of a renal abscess (Fig. 575.3). Manifestations are identical to those of pyelonephritis and include fever and flank pain. The epidemiology of the causative organism is also similar to that of pyelonephritis. **Renal abscess** can occur following a pyelonephritic infection caused by the usual uropathogens or less commonly following hematogenous spread with *S. aureus.* Most abscesses are unilateral and right-sided and can affect children of all ages (Fig. 575.4). Both acute lobar nephronia and renal abscess are associated with an increased risk of renal scarring. **Perinephric abscess** can occur secondary to contiguous infection in the perirenal area (e.g., vertebral osteomyelitis, psoas abscess) or pyelonephritis that dissects to the renal capsule. It differs from renal abscess in that it is diffuse throughout the capsule and is not walled off, although it can develop septations. As with renal abscesses, the most common organisms are *S. aureus* and *E. coli.* A perinephric abscess may not communicate with the collecting system, and, thus, abnormal findings may not be seen on urinalysis or culture.

Xanthogranulomatous pyelonephritis is a rare type of chronic renal infection characterized by granulomatous inflammation with

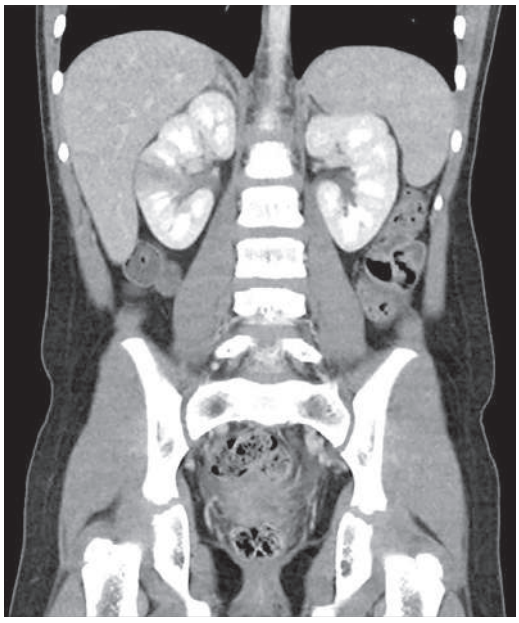

Fig. 575.1 Acute pyelonephritis seen as an area of decreased perfusion by CT scan done for abdominal pain and fever in a child who subsequently was shown to have no reflux by VCUG.

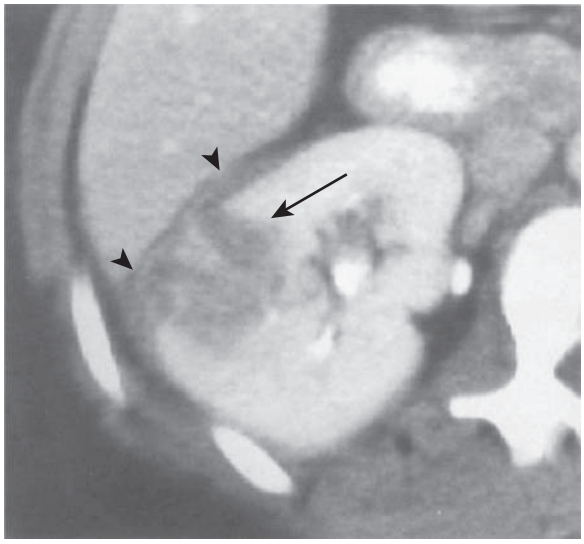

Fig. 575.2 Acute pyelonephritis with focal mass formation. The kidney shows a rounded heterogeneous mass *(arrow)* with a poorly defined margin. Inflammatory changes in the adjacent perinephric fat and renal fascial thickening *(arrowheads)* are also present. *(From Haaga JR, Boll DT, eds. CT and MRI of the Whole Body, 6th ed. Philadelphia: Elsevier; 2017. Fig. 54-131, p. 1833.)*

giant cells and foamy histiocytes. It can manifest clinically with a renal mass and nonspecific symptoms including fever, flank pain, weight loss, and malaise. Dysuria and other urinary symptoms are less common. Renal calculi, obstruction, and infection with *Proteus* spp. or *E. coli* contribute to the development of this lesion, which usually requires total or partial nephrectomy.

Alkaline encrusted pyelitis/cystitis is a rare chronic obstruction UTI caused by *Corynebacterium urealyticum*. The organism creates an alkaline urine (converting urea to ammonia), precipitating struvite and calcium phosphate resulting in stone formation and pyuria with

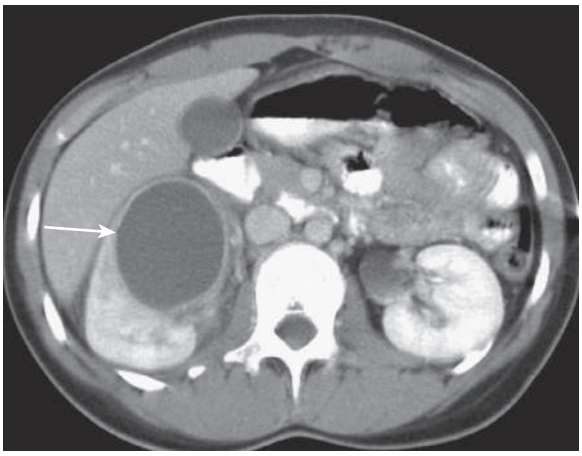

Fig. 575.3 Right renal abscess *(arrow)* shows a thick wall and low density (30 HU). Inflammatory stranding is present in the perinephric fat. *(From Haaga JR, Boll DT, eds. CT and MRI of the Whole Body, 6th ed. Philadelphia: Elsevier; 2017. Fig. 55.3, p. 1834.)*

hematuria. Risk factors include urinary tract instrumentation, congenital uropathies/anomalies, chronic illness, and immune suppression.

Cystitis

Cystitis indicates that there is only bladder involvement; symptoms include dysuria, urgency, frequency, suprapubic pain, incontinence, and possibly malodorous urine. Cystitis does not cause high fever and does not result in renal injury. Malodorous urine is suggestive but not specific for a UTI.

Acute hemorrhagic cystitis, though uncommon in immunocompetent children, is often caused by *E. coli;* it also has been attributed to adenovirus types 11 and 21. It is self-limiting, with hematuria lasting approximately 4 days. Patients receiving immunosuppressive therapy (e.g., solid-organ or bone marrow transplantation) are at higher risk for hemorrhagic cystitis; adenoviruses and polyomaviruses (i.e., JC virus and BK virus) are important causes in immunocompromised populations (see Chapter 321). Other rare types of cystitis that may be confused with infection include *eosinophilic cystitis* or *interstitial cystitis.* Eosinophilic cystitis may present with hematuria, whereas interstitial cystitis may present with irritative voiding symptoms but a negative urine culture.

PATHOGENESIS AND PATHOLOGY

Nearly all UTIs are ascending infections. The bacteria arise from the fecal flora, colonize the perineum, and enter the bladder via the urethra. In uncircumcised males, the bacterial pathogens arise from the flora beneath the prepuce. In some cases, the bacteria causing cystitis ascend to the kidney to cause pyelonephritis. Rarely, renal infection occurs by hematogenous spread, as in endocarditis or in bacteremic neonates.

If bacteria ascend from the bladder to the kidney, acute pyelonephritis can occur. Normally, the simple and compound papillae in the kidney have an antireflux mechanism that prevents urine in the renal pelvis from entering the collecting tubules. However, some compound papillae, typically in the upper and lower poles of the kidney, allow intrarenal reflux. Infected urine stimulates an immunologic and inflammatory response that can cause renal injury and scarring (Figs. 575.5 and 575.6).

Table 575.1 and Figure 575.7 outline the host risk factors for UTI. Vesicoureteral reflux (VUR) is discussed in Chapter 576. If there is grade III, IV, or V VUR and a febrile UTI, 90% of patients have evidence of acute pyelonephritis on renal scintigraphy or other imaging studies. In females, UTIs often occur at the onset of toilet training because of bowel-bladder dysfunction that occurs at that age. The child is trying to retain urine to stay dry, yet the bladder may have uninhibited contractions forcing urine out. The resulting high-pressure, turbulent urine flow and incomplete bladder emptying both increase

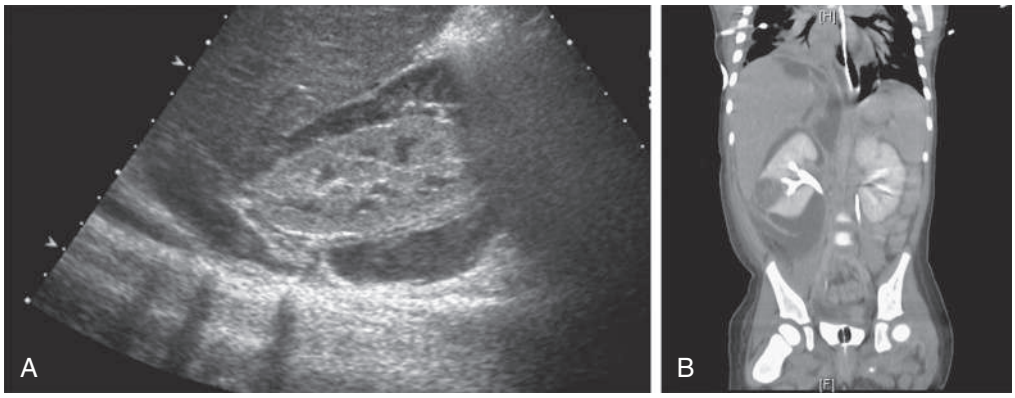

Fig. 575.4 A, Renal sonogram, 19-mo-old infant with perirenal abscess secondary to methicillin-resistant *Staphylococcus aureus*. B, CT scan demonstrates extensive perinephric and focal intrarenal abscess. Patient underwent incision and drainage.

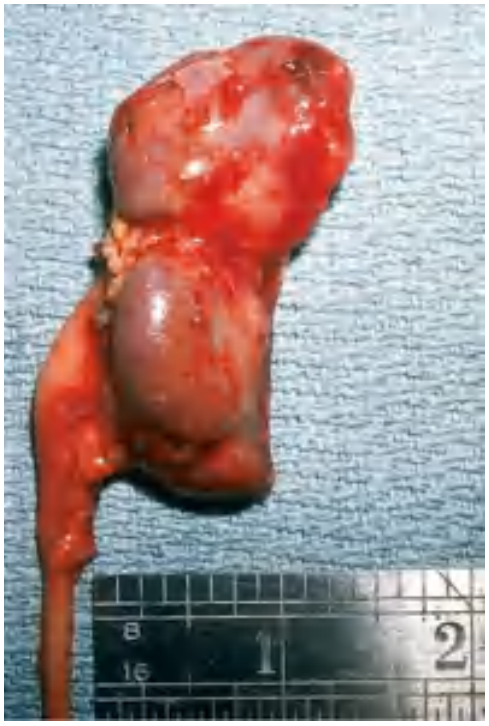

Fig. 575.5 Scarred kidney from recurrent pyelonephritis.

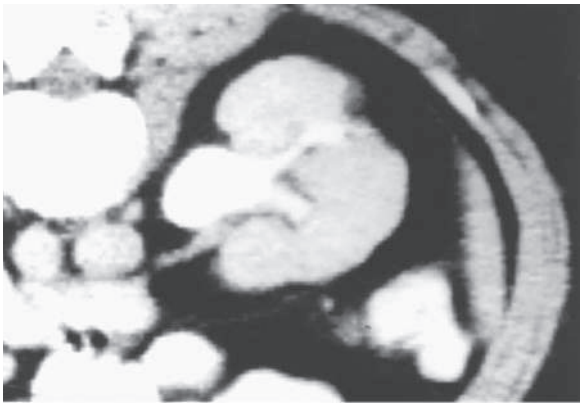

Fig. 575.6 CT scan showing an area of parenchymal thinning corresponding to an underlying calyx, characteristic of pyelonephritic scarring or reflux nephropathy.

Table 575.1 Risk Factors for Urinary Tract Infection

Female anatomy	Obstructive uropathy
Uncircumcised male	Urethral instrumentation
Age ≤1 years	Constipation
Vesicoureteral reflux	Anatomic abnormality (labial adhesion)
Toilet training	Neurogenic bladder
Voiding dysfunction	Sexual activity
Sources of external irritation (such as tight clothing, pinworm infestation)	Pregnancy

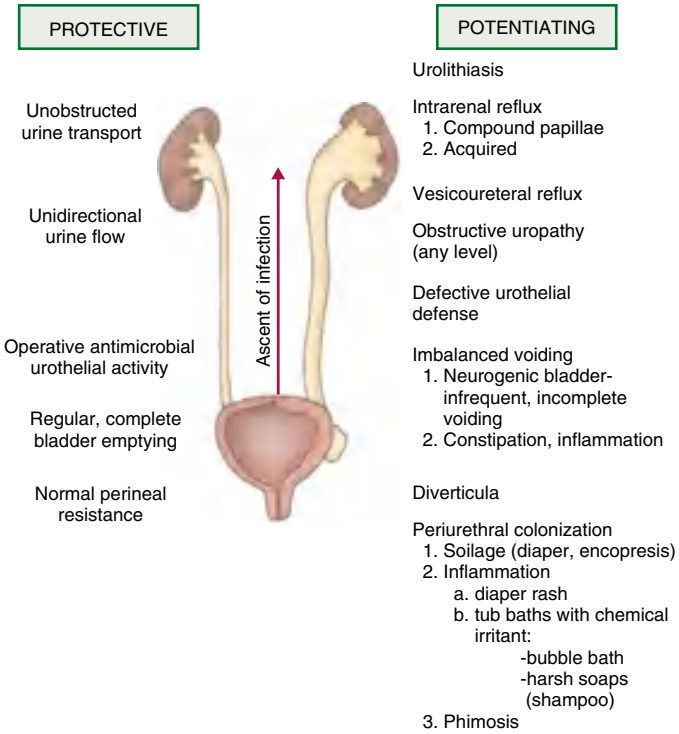

Fig. 575.7 Host factors that protect the urinary tract from infection and abnormalities that potentiate the establishment of invasive bacterial infection. *(From Holcomb III GW, Murphy JP, Ostlie DJ, eds. Holcomb and Ashcraft's Pediatric Surgery, 7th ed. Philadelphia: Elsevier; 2020. Fig. 55-3, p. 855.)*

Table 575.2 Sensitivity and Specificity of Components of Urinalysis, Alone and in Combination

TEST	SENSITIVITY (RANGE) %	SPECIFICITY (RANGE) %
Leukocyte esterase test	83 (67–94)	78 (64–92)
Nitrite test	53 (15–82)	98 (90–100)
Leukocyte esterase or nitrite positive	93 (90–100)	72 (58–91)
Microscopy (white blood cells)	73 (32–100)	81 (45–98)
Microscopy (bacteria)	81 (16–99)	83 (11–100)
Leukocyte esterase test, nitrite, or microscopy positive	99.8 (99–100)	70 (60–92)

From Finnell SM, Carroll AE, Downs SM, Subcommittee on Urinary Tract Infection. Technical report—diagnosis and management of an initial UTI in febrile infants and young children. *Pediatrics.* 2011;128:e749–e770.

the likelihood of bacteriuria. *Bowel-bladder dysfunction* can arise in school-age children who refuse to use the school bathroom, creating a state of urinary retention. Obstructive uropathy resulting in hydronephrosis increases the risk of UTI because of urinary stasis. Constipation with fecal impaction can increase the risk of UTI because it can cause bladder dysfunction.

Other host factors for UTI include anatomic abnormalities precluding normal micturition, such as a labial adhesion. This lesion acts as a barrier and causes vaginal voiding. A neurogenic bladder can predispose to UTI if there is incomplete bladder emptying and/or detrusor-sphincter dyssynergia or a resultant need for frequent catheterization. Sexual activity is associated with UTI in females due to introduction of bacteria near the urinary tract, which can be exacerbated in part because of urethral irritation and incomplete bladder emptying following intercourse.

The pathogenesis of UTI is based in part on the presence of bacterial pili or fimbriae on the bacterial surface, which allow for attachment to the uroepithelial cells. For *E. coli,* this attachment occurs through the type 1 fimbriae and P-fimbriae, which may result in bacterial uptake and replication and formation of intracellular bacterial communities. These intracellular organisms may evade the immune response, form quiescent reservoirs protected from antibiotics, and be a source of recurrent infections. Current research is attempting to prevent the initial attachment of bacteria to the bladder wall that can lead to intracellular bacterial communities and quiescent reservoirs.

DIAGNOSIS

Among children 2-24 months of age, risk factors for UTI include age younger than 12 months, being a female or uncircumcised male, temperature ≥39°C (102.2°F), fever for at least 2 days, and absence of another source of infection. Urine testing is recommended when the pretest probability of a UTI is ≥2%, and an online UTI calculator can provide probability estimates (https://uticalc.pitt.edu/). In older verbal children, urine testing should be considered when there are UTI symptoms. A positive urinalysis suggestive of infection (i.e., presence of pyuria) plus a urine culture with ≥50,000 colony-forming units (CFU)/mL of a single uropathogen are recommended for diagnosis of a UTI in a symptomatic child. In the appropriate clinical context, ≥10,000 CFU/mL may be sufficient for diagnosis, especially if the laboratory does not categorize counts between 10,000 and 100,000 CFU/mL.

There are several ways to obtain a urine sample; some are more accurate than others. In toilet-trained children, a midstream urine sample usually is satisfactory; the introitus should be cleaned before obtaining the specimen. In uncircumcised males, the prepuce must be retracted; if the prepuce is not retractable, a voided sample may be unreliable and contaminated with skin flora. For children 2-24 months who are not toilet trained, a catheterized urine sample should be obtained. Alternatively, the application of an adhesive, sealed, sterile collection bag after disinfection of the skin of the genitals can be useful only if the urinalysis and culture are negative; the negative predictive value for urinalysis from a "bag" specimen is 99%. However, a positive culture can result from skin contamination, particularly in females and uncircumcised males. If treatment is planned immediately after obtaining the urine sample, a bagged specimen *should not* be the method because of a high rate of contamination, often with mixed organisms. A suprapubic aspirate generally is unnecessary.

Inclusion of pyuria in the diagnostic criteria along with a positive urine culture helps to distinguish true UTI from asymptomatic bacteriuria or contamination. **Pyuria** is defined as ≥5 white blood cells (WBCs)/high-power field on a centrifuged specimen, ≥10 WBC/mm^3 on an enhanced urinalysis, or any **leukocyte esterase** on a dipstick. Additional urinalysis findings that support a UTI diagnosis include presence of **nitrites**. Bacteria generally require 4 hours for metabolism of nitrates to nitrites. Thus nitrites may not be detected in cases of UTI where the organism does not convert nitrates to nitrites (most notably *Enterococcus*) or if the child has urinary frequency, where there may not be enough time for the conversion to nitrites. Findings of leukocyte esterase, WBC on microscopy, or nitrites has a high sensitivity for UTI, including in febrile infants <60 days of age (Table 575.2). Microscopic hematuria is common in acute cystitis, but microhematuria alone does not suggest UTI. WBC casts in the urinary sediment suggest renal involvement, but in practice these are rarely seen.

Sterile pyuria (positive leukocytes, negative culture) may occur in partially treated bacterial UTI, viral infections, urolithiasis, renal tuberculosis, renal abscess, UTI in the presence of urinary obstruction, urethritis as a consequence of a sexually transmitted infection (see Chapter 163), inflammation near the ureter or bladder (appendicitis, Crohn disease), Kawasaki disease (see Chapter 493.1), COVID-19–associated multisystem inflammatory syndrome in children (MIS-C; see Chapter 311), schistosomiasis, neoplasm, renal transplant rejection, or interstitial nephritis (eosinophils). Prompt plating of the urine sample for culture is important, because if the urine sits at room temperature for more than 60 minutes, overgrowth of a minor contaminant can suggest a UTI when the urine might not be infected. Refrigeration is a reliable method of storing the urine until it can be cultured.

With acute renal infection, leukocytosis and neutrophilia are noted on the CBC; an elevated ESR, procalcitonin level, and CRP are common. However, these are all nonspecific markers of inflammation; thus their elevation does not prove that the child has acute pyelonephritis, and they do not need to be routinely obtained. Bacteremia in the setting of pyelonephritis is reported to occur in 3–20% of patients and is most common in infants <60 days old (with rates decreasing with increasing age in the first 60 days). For infants <60 days old or ill-appearing patients at presentation, blood cultures should be drawn before starting antibiotics, if possible.

IMAGING FINDINGS

Imaging is not needed to make the diagnosis of UTI. If there is concern about acute lobar nephronia or renal abscess (e.g., patient not responding to appropriate antibiotics), imaging should be considered. Ultrasound is the first-line imaging for screening and will likely demonstrate an enlarged kidney with a possible mass in the case of acute lobar nephronia or renal abscess. CT scan is more sensitive and specific for lobar nephronia and will typically show a wedge-shaped, lower-density area after contrast administration.

TREATMENT

Acute cystitis should be treated promptly to prevent possible progression to pyelonephritis. If the symptoms are severe, and the urinalysis shows pyuria, presumptive treatment should be started while awaiting urine culture results. If the symptoms are mild or the diagnosis is doubtful, treatment can be delayed until the results of culture are known, and the urinalysis and culture can be repeated if the results are uncertain. In **acute febrile UTI**, the clinical symptoms of cystitis and pyelonephritis are difficult to differentiate. Given the presence of systemic symptoms, it is reasonable to consider that the infection has likely progressed to the kidneys and treat for pyelonephritis. A UTI can be treated safely and effectively with oral antibiotics in the outpatient setting, including in younger children. Thus route of therapy should be based on practical considerations. Parenteral therapy should be used in children who are dehydrated, are vomiting, are unable to drink fluids, have complicated infection, or in whom urosepsis is a possibility. Infants less than 1 month of age with suspected febrile UTI are typically hospitalized and started on parenteral antibiotics while awaiting results of a sepsis evaluation and can be converted to oral therapy if there is no concern for meningitis and they are otherwise clinically well. Infants 1-2 months of age can be managed as an outpatient unless hospitalization is indicated for other reasons (e.g., emesis, dehydration). Although infants with bacteremic UTI are often treated with longer parenteral courses, duration of therapy has not been associated with UTI relapse.

Local antimicrobial sensitivity patterns should be considered when selecting empiric antibiotic treatment. For oral treatment, cephalexin is a commonly used narrow-spectrum empiric option, as overall rates of *E. coli* resistance to first-generation cephalosporins are low. In areas with high rates of *E. coli* resistance to first-generation cephalosporins, oral third-generation cephalosporins such as cefixime can be appropriate empiric options and are effective against a variety of gram-negative organisms. Trimethoprim-sulfamethoxazole (TMP-SMX) may also be used, though resistance is increasing in some areas. Nitrofurantoin can be used for cystitis but should not be used routinely in children with a febrile UTI, because it does not achieve significant renal tissue levels. The oral fluoroquinolone ciprofloxacin can be considered for UTI caused by *P. aeruginosa* or resistant microorganisms when there are no other oral antibiotic options. However, clinical treatment with fluoroquinolones in young children should be used with caution because of potential cartilage damage. For parenteral treatment in hospitalized children 1 month and older, ceftriaxone is a reasonable choice until culture results are available to determine whether a narrower-spectrum antibiotic can be used. Ampicillin plus either gentamicin or a third-generation cephalosporin are often used empirically in neonates. If prior urine culture results have grown resistant or atypical organisms, other antibiotic choices may be prudent on a case-by-case basis.

A repeat urine culture after the termination of UTI treatment is not routinely needed. Urine cultures are typically negative within 24 hours of initiation of antibiotic therapy; therefore a urine culture during treatment is almost invariably negative. Most children exhibit clinical improvement (afebrile) within 48-72 hours of antibiotic initiation. Recommended duration of therapy is generally 3-5 days for cystitis and 7-10 days for uncomplicated pyelonephritis. Atypical features include failure to respond within 48-72 hours of appropriate antibiotics; poor urine flow; an abdominal, flank, or suprapubic mass; sepsis; or an elevated creatinine level. Atypical features should prompt further evaluation.

Acute Lobar Nephronia, Renal Abscess, and Perinephric Abscess

Acute lobar nephronia is treated with the same antibiotics as pyelonephritis. The recommended duration of treatment is 14-21 days; one study suggested higher treatment failure in the group treated for shorter duration. Children with a renal or perirenal abscess or with infection in obstructed urinary tracts can require percutaneous or surgical drainage in addition to antibiotic therapy and other supportive measures (see Fig. 575.4). Percutaneous drainage is typically attempted prior to surgical intervention. Medical management alone has been successful in treating small-to-moderate renal abscesses. Although some studies have commented that resolution with antibiotics alone are more likely in abscesses 3 cm or less, some patients with abscesses >3 cm have been managed successfully with IV antibiotics only. Thus a 48-hour trial of IV antibiotics prior to percutaneous drainage may be warranted in otherwise stable children. Few studies address the role of oral antibiotic therapy for renal abscess. Traditionally, patients received 10-14 days of IV antibiotics, followed by 2-4 weeks of oral antibiotic therapy targeted against the known organism (or the likely causes of *E. coli* and *S. aureus* if the organism was unknown). The increasing use of oral antibiotics for other serious infections (e.g., osteomyelitis) suggests that an earlier transition to oral therapy for renal abscess is likely feasible. Kidney loss is reported to occur in 10–20% of cases of renal abscess. Perinephric abscesses may be managed with IV antibiotics alone or with percutaneous drainage if the area is large or causing impaired kidney function. Identification of a causative organism can be an additional advantage of percutaneous drainage of a perinephric abscess because the infection may remain isolated from the collecting system based on the location.

Other Potential Treatment or Prevention Options

There is interest in probiotic therapy as well as cranberry juice to *prevent* UTIs. Studies are ongoing and a probiotic containing a non-uropathogenic *E. coli* called Nissle 1917 is available in Europe and other parts of the world. These bacteria may inhibit growth of other bacteria. Cranberry juice may prevent bacterial adhesion and biofilm formation, hypothesized to be via proanthocyanidin (PAC). Currently there is insufficient evidence regarding the use of these therapies in children to reduce UTIs.

The main consequences of chronic renal damage caused by pyelonephritis are arterial hypertension and end-stage renal insufficiency; when they are found, they should be treated appropriately (see Chapters 494 and 572). Even without chronic renal damage, the consequences of infections include lost days from school and work, uncomfortable symptoms, and exposure to antibiotics that change the healthy microbiome.

IMAGING STUDIES IN CHILDREN WITH A FEBRILE UTI

The primary goal of imaging studies in children with a febrile UTI is to identify anatomic abnormalities that predispose to future infection, such as high-grade VUR, posterior urethral valves, or other obstructive uropathy. Imaging is usually unnecessary in children with afebrile cystitis. Historically, children either underwent a renal sonogram plus a voiding cystourethrogram (VCUG) in a "bottom-up" approach, or a dimercaptosuccinic acid (DMSA) renal scan first to identify areas of acute pyelonephritis (Fig. 575.8) in a "top-down" approach. If the DMSA scan was positive, then a VCUG was performed (Fig. 575.9) because up to 90% of children with dilating reflux have a positive DMSA scan. In the past decade, with increasing evidence that most children with first-time UTI have normal genitourinary tracts and the unclear benefit of early detection of VUR, most national guidelines recommend selective imaging for children with UTI. Though the sensitivity of renal-bladder ultrasounds for detecting VUR is poor, there is no established harm of nondetection of VUR after a first UTI.

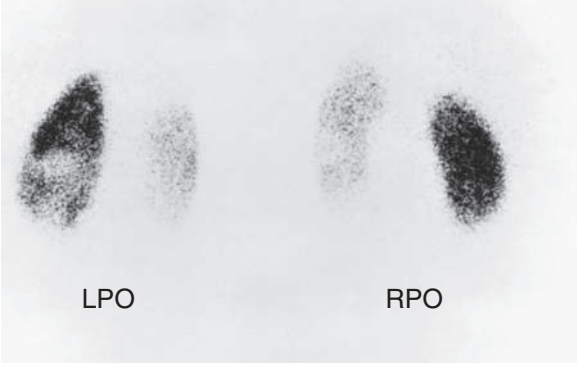

Fig. 575.8 DMSA renal scan showing bilateral photopenic areas indicating acute pyelonephritis and renal scarring. LPO, left posterior oblique; RPO, right posterior oblique.

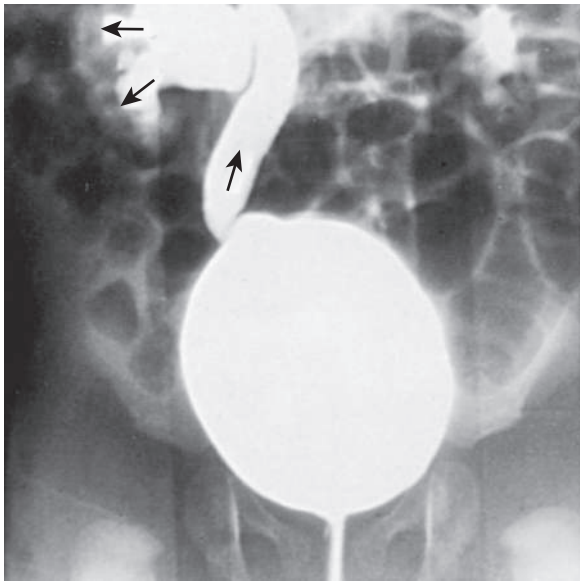

Fig. 575.9 Intrarenal reflux. VCUG in an infant boy with a history of a UTI. Note the right VUR with ureteral dilation, with opacification of the renal parenchyma representing intrarenal reflux.

Most experts still recommend initial ultrasound of the kidneys, ureters, and bladder for children 2-24 months with a first febrile UTI. VCUG should be obtained if the ultrasound study indicates hydronephrosis, scarring, or other findings suggestive of high-grade (e.g., grades IV-V) reflux or obstructive uropathy, or if the patient has other atypical complex features. Further, a VCUG should be obtained if the child has a recurrent febrile UTI (Table 575.3). The rate of renal scarring increases between days 2 and 3 of fever; this makes the prompt evaluation and appropriate treatment of a recurrent UTI important. The risk of scarring also increases with the number of episodes of pyelonephritis and with higher grades of reflux.

The NICE (National Institute for Health and Care Excellence, UK) guidelines for diagnosis, management, and imaging after UTI were released in 2022 (Table 575.4). These recommendations divided children into those younger than 6 months, 6 months to younger than 3 years, and 3 years and older. An initial renal-bladder ultrasound is recommended for all children younger than 6 months, and a VCUG only if atypical features (including non–*E. coli* infection, sepsis or bacteremia, failure to respond to antibiotics within 48 hours), recurrent UTI, or abnormal ultrasound findings. For children age 6 months to younger than 3 years who have a UTI with atypical features or recurrent UTI, an ultrasound is recommended, and if risk factors are present, then also a VCUG should also be obtained (see Table 575.4). No imaging is suggested for otherwise first-time, typical UTI in this age group. When ultrasound is recommended, the optimal timing for obtaining it is unclear. Most national guidelines recommend an ultrasound during the acute infection if there is concern for obstruction (e.g., not responding to antibiotics, elevated creatinine, poor urine flow) but otherwise nonurgently within 2-6 weeks after the UTI as routine ultrasound during the acute infection rarely changes management.

PREVENTION OF RECURRENCES

In a child with recurrent UTIs, identification of predisposing factors is beneficial. Bowel and bladder dysfunction is a very important contributor to recurrent UTIs and is one of the main reasons for an increase in UTIs around the time of toilet training. Bladder dysfunction is manifested by urgency, wetting, and especially "Vincent's curtsy" (children squat on their heels in response to an uninhibited bladder contraction) (see Chapter 580). In toilet-trained children, a thorough history and use of urodynamic studies and measurement of postvoid residual volumes may be helpful in

Table 575.3 Guideline Recommendations for Diagnostic Evaluation Following a Febrile Urinary Tract Infection in Infants

GUIDELINE	ULTRASONOGRAPHY	VCUG	LATE DMSA SCAN
National Institute for Health and Care Excellence (NICE)	See Table 575.4		
American Academy of Pediatrics (retired)	Yes	If abnormal ultrasonogram or febrile recurrence	No
Italian Society for Paediatric Nephrology (ISPN)	Yes	If abnormal ultrasonogram, non-*Escherichia coli* infection, or febrile recurrence	If grade IV-V VUR
Spanish Association of Paediatrics	Yes, if age <6 months, atypical infection,* or recurrence	If abnormal ultrasonogram, atypical infection,* or recurrence	If atypical infection* or recurrence
Swiss consensus recommendations	Yes	If abnormal ultrasonogram, atypical infection,† or febrile recurrence	No

*Defined as fever >48 hours after appropriate antibiotics, sepsis, non–*E. coli* infection, acute kidney injury, or abdominal or vesical mass.
†Defined as failure to respond to appropriate antibiotics within 48 hours, non–*E. coli* infection, increased creatinine, abnormal electrolytes, hypertension, or poor urine flow.
VCUG, Voiding cystourethrogram; DMSA, dimercaptosuccinic acid; VUR, vesicoureteral reflux.

Table 575.4 NICE Recommended Imaging Schedule for Children with Urinary Tract Infection

CHILD AGE AND TESTS	TYPE OF INFECTION		
	RESPONDS WELL TO TREATMENT WITHIN 48 HR	ATYPICAL INFECTION*	RECURRENT INFECTION
CHILDREN YOUNGER THAN 6 MO OLD			
Ultrasound scan during acute infection	No	Yes	Yes
Ultrasound scan within 6 wk of infection	Yes	No	No
DMSA scan 4-6 mo after acute infection	No	Yes	Yes
VCUG	Consider if ultrasound scan abnormal	Yes	Yes
CHILDREN 6 MO TO YOUNGER THAN 3 YR OLD			
Ultrasound scan during acute infection	No	Yes	No
Ultrasound scan within 6 wk of infection	No	No	Yes
DMSA scan 4-6 mo after acute infection	No	Yes	Yes
VCUG	No	Not routine; consider if dilation on ultrasound, poor urine flow, non–*E. coli* infection, or family history of vesicoureteral reflux	
CHILDREN 3 YR OR OLDER			
Ultrasound scan during acute infection	No	Yes	No
Ultrasound scan within 6 wk of infection	No	No	Yes
DMSA scan 4-6 mo after acute infection	No	No	Yes
VCUG	No	No	No

*Defined as seriously ill, poor urine flow, abdominal or bladder mass, raised creatinine, sepsis or bacteriemia, failure to respond to appropriate antibiotics within 48 hours, or infection with non–*E. coli* organisms.

NICE, National Institute for Health and Care Excellence; DMSA, Dimercaptosuccinic acid; VCUG, voiding cystourethrogram.

Adapted from National Institute for Health and Clinical Excellence. Urinary tract infection in children: Diagnosis, treatment, and long-term management. NICE clinical guidelines, no. 224. London: RCOG Press; 2022. Tables 4–6.

identifying children with bladder dysfunction that may contribute to UTI. Tightening the pelvic floor during urination can sometimes be seen on a VCUG as a **spinning-top urethra** (Fig. 575.10). An ultrasound may document residual urine and possibly a thick bladder wall. Urodynamics may show an intermittent stream with increased activity in the pelvic floor muscles. Some children with UTI may also have constipation (see Chapter 378.3). Behavioral modification, with treatment of constipation as described in Chapter 580, often is effective at reducing recurrent UTI from constipation.

Routine use of antibiotic prophylaxis is not recommended for children with a first episode of pyelonephritis and an otherwise anatomically normal urinary tract. Urologic conditions that can cause recurrent UTIs that might benefit from long-term antibiotic prophylaxis include neurogenic bladder, urinary tract stasis and obstruction, severe VUR (see Chapter 576), and urinary calculi. The RIVUR study was a randomized trial of TMP-SMX prophylaxis for patients with a history of UTI and diagnosed grades I-IV VUR. Although the UTI recurrence rate was decreased by half from 30% in the group not receiving prophylaxis to 15% in those receiving prophylaxis, rates of renal scarring were the same in both groups. Additionally, the rates of UTI caused by resistant organisms increased in the group receiving prophylaxis. Although the use of prophylaxis can decrease rates of recurrence, routine prophylaxis is not recommended for children with VUR (especially lower-grade VUR) due to the increase in antibiotic resistance, need for daily medication in children, and lack of change in renal scarring.

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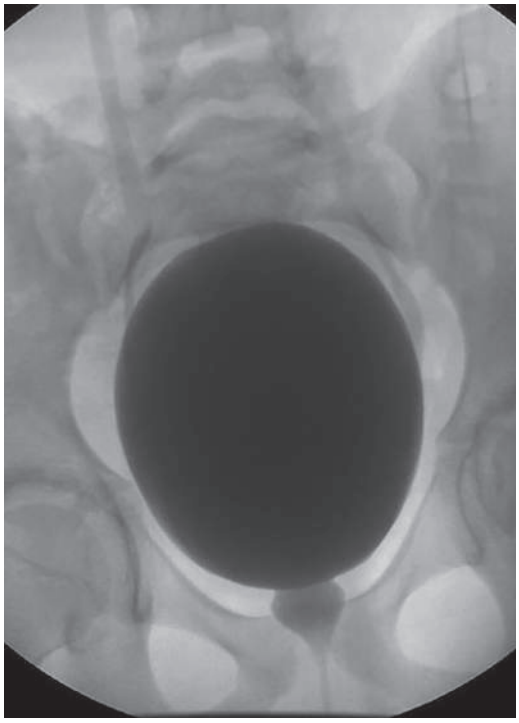

Fig. 575.10 VCUG shows contraction of the pelvic floor and external sphincter during voiding, leading to a dilated posterior urethra and bilateral reflux.

Chapter 576

Vesicoureteral Reflux

Heather N. Di Carlo and Chad B. Crigger

Vesicoureteral reflux (VUR) describes the retrograde flow of urine from the bladder to the ureter and kidney. The ureteral attachment to the bladder normally is oblique, between the bladder mucosa and detrusor muscle, creating a flap-valve mechanism that prevents VUR (Fig. 576.1). VUR occurs when the submucosal tunnel between the mucosa and detrusor muscle is short or absent. Affecting 1–2% of children, VUR usually is congenital and often is familial. VUR is present in approximately 30% of females who had a urinary tract infection and in 5–15% of infants with antenatal hydronephrosis.

VUR predisposes to kidney infection **(pyelonephritis)** by facilitating the transport of bacteria from the bladder to the upper urinary tract (see Chapter 575). The inflammatory reaction caused by pyelonephritis can result in renal injury or scarring, also termed **reflux-related renal injury** or **reflux nephropathy.** In children with a febrile urinary tract infection, those with VUR are three times more likely to develop renal injury compared with those without VUR. Extensive **renal scarring** impairs renal function and can result in renin-mediated hypertension (see Chapter 494), renal insufficiency or end-stage renal disease (see Chapter 572), impaired somatic growth, and morbidity during pregnancy. Scarring associated with reflux may be present at birth or develop in the absence of infection if there is significant bladder-sphincter discoordination during voiding.

In the past, reflux nephropathy accounted for as much as 15–20% of end-stage renal disease in children and young adults. With greater attention to the management of UTIs and a better understanding of VUR, end-stage renal disease secondary to reflux nephropathy is uncommon. Reflux nephropathy remains a common cause of hypertension in children. VUR in the absence of infection or elevated bladder pressure (e.g., neuropathic bladder, posterior urethral valves) rarely causes renal injury.

CLASSIFICATION

VUR severity is graded using the International Reflux Study (IRS) classification of I-V and is based on the appearance of the urinary tract on a contrast **voiding cystourethrogra**m (VCUG) (Figs. 576.2 and 576.3). The higher the VUR grade the greater the likelihood of renal injury. VUR severity is an indirect indication of the degree of abnormality of the ureterovesical junction.

VUR may be primary or secondary (Table 576.1). **Bladder-bowel dysfunction (BBD)** can worsen preexisting VUR if there is a marginally competent ureterovesical junction. In the most severe cases, there is such massive VUR into the upper tracts that the bladder becomes overdistended. This condition, the **megacystis-megaureter syndrome,** occurs primarily in males and may be unilateral or bilateral (Fig. 576.4). Reimplantation of the ureters into the bladder to correct VUR corrects the condition.

Primary VUR appears to be an autosomal dominant inherited trait with variable penetrance. Approximately 35% of siblings of children with VUR also have VUR, and VUR is found in nearly half of newborn siblings. The likelihood of a sibling having VUR is independent of the grade of VUR or sex of the index child. Approximately 12% of asymptomatic siblings with VUR have evidence of renal scarring. In addition, 50% of children born to women with a history of VUR also have VUR. The American Urological Association Vesicoureteral Reflux Guidelines Panel stated that, *in siblings of individuals with VUR, a VCUG or radionuclide cystogram is recommended if there is evidence of a renal cortical abnormality or renal size asymmetry on sonography, or if the sibling has a history of febrile UTI*. Otherwise, screening is optional. VUR may be suggested on a prenatal ultrasound that demonstrates hydronephrosis or hydroureteronephrosis.

Approximately 1 in 125 children has a **duplication** of the upper urinary tract, in which two ureters rather than one drain the kidney. Duplication may be partial or complete. In partial duplication, the

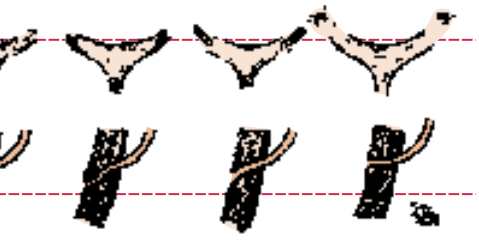

Fig. 576.1 Normal and abnormal configuration of the ureteral orifices. Shown from *left* to *right*, progressive lateral displacement of the ureteral orifices and shortening of the intramural tunnels. *Top*, Endoscopic appearance. *Bottom*, Sagittal view through the intramural ureter.

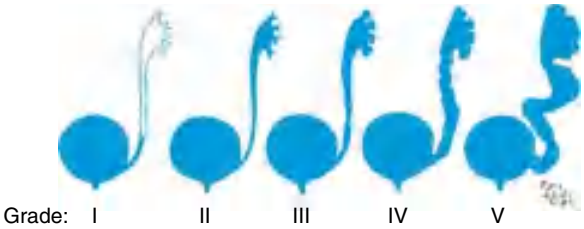

Fig. 576.2 Grading of VUR. Grade I: VUR into a nondilated ureter. Grade II: VUR into the upper collecting system without dilation. Grade III: VUR into a dilated ureter and/or blunting of the calyceal fornices. Grade IV: VUR into a grossly dilated ureter. Grade V: massive VUR, with significant ureteral dilation and tortuosity and loss of the papillary impression.

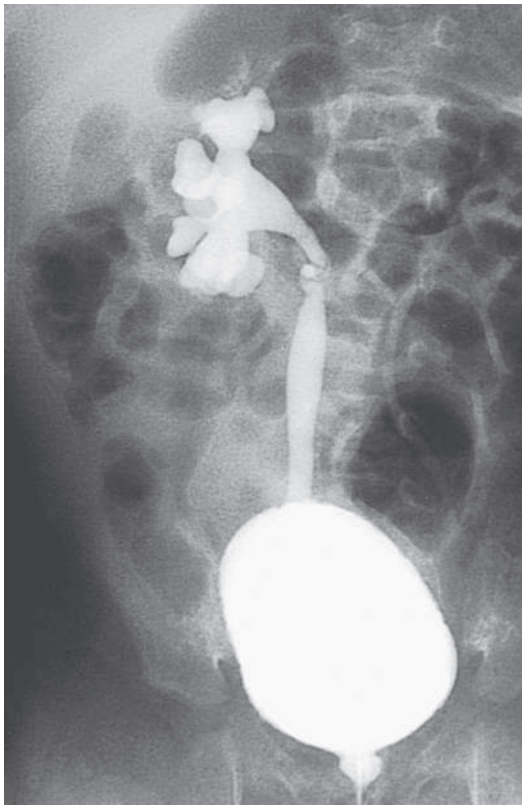

Fig. 576.3 VCUG showing grade IV right VUR.

Table 576.1 Classification of Vesicoureteral Reflux

TYPE	CAUSE
Primary	Congenital incompetence of the valvular mechanism of the vesicoureteral junction
Primary associated with other malformations of the ureterovesical junction	Ureteral duplication Ureterocele with duplication Ureteral ectopia Paraureteral diverticula
Secondary to increased intravesical pressure	Neuropathic bladder Nonneuropathic bladder dysfunction Bladder outlet obstruction
Secondary to inflammatory processes	Severe bacterial cystitis Foreign bodies Vesical calculi Clinical cystitis
Secondary to surgical procedures involving the ureterovesical junction	Surgery

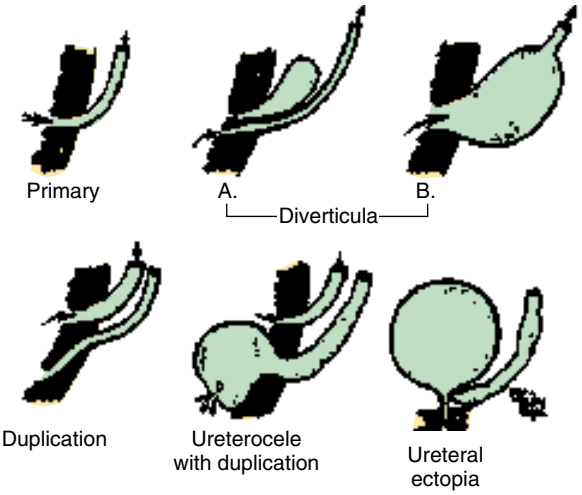

Fig. 576.5 Various anatomic defects of the ureterovesical junction associated with VUR.

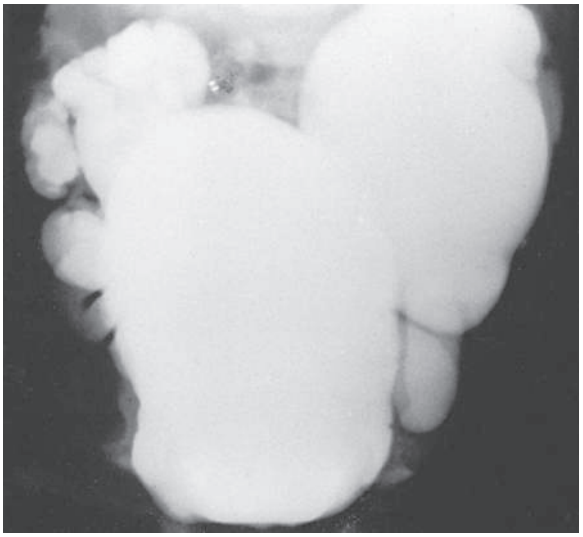

Fig. 576.4 VCUG in a newborn with megacystis-megaureter syndrome. Note the massive ureteral dilation caused by high-grade VUR. The bladder is very distended. There was no urethral obstruction or neuropathic dysfunction.

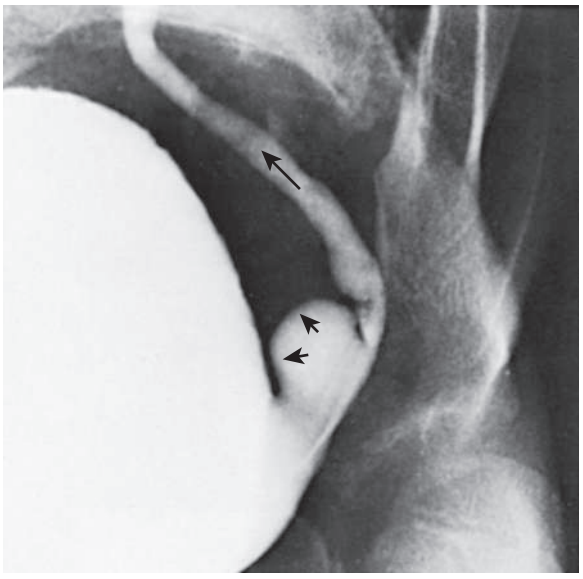

Fig. 576.6 VUR and bladder diverticulum. The VCUG demonstrates left VUR and a paraureteral diverticulum.

ureters join above the bladder, and there is one ureteral orifice. In complete duplication, the attachment of the lower pole ureter to the bladder is superior and lateral to the upper pole ureter. The valvelike mechanism for the lower pole ureter often is marginal, and VUR into the lower ureter occurs in as many as 50% of cases (Fig. 576.5). VUR occurs into both the lower and upper systems in some persons. With a duplication anomaly, some patients have an **ectopic ureter**, in which the upper pole ureter drains outside the bladder (see Chapter 577 and Figs. 577.6 and 577.7). If the ectopic ureter drains into the bladder neck, typically it is obstructed and refluxes. Duplication anomalies also are common in children with a **ureterocele**, which is a cystic swelling of the intramural portion of the distal ureter. These patients often have VUR into the associated lower pole ureter or the contralateral ureter. In addition, generally VUR is present when the ureter enters a bladder diverticulum (Fig. 576.6).

VUR is present at birth in 25% of children with **neuropathic bladder,** as occurs in myelomeningocele (see Chapters 579 and 631.4), sacral agenesis, and many cases of high imperforate anus. VUR is seen in 50% of males with posterior urethral valves. VUR with increased intravesical pressure (as in detrusor-sphincter discoordination or bladder outlet obstruction) can result in renal injury because of increased intravesical pressure transmitted to the upper urinary tract, even in the absence of infection.

Primary VUR occurs in association with several congenital urinary tract abnormalities. Of children with a multicystic dysplastic kidney or renal agenesis (see Chapter 574), 15% have VUR into the contralateral kidney, and 10–15% of children with a ureteropelvic junction obstruction have VUR into either the hydronephrotic kidney or the contralateral kidney. As such, a diagnosis of VUR should prompt complete investigation to rule out concomitant pathology contralaterally.

CLINICAL MANIFESTATIONS

VUR usually is discovered during evaluation for a UTI (see Chapter 575). Among these children, 80% are female, with an average age at diagnosis of 2-3 years. In other children, a VCUG is performed during evaluation of BBD, renal insufficiency, hypertension, or other suspected pathologic process of the urinary tract. Primary VUR also may be discovered during evaluation for antenatal hydronephrosis. In this select population, 80% of affected children are male, and the VUR

grade usually is higher than in females whose VUR is diagnosed following a UTI. The UTI may be symptomatic, an isolated febrile event, or more often both febrile and symptomatic (abdominal pain, dysuria). BBD (constipation) may be present in 50% of children with reflux and a UTI.

DIAGNOSIS

Diagnosis of VUR requires catheterization of the bladder, instillation of a solution containing iodinated contrast or a radiopharmaceutical, and radiologic imaging of the lower and upper urinary tract (a contrast VCUG or radionuclide cystogram, respectively). The bladder and upper urinary tracts are imaged during bladder filling and voiding. VUR occurring during bladder filling is termed *low-pressure* VUR; VUR during voiding is termed *high-pressure* VUR. *VUR in children with low-pressure VUR is significantly less likely to resolve spontaneously than in children who exhibit only high-pressure VUR.* Radiation exposure during a radionuclide cystogram is significantly less than that from a contrast VCUG. Low-dose radiation contrast VCUG provides more anatomic information, such as demonstration of a duplex collecting system, ectopic ureter, paraureteral (bladder) diverticulum, bladder outlet obstruction in males, upper urinary tract stasis, and signs of voiding dysfunction, such as a **spinning-top** urethra in females. The VUR grading system is based on the appearance on contrast VCUG, and the grade reported is the maximum grade observed during the study. For follow-up evaluation, some prefer the radionuclide cystogram because of the lower radiation exposure (Fig. 576.7), although it is difficult to determine whether the VUR severity has changed and the grading system for the radionuclide study is different than the standard IRS grading system.

Fig. 576.7 Radionuclide cystogram shows bilateral VUR.

Children undergoing cystography may be psychologically traumatized by the catheterization. Careful preparation by caregivers, use of Child Life specialists, or administration of oral or nasal midazolam (for sedation and amnesia) or propofol before the study can result in a less-distressing experience.

Indirect cystography is a technique of detecting VUR without catheterization that involves injecting an intravenous radiopharmaceutical that is excreted by the kidneys, waiting for it to be excreted into the bladder, and imaging the lower urinary tract while the patient voids. This technique detects only 75% of VUR cases. Another technique, which avoids radiation exposure, involves instilling sonographic contrast medium through a urethral catheter. The kidneys are imaged sonographically to determine whether any of the material refluxes. This technique is currently investigational only.

After VUR is diagnosed, assessment of the upper urinary tract is important. The goal of upper tract imaging is to assess whether renal scarring and associated urinary tract anomalies are present. Renal imaging typically is performed with a renal sonogram and/or renal scintigraphy (Fig. 576.8; see Chapter 575).

The child should be evaluated for BBD, including urgency, frequency, diurnal incontinence, infrequent voiding, or a combination of these (see Chapter 575). Children with an overactive bladder often undergo a regimen of behavioral modification with timed voiding, treatment of constipation, and, on occasion, anticholinergic therapy.

After diagnosis, the child's height, weight, and blood pressure should be measured and monitored. If upper tract imaging shows renal scarring, a serum creatinine measurement should be obtained. The urine should be assessed for infection and proteinuria.

NATURAL HISTORY

The incidence of reflux-related renal scarring increases with VUR grade. With bladder growth and maturation, the VUR grade often resolves or improves. *Lower grades of VUR are much more likely to resolve than are higher grades.* For grade I and II VUR, the likelihood of resolution is similar regardless of age at diagnosis and whether it is unilateral or bilateral. For grade III, a younger age at diagnosis and unilateral VUR usually are associated with a higher rate of spontaneous resolution (Fig. 576.9). Bilateral grade IV VUR is much less likely to resolve than is unilateral grade IV VUR. Grade V VUR rarely resolves. The mean age at VUR resolution is 6 years. *BBD and grade III-V VUR are the most common risk factors for recurrent febrile UTI and new renal scarring.*

Sterile VUR does not usually cause renal injury in the absence of infection, but in situations with high-pressure VUR, as in children with posterior urethral valves, neuropathic bladder, and nonneurogenic neurogenic bladder (i.e., **Hinman syndrome**), sterile VUR can cause significant renal damage. Children with high-grade VUR who acquire

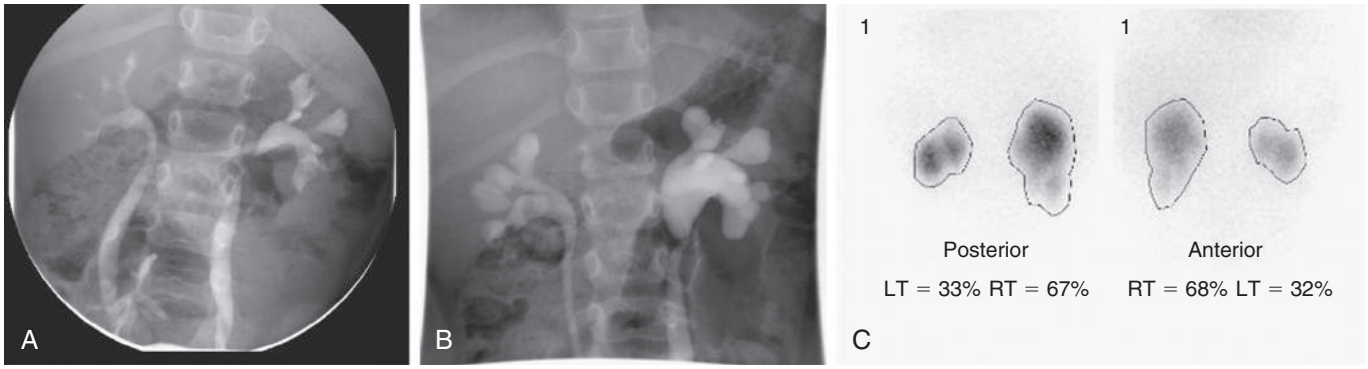

Fig. 576.8 A, VCUG in a 3-yr-old child with two febrile UTIs shows bilateral grade III VUR. B, At 5 years, repeat VCUG shows worsening VUR and calyceal clubbing, indicating renal scarring. C, At 11 years, renin-mediated hypertension has developed. Dimercaptosuccinic acid (DMSA) renal scan shows significant VUR-related renal scarring.

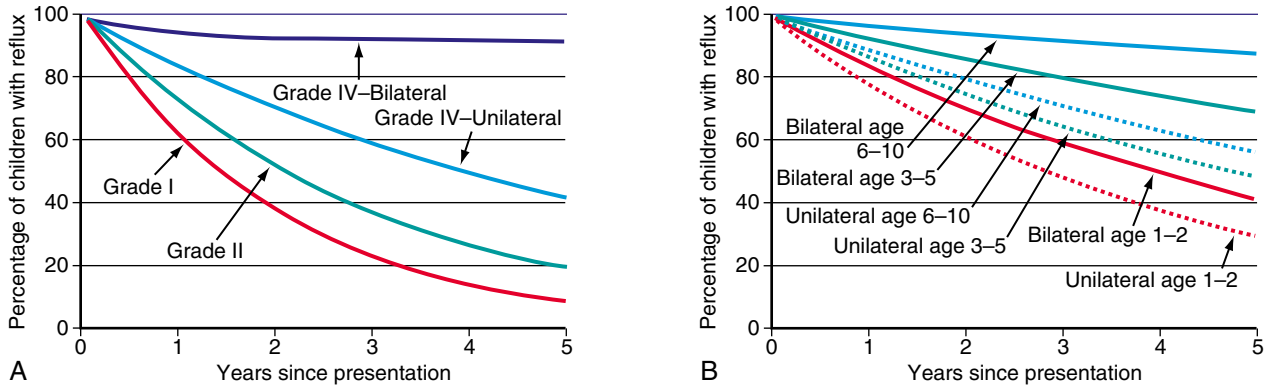

Fig. 576.9 A, Percentage chance of VUR persistence, grades I, II, and IV, for 1-5 years after presentation. B, Percentage chance of VUR persistence by age at presentation, grade III, for 1-5 years after presentation. *(From Elder JS, Peters CA, Arant BS Jr, et al. Pediatric Vesicoureteral Reflux Guidelines Panel summary report on the management of primary vesicoureteral reflux in children. J Urol. 1997;157:1846–1851.)*

a UTI are at significant risk for acute and recurrent pyelonephritis and new renal scarring (see Fig. 576.8).

TREATMENT

The goals of treatment are to prevent pyelonephritis, VUR-related renal injury, and other complications of VUR. Medical therapy is based on the principle that VUR often resolves over time and that if UTIs can be prevented, the morbidity or complications of VUR may be avoided without surgery. Medical therapy includes observation with behavioral modification or behavioral modification with antimicrobial prophylaxis in some patients. The basis for surgical therapy is that in selected children, ongoing VUR has caused or has significant potential for causing renal injury or other VUR-related complications, and that elimination of VUR minimizes the risk of these problems. Therapy for VUR should be individualized based on a particular patient's risk factors.

Observation

In children undergoing observation, therapeutic emphasis is directed at minimizing the risk of UTI by behavioral modification. These methods include timed voiding during the day, ensuring regular fecal elimination, increased fluid intake, periodic assessment of satisfactory bladder emptying, and prompt assessment and treatment of UTIs, particularly febrile UTIs. This approach is most appropriate for children with grade I and II VUR, and perhaps older children with persistent VUR and normal kidneys who have not experienced clinical pyelonephritis.

Antimicrobial Prophylaxis

In the past, daily antimicrobial prophylaxis was recommended as an initial approach to most children with VUR. However, several prospective clinical trials question the benefit of prophylaxis in children with VUR. The risk of recurrent UTI is highest in patients with grade III or IV reflux, those with BBD, and those whose first reflux-associated UTI was *febrile* rather than just symptomatic without fever. Antibiotic prophylaxis after a reflux-associated UTI decreases the risk of recurrent UTI but may increase the risk of developing resistant bacteria. In one study, antibiotic prophylaxis reduced the risk of new renal scars in children with grade III or IV reflux, while in another larger study, antibiotic prophylaxis did not affect the incidence of new renal scars in those with severe reflux (approximately 10% developed new scars regardless of prophylaxis).

Surgery

The purpose of surgical therapy is to minimize the risk of febrile UTI from ongoing VUR and nonsurgical therapy (observation or prophylaxis with follow-up testing). VUR can be corrected through a lower abdominal or inguinal incision (open), laparoscopically (with or without robotic assistance), or endoscopically with subureteral injection of a bulking agent.

Surgical management involves modifying the abnormal ureterovesical attachment. The operation can be performed from either outside (extravesical) or inside the bladder (intravesical). When VUR is associated with severe ureteral dilation (i.e., megaureter), the ureter must be tailored or narrowed to a more normal size to allow a smaller length:width ratio for the intramural tunnel, and a corner of the bladder is attached to the psoas tendon, forming a *psoas hitch.* Most children can be discharged 1-2 days following the surgical procedure. If the refluxing kidney is poorly functioning, nephrectomy or nephroureterectomy is indicated. Minimally invasive approaches with **laparoscopic** and **robotic-assisted laparoscopic ureteral reimplantation** offer alternatives to open surgical management; as experience with these procedures grows, success rates are approaching that of open surgery.

The success rate of conventional open ureteral reimplantation in children with primary VUR is >95–98% for grades I-IV, with 2% experiencing persistent VUR and 1% having ureteral obstruction that requires correction. The success rate is so high that many pediatric urologists do not perform a postoperative VCUG unless the child develops clinical pyelonephritis. For grade V VUR, the success rate is approximately 80%. In lower grades of VUR, a failed reimplantation is most likely to occur in children with undiagnosed BBD. In children with secondary VUR (posterior urethral valves, neuropathic bladder), the success rate is slightly lower than with primary VUR. The risk of pyelonephritis in children with grade III and IV VUR is significantly lower following open surgical correction compared with medical management. *Surgical repair will not reverse renal scarring or lead to improvement in renal function.*

Endoscopic repair of VUR involves injection of a bulking agent through a cystoscope just beneath the ureteral orifice, creating an effective flap-valve (Figs. 576.10 and 576.11). In 2001, the US Food and Drug Administration (FDA) approved the use of a biodegradable material, dextranomer microspheres suspended in hyaluronic acid (Dx-HA) (Deflux), for subureteral injection. The advantage of subureteral injection is that it is a noninvasive outpatient procedure (performed under general anesthesia) with no recovery time. The success rate is 70–80% and is highest for lower grades of VUR. If the first injection is unsuccessful, one or two repeat injections can be performed. The VUR recurrence rate is approximately 10–20%. In other areas of the world, a polyacrylamide hydrogel is used for endoscopic injection. The success rate with this product, which is not approved in the United States, is similar to Dx-HA, but the risk of reflux recurrence is significantly less.

CURRENT VESICOURETERAL REFLUX GUIDELINES

The long-standing belief regarding the benefit of antibiotic prophylaxis in children with VUR has been questioned. Multiple randomized, controlled prospective trials suggested that the risk of UTI in children with VUR is not reduced by prophylaxis. Most of the children in these trials had grade I-III VUR, and few younger than 1 year of age were studied.

In contrast, the PRIVENT (Prevention of Recurrent Urinary Tract Infection in Children with Vesicoureteric Reflux and Normal Renal Tracts) trial from Australia showed significant benefit to prophylaxis in children with VUR. The Swedish VUR Trial in Children studied children younger than 2 years of age with grades III and IV VUR; they compared antibiotic prophylaxis (nitrofurantoin) with observation and endoscopic injection therapy. Females in the surveillance group had a significantly higher incidence of febrile UTI and new renal scarring compared with the other treatment groups. The largest randomized trial (RIVUR [Randomized Intervention for Children with Vesicoureteral Reflux]) enrolled more than 600 children and demonstrated a reduction in the recurrence rate of UTIs with no reduction in the occurrence of renal scarring with antibiotic prophylaxis, but the prevalence of renal scarring at study entry was low.

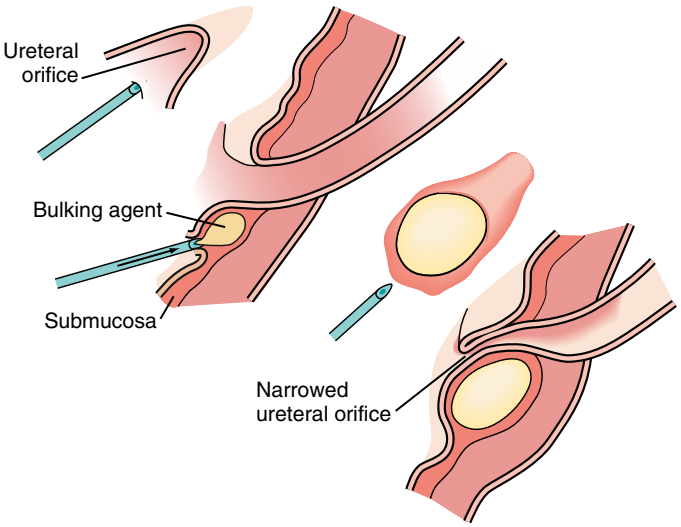

Fig. 576.10 Endoscopic correction of VUR. Through a cystoscope, a needle is inserted into the submucosal plane deep to the ureteral orifice, and a bulking agent is injected, creating a flap-valve to prevent VUR. *(Adapted from Ortenberg J. Endoscopic treatment of vesicoureteral reflux in children. Urol Clin North Am. 1998;25:151–156.)*

Prophylaxis is recommended by the American Urologic Association (AUA) in children at greatest risk for VUR-related renal injury (i.e., those <1 year of age). In addition, evaluation for bladder and bowel dysfunction is considered a standard part of initial and ongoing patient evaluation in children with VUR. Because children with BBD and VUR are much more likely to have recurrent UTIs and renal scarring, prophylaxis is recommended for these children. In children with VUR who are being managed by surveillance, if a febrile UTI occurs, prophylaxis is recommended. The decision whether to recommend observation, medical therapy, or surgery is based on the risk of VUR to the patient, the likelihood of spontaneous resolution, and the parents' and patient's preferences; the family should understand the risks and benefits of each treatment approach.

Another aspect of VUR management pertains to screening. VUR is known to be a familial disorder with autosomal dominant transmission with variable penetrance. The advantage of early VUR detection is to implement treatment before a potentially damaging episode of clinical pyelonephritis. In siblings of an index patient with VUR, optional management includes screening of asymptomatic siblings or offspring with a renal ultrasound or VCUG. The AUA recommends that a VCUG should be obtained if a screening ultrasound demonstrated a renal abnormality or if the sibling had a UTI.

The AUA also determined that female newborns with renal pelvic dilation were more likely than male newborns to have VUR. The AUA recommends that a VCUG be performed in neonates with grade III-IV *antenatal* hydronephrosis (moderate to severe pelvicalyceal dilation), hydroureter, or an abnormal bladder. In children with less severe renal pelvic dilation, an observational approach without screening for VUR, with prompt treatment of any UTI, is appropriate. However, the AUA also indicated that obtaining a VCUG is considered an appropriate option for neonates with lesser grades of hydronephrosis.

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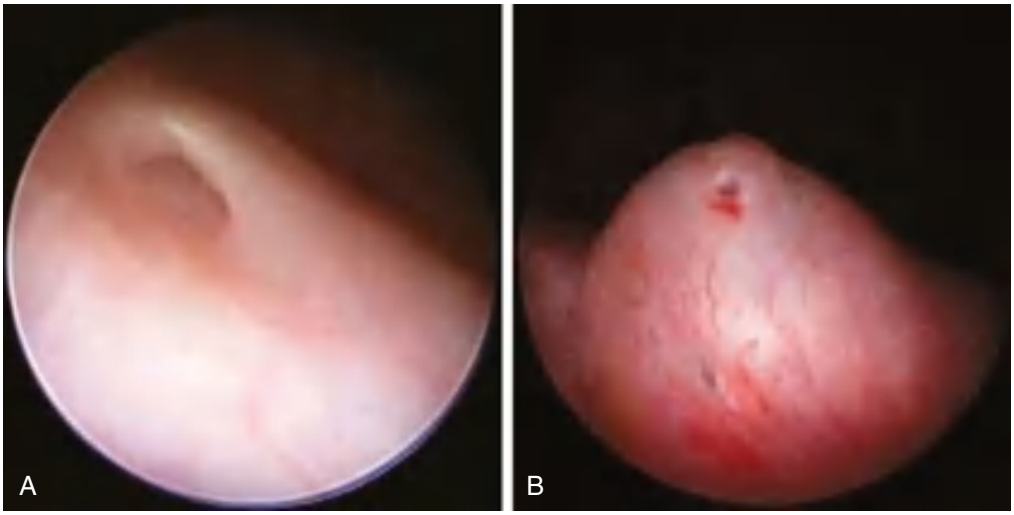


Fig. 576.11 A, Endoscopic view of right vesicoureteral refluxing ureter. B, The same ureter after subureteral injection of dextranomer microspheres.

Chapter 577

Obstruction of the Urinary Tract

Heather N. Di Carlo and Chad B. Crigger

Most childhood obstructive lesions are congenital, although urinary tract obstruction can be caused by trauma, neoplasia, calculi, inflammatory processes, or surgical procedures. Obstructive lesions occur at any level from the urethral meatus to the calyceal infundibula (Table 577.1). The pathophysiologic effects of obstruction depend on its level, the extent of involvement, the child's age at onset, and whether it is acute or chronic.

ETIOLOGY

Severe ureteral obstruction early in fetal life results in renal dysplasia, ranging from multicystic kidney, which is associated with ureteral or ureteropelvic junction (UPJ) atresia (see Fig. 574.3), to various degrees of histologic renal cortical dysplasia that are seen with less severe obstruction. **Chronic ureteral obstruction** in late fetal life or after birth results in dilation of the ureter, renal pelvis, and calyces with alterations of renal parenchyma ranging from minimal tubular changes to dilation of Bowman's space, glomerular fibrosis, and interstitial fibrosis. After birth, infection can complicate obstruction and worsen renal damage.

Prenatal screening with ultrasonography (US) may detect **antenatal hydronephrosis** (ANH), which is graded by the trimester and the anterior-posterior diameter of the renal pelvis (Table 577.2); most are mild. Table 577.3 notes the eventual etiology. Risk stratification for prenatal (Fig. 577.1) and postnatal (Fig. 577.2) urinary tract dilation (UTD) helps plan for further evaluation and treatment.

CLINICAL MANIFESTATIONS

Obstruction of the urinary tract generally causes **hydronephrosis,** which typically is asymptomatic in its early phases. An obstructed kidney secondary to a **ureteropelvic junction (UPJ) obstruction** or **ureterovesical junction obstruction** can manifest as a unilateral mass or cause upper abdominal or flank pain on the affected side. Pyelonephritis can occur because of urinary stasis. An upper urinary tract stone can occur, causing abdominal and flank pain and hematuria. With bladder outlet obstruction, the urinary stream may be weak; urinary tract infection (UTI; see Chapter 575) is common. Many of these lesions are identified by antenatal US; an abnormality involving the genitourinary tract is suspected in as many as 1 in 50 fetuses (see Table 577.3).

Obstructive renal insufficiency can manifest itself by failure to thrive, vomiting, diarrhea, or other nonspecific signs and symptoms. In older children, **infravesical obstruction** can be associated with overflow urinary incontinence or a poor urine stream. **Acute ureteral obstruction** causes flank or abdominal pain; there may be nausea and vomiting. Chronic ureteral obstruction can be silent or can cause vague abdominal or typical flank pain with increased fluid intake (such as in Dietl's crisis).

DIAGNOSIS

Urinary tract obstruction may be diagnosed prenatally by US, which typically shows hydronephrosis and occasionally a distended bladder. More complete evaluation, including imaging studies, should be undertaken in these children in the neonatal period.

A multidisciplinary consensus group has standardized the fetal evaluation and early postnatal management of babies with ANH. The US parameters include the anterior-posterior renal pelvic diameter (APRPD), **calyceal dilation,** whether the ANH involves the major and/or minor calyces, the parenchymal thickness and appearance, whether the ureter is normal or abnormal, and whether the bladder is normal or abnormal. Normal values for UTD are based on the APRPD:

Antenatal	16-27 weeks	<4 mm
	≥28 weeks	<7 mm
Postnatal	(>48 hours)	<10 mm

Assuming there is no calyceal dilation, the kidneys have a normal appearance, and the ureter and bladder are normal, the study is considered normal.

The consensus group then categorized ANH into antenatal and postnatal risk groups. For antenatal ANH, there are two risk groups: low and high (see Fig. 577.1). For postnatal ANH, there are three risk groups: low,

Table 577.1 Types and Causes of Urinary Tract Obstruction

LOCATION	CAUSE
Infundibula	Congenital Calculi Inflammatory (tuberculosis) Traumatic Postsurgical Neoplastic
Renal pelvis	Congenital (infundibulopelvic stenosis) Inflammatory (tuberculosis) Calculi Neoplasia (Wilms tumor, neuroblastoma)
Ureteropelvic junction	Congenital stenosis Calculi Neoplasia Inflammatory Postsurgical Traumatic
Ureter	Congenital obstructive megaureter Midureteral structure Ureteral ectopia Ureterocele Retrocaval ureter Ureteral fibroepithelial polyps Ureteral valves Calculi Postsurgical Extrinsic compression Neoplasia (neuroblastoma, lymphoma, and other retroperitoneal or pelvic tumors) Inflammatory (Crohn disease, chronic granulomatous disease) Hematoma, urinoma Lymphocele Retroperitoneal fibrosis
Bladder outlet and urethra	Neurogenic bladder dysfunction (functional obstruction) Posterior urethral valves Anterior urethral valves Diverticula Urethral strictures (congenital, traumatic, or iatrogenic) Urethral atresia Ectopic ureterocele Meatal stenosis (males) Calculi Foreign bodies Phimosis Extrinsic compression by tumors Urogenital sinus anomalies

Table 577.2 Definition of Antenatal Hydronephrosis by Anterior-Posterior Diameter

DEGREE OF ANTENATAL HYDRONEPHROSIS	SECOND TRIMESTER	THIRD TRIMESTER
Mild	4–6 mm	7 to 9 mm
Moderate	7–10 mm	10–15 mm
Severe	>10 mm	>15 mm

From Nguyen HT, Herndon CDA, Cooper C, et al. The Society for Fetal Urology consensus statement on the evaluation and management of antenatal hydronephrosis. *J Pediatr Urol.* 2010;6:212–231. Table 2.

Table 577.3 Etiology of Antenatal Hydronephrosis

ETIOLOGY	INCIDENCE
Transient hydronephrosis	41–88%
Ureteropelvic junction obstruction	10–30%
Vesicoureteral reflux	10–20%
Ureterovesical junction obstruction/ megaureters	5–10%
Multicystic dysplastic kidney	4–6%
Posterior urethral valve/urethral atresia	1–2%
Ureterocele/ectopic ureter/duplex system	5–7%
Others: prune-belly syndrome, cystic kidney disease, congenital ureteric strictures, megalourethra	Uncommon

From Nguyen HT, Herndon CDA, Cooper C, et al. The Society for Fetal Urology consensus statement on the evaluation and management of antenatal hydronephrosis. *J Pediatr Urol.* 2010;6:212–231. Table 5.

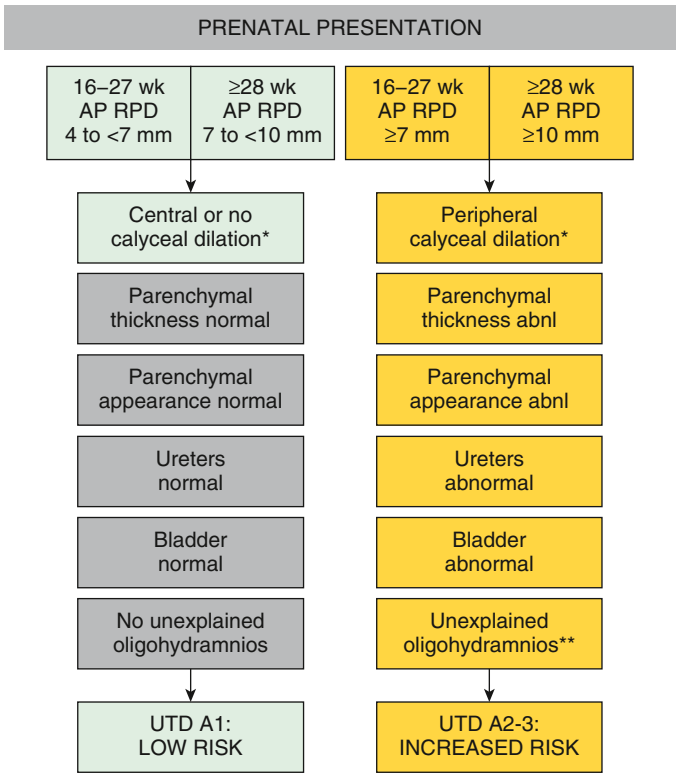
intermediate, and high (see Fig. 577.2). The panel recommended that all seven urinary tract parameters be described in a written report.

For antenatal presentation, if the APRPD is 4-7 mm at 16-27 weeks or 7-10 mm at ≥28 weeks and there is central or no calyceal dilation, the fetus is categorized as having **UTD A1**, **Low Risk**. In follow-up for UTD A1, the panel suggested one additional antenatal US at ≥32 weeks, and after birth, a renal US at >48 hours to 1 month of age and a second renal US 6 months later. Genetic screening is not indicated unless there are associated congenital malformations.

If the APRPD is ≥7 mm at 16-27 weeks or ≥10 mm at ≥28 weeks, with any peripheral calyceal dilation or any other upper urinary tract abnormality, the fetus is classified as having **UTD A2-3,** or **Increased Risk**. The assigned risk is based on the most concerning feature. For UTD A2-3, the panel recommends a follow-up US in 4-6 weeks, although with suspected **posterior urethral valves** (PUVs) or severe bilateral hydronephrosis, more frequent follow-up was recommended until delivery. Following delivery, a renal US after 48 hours but before 1 month is suggested, again with more immediate evaluation if PUV is suspected or there is significant bilateral hydronephrosis. In addition, specialist consultation with pediatric urology or nephrology is recommended.

For postnatal presentation, at >48 hours an APRPD <10 mm is **Normal.** If the APRPD is 10-15 mm and there is central calyceal dilation, but all other parameters are normal, the infant is classified as having **UTD P1, Low Risk**. Society of Fetal Urology (SFU) hydronephrosis grades 1 and 2 correspond to UTD P1. The panel recommends a follow-up renal US in 1-6 months. *A voiding cystourethrogram (VCUG) and antibiotic prophylaxis are optional and at the discretion of the clinician. A renal scan is not recommended.*

If the postnatal APRPD is ≥15 mm and there is peripheral calyceal dilation and/or abnormal ureters, the infant is classified as having **UTD P2, Intermediate Risk**. SFU hydronephrosis grade 3 corresponds to UTD P2. The panel recommends a follow-up renal US in 1-3 months.



*Central and peripheral calyceal dilation may be difficult to evaluate early in gestation

**Oligohydramnios is suspected to result from a GU cause

Fig. 577.1 Urinary tract dilation (UTD) risk stratification: prenatal presentation for UTD A1 (low risk) and UTD A2-3 (increased risk). Note: Classification is based on the presence of the most concerning feature. For example, a fetus with an APRPD within the UTD A1 range but with peripheral calyceal dilation would be classified as UTD A2-3. GU, Genitourinary. *(From Nguyen HT, Benson CB, Bromley B, et al. Multidisciplinary consensus on the classification of prenatal and postnatal urinary tract dilation [UTD classification system]. J Pediatr Urol. 2014;10:982–998. Fig. 3.)*

VCUG, antibiotic prophylaxis, and a functional renal scan are optional and at the discretion of the clinician.

If the APRPD is ≥15 mm and there is peripheral calyceal dilation, abnormal parenchymal thickness, abnormal parenchymal appearance, abnormal ureters, and/or abnormal bladder, the infant is classified as having **UTD P3, High Risk**. SFU hydronephrosis grade 4 corresponds to UTD P3. The panel recommends a follow-up renal US in 1 month. *A VCUG and antibiotic prophylaxis are recommended. A functional renal scan is optional and at the discretion of the clinician (but is virtually always recommended).*

PHYSICAL FINDINGS

Urinary tract obstruction is often silent. In the newborn infant, a palpable abdominal mass most commonly is a hydronephrotic or multicystic dysplastic kidney. With PUVs, which constitute an infravesical obstructive lesion in males, a walnut-sized mass representing the bladder is palpable just above the pubic symphysis. A **patent draining urachus** also can suggest urethral obstruction. **Urinary ascites** in the newborn usually is caused by renal or bladder urinary extravasation secondary to PUVs. Infection and sepsis may be the first indications of an obstructive lesion of the urinary tract. The combination of infection and obstruction poses a serious threat to infants and children and generally requires parenteral administration of antibiotics and drainage of the obstructed kidney. Renal US should be performed in all children during the acute stage of an initial febrile UTI.

IMAGING STUDIES

Renal Ultrasound

Hydronephrosis is the most common characteristic of obstruction (Fig. 577.3). Upper UTD is not diagnostic of obstruction and often

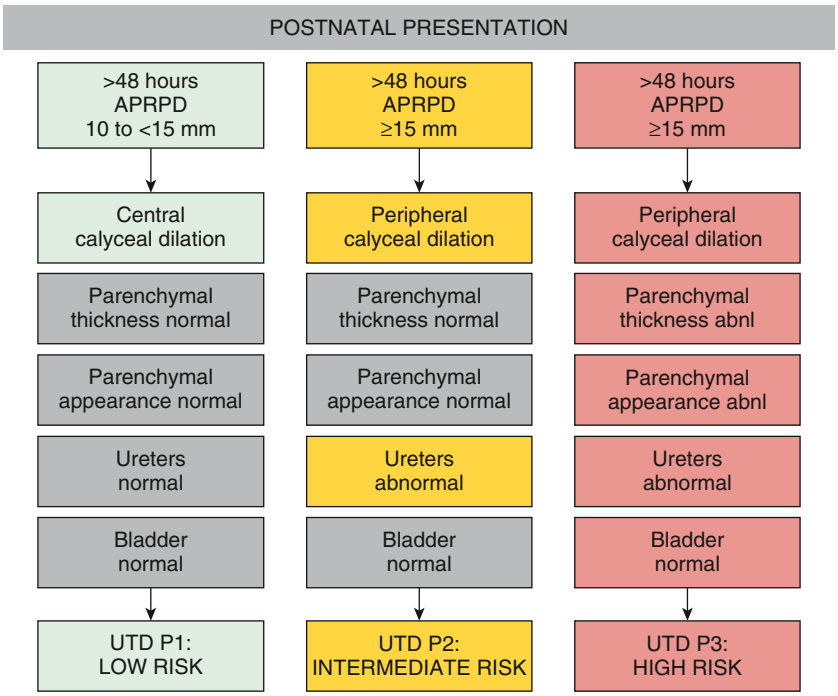


Fig. 577.2 Urinary tract dilation (UTD) risk stratification: postnatal presentation for UTD P1 (low risk), UTD P2 (intermediate risk), and UTD P3 (high risk). Note: Stratification is based on the most concerning ultrasound finding. For example, if the APRPD is in the UTD P1 range but there is peripheral calyceal dilation, the classification is UTD P2. Similarly, the presence of parenchymal abnormalities (abnl) denotes a UTD P3 classification, regardless of APRPD measurement. *(From Nguyen HT, Benson CB, Bromley B, et al. Multidisciplinary consensus on the classification of prenatal and postnatal urinary tract dilation [UTD classification system]. J Pediatr Urol. 2014;10:982–998. Fig. 6.)*

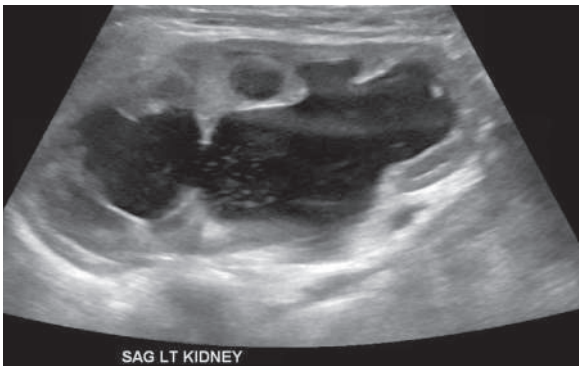


Fig. 577.3 US image of the left kidney with marked pelvic and calyceal dilation (grade 4 hydronephrosis) in a newborn with ureteropelvic junction obstruction.

persists after surgical correction of a significant obstructive lesion. Dilation can result from vesicoureteral reflux (VUR), or it may be a manifestation of abnormal development of the urinary tract, even when there is no obstruction. Renal length, degree of caliectasis and parenchymal thickness, and presence or absence of ureteral dilation should be assessed. In addition to the UTD system, most pediatric urologists also grade the severity of hydronephrosis from 1-4 using the SFU grading scale (Table 577.4). The clinician should ascertain that the contralateral kidney is normal, and the bladder should be imaged to see whether the bladder wall is thickened, the lower ureter is dilated, and bladder emptying is complete. In acute or intermittent obstruction, the dilation of the collecting system may be minimal, and US may be misleading.

Voiding Cystourethrogram

In neonates and infants with congenital grade 3 or 4 hydronephrosis and in any child with ureteral dilation, a **contrast VCUG** should be obtained, because the dilation is secondary to VUR in 15% of cases.

Table 577.4 Society for Fetal Urology Grading System for Hydronephrosis

GRADE OF HYDRONEPHROSIS	RENAL IMAGE	
	CENTRAL RENAL COMPLEX	RENAL PARENCHYMAL THICKNESS
0	Intact	Normal
1	Slight splitting	Normal
2	Evident splitting, complex confined within renal border	Normal
3	Wide splitting, pelvis dilated outside renal border, calyces uniformly dilated	Normal
4	Further dilation of pelvis and calyces (calyces may appear convex)	Thin

After Maizels M, Mitchell B, Kass E, et al. Outcome of nonspecific hydronephrosis in the infant: a report from the registry of the Society for Fetal Urology. *J Urol.* 1994;152:2324–2327.

In males, the VCUG also is performed to rule out urethral obstruction, particularly in cases of suspected PUVs. In older children, the urinary flow rate can be measured noninvasively with a urinary flowmeter. Decreased flow with a normal bladder contraction suggests infravesical obstruction (e.g., PUVs, urethral stricture). When the urethra cannot be catheterized to obtain a VCUG, the clinician should suspect a urethral stricture or an obstructive urethral lesion. Retrograde urethrography with contrast medium injected into the urethral meatus helps delineate the anatomy of the urethral obstruction.

Radioisotope Studies

Renal scintigraphy is used to assess renal anatomy and function. The two most commonly used radiopharmaceuticals are mercaptoacetyl triglycine (MAG-3) and technetium-99m–labeled dimercaptosuccinic acid (DMSA). MAG-3, which is excreted by renal tubular secretion, is used to assess differential renal function, and when furosemide is administered, drainage also can be measured. DMSA is a renal cortical imaging agent and is used to assess differential renal function and to demonstrate whether renal scarring is present. It is used infrequently in children with obstructive uropathy.

In a MAG-3 diuretic renogram, a small dose of technetium-labeled MAG-3 is injected intravenously (Figs. 577.4 and 577.5). During the first 2-3 minutes, renal parenchymal uptake is analyzed and compared, allowing computation of differential renal function.

Subsequently, excretion is evaluated. After 20 minutes, furosemide 1 mg/kg 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 10-15 minutes, termed the half-time ($t_{1/2}$). If there is significant upper tract obstruction, the $t_{1/2}$ usually is longer than 20 minutes. A $t_{1/2}$ of 15-20 minutes is indeterminate. An elevated $t_{1/2}$ is suggestive but not diagnostic of obstruction. The images generated usually provide an accurate assessment of the site of obstruction. Numerous variables affect the outcome of the diuretic renogram. Newborn kidneys are functionally immature, and, in the first month of life, normal kidneys might not demonstrate normal drainage after diuretic administration. Patient dehydration prolongs parenchymal transit and can blunt the diuretic response. As such, renal scintigraphy is usually performed after 8 weeks of life in an appropriately hydrated infant. Giving an insufficient dose of furosemide can result in slow drainage. If VUR is present, continuous bladder drainage is mandatory to prevent the radionuclide from refluxing from the bladder into the dilated upper tract, which would prolong the washout phase.

Magnetic Resonance Urography

Magnetic resonance (MR) urography is also used to evaluate suspected upper urinary tract pathology. The child is hydrated and given intravenous furosemide. Gadolinium-diethylene tetrapentaacetic acid is injected, and routine T1 weighted and fat-suppressed fast spin-echo T2 weighted imaging is performed through the kidneys, ureters, and bladder. This study provides superb images of the pathology, and methodology permits assessment of differential renal function and drainage (Fig. 577.6). There is no radiation exposure; however, young children need sedation or anesthesia. It is used primarily when renal US and radionuclide imaging fail to delineate complex pathology.

Computed Tomography

In children with a suspected ureteral calculus (see Chapter 584), noncontrast, low-dose spiral CT of the abdomen and pelvis is a standard method of demonstrating whether a calculus is present, its location, and whether there is significant proximal hydronephrosis. This study may be ordered when a renal/bladder US is inconclusive. The disadvantage of CT is the significant radiation exposure, and it should be used only when the results will direct management decisions.

Ancillary Studies

In unusual cases, an **antegrade pyelogram** (insertion of a percutaneous nephrostomy tube and injection of contrast agent) can be performed to assess the anatomy of the upper urinary tract. This procedure usually requires general anesthesia. In addition, an **antegrade pressure-perfusion flow study** (Whitaker test) may be performed, in which fluid is infused at a measured rate, usually 10 mL/min. The pressures

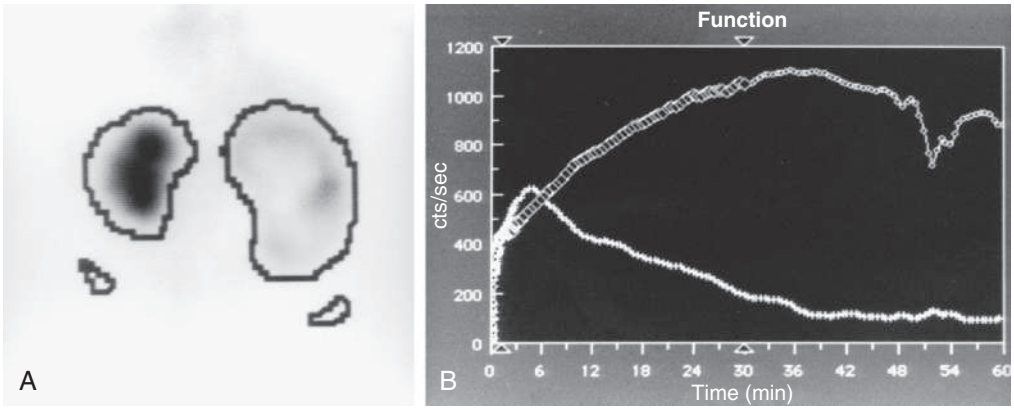


Fig. 577.4 MAG-3 diuretic renogram of a 6-wk-old infant with severe right hydronephrosis. The right kidney is on the *right* side of the image. A, Differential renal function: left kidney 70%, right kidney 30%. B, After administration of furosemide, drainage from the left kidney was normal and drainage from the right kidney was slow, consistent with right UPJ obstruction. Pyeloplasty was performed on the right kidney.

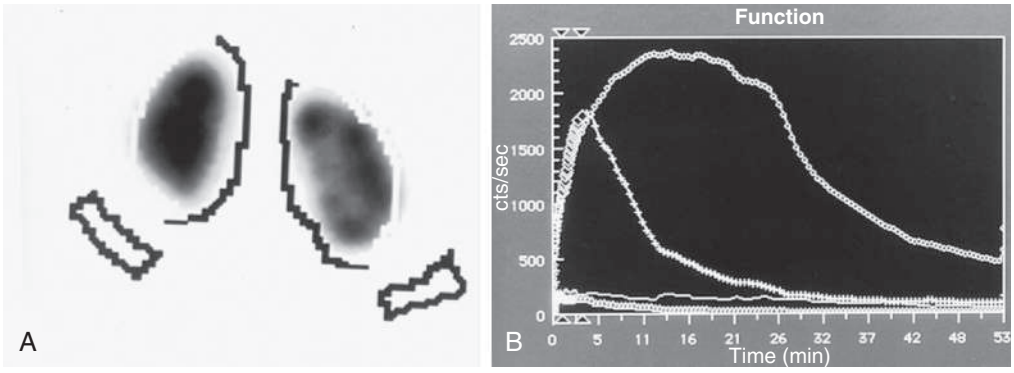


Fig. 577.5 A, MAG-3 diuretic renogram at 14 mo of age shows equal function in the two kidneys. B, Prompt drainage after the administration of furosemide.

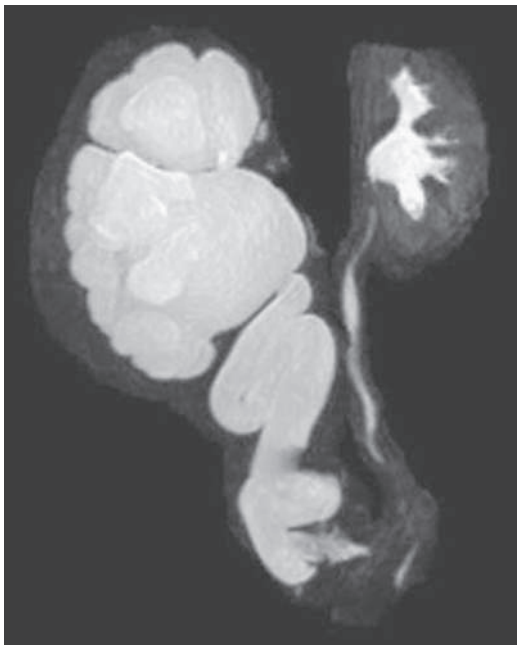


Fig. 577.6 MR urogram in boy with distal ureterovesical obstruction.

in the renal pelvis and the bladder are monitored during this infusion, and pressure differences exceeding 20 cm H_2O suggest obstruction. In other cases, cystoscopy with retrograde pyelography provides excellent images of the upper urinary tract (Fig. 577.7).

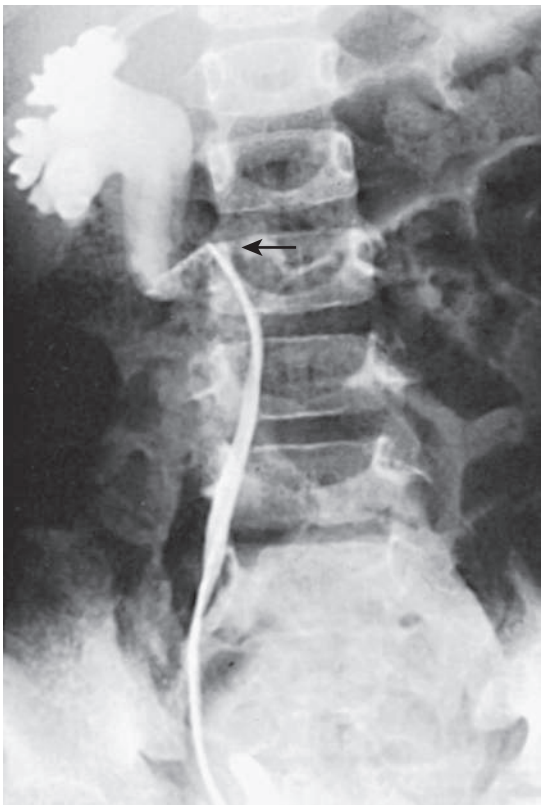


Fig. 577.7 Retrograde pyelogram showing medial deviation of a dilated upper ureter to the level of the third lumbar vertebra *(arrow)*, characteristic of a retrocaval ureter.

SPECIFIC TYPES OF URINARY TRACT OBSTRUCTION AND THEIR TREATMENT

Hydrocalycosis

Hydrocalycosis refers to a localized dilation of the calyx caused by obstruction of its infundibulum, termed **infundibular stenosis.** This condition can be developmental in origin or secondary to inflammatory processes, such as UTI. It usually is discovered during evaluation for pain or UTI. The diagnosis of infundibular stenosis is usually established by sonograph and CT scan or MR urography.

Ureteropelvic Junction Obstruction

UPJ obstruction is the most common obstructive lesion in childhood and usually is caused by intrinsic stenosis (see Figs. 577.3-577.5). An accessory artery to the lower pole of the kidney can also cause extrinsic obstruction. The typical appearance on US is grade 3 or 4 hydronephrosis without a dilated ureter and a clear transition point. UPJ obstruction may present on antenatal sonography revealing fetal hydronephrosis; as a palpable renal mass in a newborn or infant; as abdominal, flank, or back pain; as a febrile UTI; or as hematuria after minimal trauma. Approximately 60% of cases occur on the left side; the male:female ratio is 2:1. *UPJ obstruction is bilateral in only 10% of cases*. In kidneys with UPJ obstruction, renal function may be significantly impaired from pressure atrophy, but approximately half of affected kidneys have relatively normal glomerular function. The anomaly is corrected by performing a **pyeloplasty**, in which the stenotic segment is excised, and the normal ureter and renal pelvis are reattached. Success rates are 91–98%. Pyeloplasty can be performed using laparoscopic techniques, often robotic assisted using the da Vinci robot.

Lesser degrees of UPJ narrowing might cause mild hydronephrosis, which usually is nonobstructive, and typically these kidneys function normally. The spectrum of UPJ abnormalities has been referred to as **anomalous UPJ**. Another cause of mild hydronephrosis is fetal folds of the upper ureter, which also are nonobstructive.

The diagnosis can be difficult to establish in an asymptomatic infant in whom dilation of the renal pelvis is found incidentally in a prenatal US. After birth, the sonographic study is repeated to confirm the prenatal finding. A VCUG is necessary because 10–15% of patients have ipsilateral vesicoureteral reflux. Because neonatal oliguria can cause temporary decompression of a dilated renal pelvis, it is ideal to perform the first postnatal US after the third day of life. Delaying the US may be impractical. *If no dilation is found on the initial US, a repeat study should be performed at 1 month of age*. If the kidney shows grade 1 or 2 hydronephrosis and the renal parenchyma appears normal, a period of observation usually is appropriate, with sequential renal US studies to monitor the severity of hydronephrosis, and the hydronephrosis usually disappears. Antibiotic prophylaxis is *not* indicated for children with mild hydronephrosis. If the hydronephrosis is grade 3 or 4, spontaneous resolution is less likely, and obstruction is more likely to be present, particularly if the renal pelvic diameter is 3 cm. A diuretic renogram with MAG-3 is performed at 4-6 weeks of age. If there is poor upper tract drainage or the differential renal function is poor, pyeloplasty is recommended. After pyeloplasty the differential renal function often improves, and improved drainage with furosemide stimulation is expected.

If the differential function on renography is normal and drainage is satisfactory, the infant can be followed with serial US studies, even with grade 4 hydronephrosis. If the hydronephrosis remains severe with no improvement, a repeat diuretic renogram after 6-12 months can help in the decision between continued observation and surgical repair. Prompt surgical repair is indicated in infants with an abdominal mass, bilateral severe hydronephrosis, a solitary kidney, or diminished function in the involved kidney. In unusual cases in which the differential renal function is <10% but the kidney has some function, insertion of a percutaneous nephrostomy tube allows drainage of the hydronephrotic kidney for a few weeks to allow reassessment of renal function. In older children who present with symptoms, the diagnosis of UPJ obstruction usually is established by US and diuretic renography.

The differential diagnosis includes megacalycosis, a congenital nonobstructive dilation of the calyces without pelvic or ureteric dilation; VUR with marked dilation and kinking of the ureter; midureteral or

distal ureteral obstruction when the ureter is not well visualized on the urogram; and retrocaval ureter.

Midureteral Obstruction

Congenital ureteral stenosis or a ureteral valve in the midureter is rare. It is corrected by excision of the strictured segment and reanastomosis of the normal upper and lower ureteral segments. A **retrocaval ureter** is an anomaly in which the upper right ureter travels posterior to the inferior vena cava. In this anomaly, the vena cava can cause extrinsic compression and obstruction. A retrograde pyelogram or MR urogram shows the right ureter to be medially deviated at the level of the third lumbar vertebra (see Fig. 577.7). Surgical treatment consists of transection of the upper ureter, moving it anterior to the vena cava, and reanastomosing the upper and lower segments. Repair is necessary only when obstruction is present. Retroperitoneal tumors, fibrosis caused by surgical procedures, inflammatory processes (as in chronic granulomatous disease), and radiation therapy can cause acquired midureteral obstruction.

Ectopic Ureter

A ureter that drains outside the bladder is referred to as an ectopic ureter. This anomaly is three times as common in females as in males and usually is detected prenatally. The ectopic ureter typically drains the upper pole of a duplex collecting system (two ureters).

In females, approximately 35% of these ureters enter the urethra at the bladder neck; 35% enter the urethrovaginal septum; 25% enter the vagina; and a few drain into the cervix, uterus, Gartner duct, or a urethral diverticulum. Often the terminal aspect of the ureter is narrowed, causing **hydroureteronephrosis**. Apart from the ectopic ureter entering the bladder neck, in females an ectopic ureter causes continuous urinary incontinence from the affected renal moiety. UTI is common because of urinary stasis.

In males, ectopic ureters enter the posterior urethra (above the external sphincter) in 47%, the prostatic utricle in 10%, the seminal vesicle in 33%, the ejaculatory duct in 5%, and the vas deferens in 5%. Consequently, in males, an ectopic ureter does not cause incontinence, and most patients present with a UTI or epididymitis.

Evaluation includes a renal US, VCUG, and renal scan, which demonstrates whether the affected segment has significant function. The US shows the affected hydronephrotic kidney or dilated upper pole and ureter down to the bladder (Fig. 577.8). If the ectopic ureter drains into the bladder neck (female), a VCUG usually shows reflux into the ureter. Otherwise, there is no reflux into the ectopic ureter, but there may be reflux into the ipsilateral lower pole ureter or contralateral collecting system.

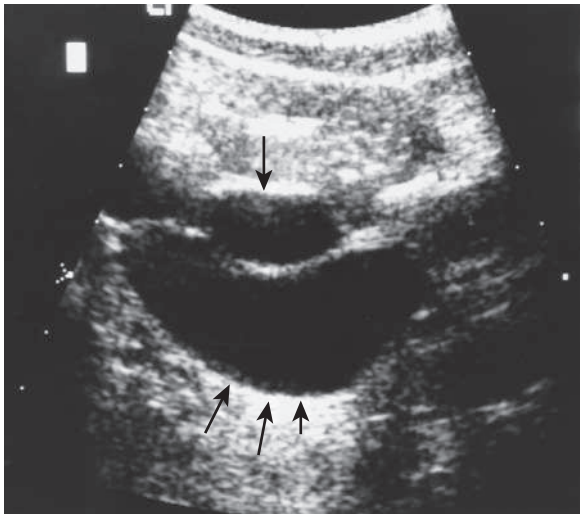


Fig. 577.8 US image of the right dilated ureter *(bottom arrows)* extending behind and caudal to a nearly empty bladder *(top arrow)* in a female with urinary incontinence and ectopic ureter draining into the vagina.

Treatment depends on the status of the renal unit drained by the ectopic ureter. If there is satisfactory function, ureteral reimplantation into the bladder or **ureteroureterostomy** (anastomosing the ectopic upper pole ureter into the normally inserting lower pole ureter) is indicated. If function is poor, partial or total nephrectomy is indicated. In many centers this procedure is done laparoscopically, often with robotic assistance.

Ureterocele

A ureterocele is a cystic dilation of the terminal ureter and is obstructive because of a pinpoint ureteral orifice. Ureteroceles are much more common in females than in males. Affected children usually are discovered by prenatal US, but some present with a febrile UTI. Ureteroceles may be ectopic, in which case the cystic swelling extends through the bladder neck into the urethra, or orthotopic, in which case the ureterocele is entirely within the bladder. Both orthotopic and ectopic ureteroceles can be bilateral.

In females, ureteroceles nearly always are associated with ureteral duplication (Fig. 577.9), whereas in 50% of affected males there is only one ureter. When associated with a duplication anomaly, the ureterocele drains the upper renal moiety, which commonly functions poorly or is dysplastic because of congenital obstruction. The lower pole ureter drains into the bladder superior and lateral to the upper pole ureter and may reflux.

An **ectopic ureterocele** extends submucosally through the bladder neck into the urethra. Rarely, large ectopic ureteroceles can cause bladder outlet obstruction and retention of urine with bilateral hydronephrosis. In females, the ureterocele can prolapse from the urethral meatus. US is effective in demonstrating the ureterocele and whether the associated obstructed system is duplicated or single. VCUG usually shows a filling defect in the bladder, sometimes large, corresponding to the ureterocele, and it often shows reflux into the adjacent lower pole collecting system with typical findings of a "drooping lily" appearance to the kidney. Nuclear renal scintigraphy is most accurate in demonstrating whether the affected renal moiety has significant function.

Treatment of ectopic ureteroceles depends on whether the upper pole functions on renal scan and whether there is reflux into the lower pole ureter. If there is nonfunction of the upper pole of the kidney and there is no reflux, treatment usually involves laparoscopic, robotic, or open excision of the obstructed upper pole and most of the associated ureter. If there is function in the upper pole or significant reflux into the lower pole ureter, or if the patient is septic from infection of the hydronephrotic kidney, then transurethral incision with cautery is appropriate initial therapy to decompress the ureterocele. Reflux into the incised ureterocele is common, and subsequent excision of the ureterocele and ureteral reimplantation usually is necessary. An alternative method is to perform an upper-to-lower ureteroureterostomy, allowing the obstructed upper pole ureter to drain through the normal lower ureter; this procedure often is performed with minimally invasive laparoscopic (robotic) technique or through a small incision.

Orthotopic ureteroceles are associated with duplicated or single collecting systems, and the orifice is in the expected location in the bladder (Fig. 577.10). These anomalies usually are discovered during an investigation for prenatal hydronephrosis or a UTI. US is sensitive for detecting the ureterocele in the bladder and hydroureteronephrosis. Transurethral incision of the ureterocele effectively relieves the obstruction, but it can result in VUR, necessitating ureteral reimplantation later. Some prefer open excision of the ureterocele and reimplantation as the initial form of treatment. Small, simple ureteroceles discovered incidentally without upper tract dilation generally do not require treatment. Rarely, a large ureterocele occupying much of the bladder lumen can result in bilateral hydronephrosis by obstructing drainage of the contralateral ureteral orifice.

Megaureter

Table 577.5 presents a classification of megaureters (dilated ureter). Numerous disorders can cause ureteral dilation, and many are nonobstructive.

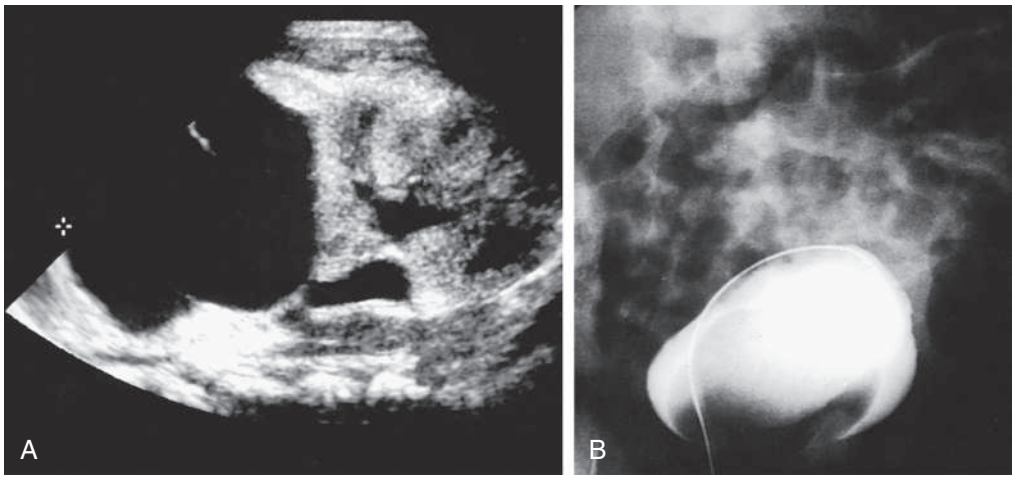


Fig. 577.9 A, Infant with ectopic ureterocele. US of the left kidney shows massive dilation of the upper pole and a normal lower pole. B, VCUG shows large ureterocele, draining the left upper pole, in the bladder. No reflux is present.

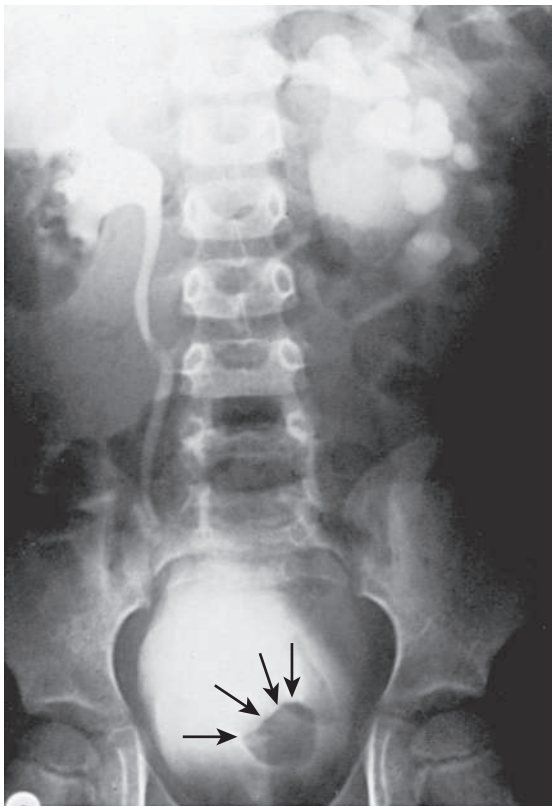


Fig. 577.10 Simple intravesical ureterocele. The excretory urogram shows left hydronephrosis and a round filling defect *(arrows)* on the left side of the bladder corresponding to a simple ureterocele causing left ureteral obstruction. This lesion was treated by transurethral incision and drainage of the ureterocele.

Megaureters usually are discovered during antenatal US or during workup for postnatal UTI, hematuria, or abdominal pain. A careful history, physical examination, and VCUG identify causes of secondary megaureters and refluxing megaureters, as well as the prune-belly syndrome. Primary obstructed megaureters and nonobstructed megaureters represent varying degrees of severity of the same anomaly.

The **primary obstructed nonrefluxing megaureter** results from abnormal development of the distal ureter, with collagenous tissue replacing the muscle layer. Normal ureteral peristalsis is disrupted, and the proximal ureter widens. In most cases there is not a true stricture. On intravenous pyelogram or an MR urogram, the distal ureter is more dilated in its distal segment and tapers abruptly at or above the junction of the bladder (Fig. 577.11). The lesion may be unilateral or bilateral. Significant hydroureteronephrosis suggests obstruction. Megaureter predisposes to UTI, urinary stones, hematuria, and flank pain because of urinary stasis. In most cases, diuretic renography and sequential sonographic studies can reliably differentiate obstructed from nonobstructed megaureters. In most nonobstructed megaureters, the hydroureteronephrosis diminishes gradually (Fig. 577.12). Truly obstructed megaureters require surgical treatment, with excision of the narrowed segment, ureteral tapering, and reimplantation of the ureter. The results of surgical reconstruction usually are good, but the prognosis depends on preexisting renal function and whether complications develop.

If differential renal function is normal (>45%) and the child is asymptomatic, it is safe to manage the patient with observation with serial US and periodic diuretic renography to monitor renal function and drainage. In children with grade 4 hydroureteronephrosis, prophylactic antimicrobial therapy should be prescribed, as these children are prone to upper UTI. If renal function deteriorates, upper urinary tract drainage slows, or UTI occurs, ureteral reimplantation is recommended. Approximately 25% of children with a nonrefluxing megaureter undergo ureteral reimplantation.

Prune-Belly Syndrome

Prune-belly syndrome, also called **triad syndrome** (lax abdominal wall muscles, urinary tract distention, intrabdominal testis) or **Eagle-Barrett syndrome,** occurs in approximately 1 in 40,000 births; 95% of affected children are male. The characteristic association occurs in a wide spectrum with deficient (hypoplastic) abdominal muscles, undescended testes, and urinary tract abnormalities (Fig. 577.13 and Table 577.6). Oligohydramnios and pulmonary hypoplasia are common complications in the perinatal period. Urinary tract abnormalities include massive (usually unobstructed) dilation of the ureters and upper tracts and a very large hypotonic bladder, with a patent urachus or a urachal diverticulum. Most patients have VUR. The prostatic urethra is usually dilated, and the prostate is hypoplastic. The anterior urethra may be dilated, resulting in a **megalourethra**. In severe cases, there is urethral stenosis or atresia. The kidneys show various degrees of dysplasia, and the testes are typically intraabdominal. Malrotation of the bowel is often present. Cardiac abnormalities occur in 10% of cases; >50% have abnormalities of the musculoskeletal system, including limb abnormalities and scoliosis. In the females, rare anomalies of the urethra, uterus, and vagina usually are present. Pathogenic variants in *FLNA* and possibly *MYOCD* or *HNF1β* have been reported; the disorder is usually sporadic, although rare instances of familial cases occur.

Many neonates with prune-belly syndrome have difficulty with effective bladder emptying because the bladder musculature is poorly

Table 577.5 Classification of Megaureter

REFLUXING		OBSTRUCTED		NONREFLUXING AND NONOBSTRUCTED	
PRIMARY	**SECONDARY**	**PRIMARY**	**SECONDARY**	**PRIMARY**	**SECONDARY**
Primary reflux	Neuropathic bladder	Intrinsic (primary obstructed megaureter)	Neuropathic bladder	Nonrefluxing, nonobstructive	Diabetes insipidus
Megacystic-megaureter syndrome	Hinman syndrome	Ureteral valve	Hinman syndrome		Infection
Ectopic ureter	Posterior urethral valves	Ectopic ureter	Posterior urethral valves		Persistent after relief of obstruction
Prune-belly syndrome	Bladder diverticulum Postoperative	Ectopic ureterocele	Ureteral calculus Extrinsic Postoperative		

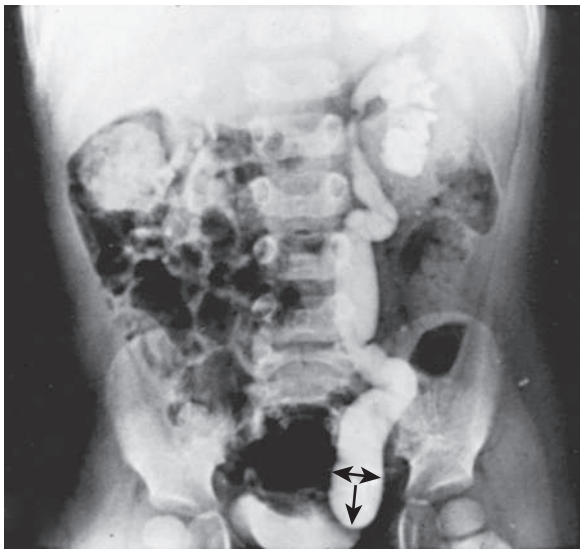


Fig. 577.11 Obstructed nonrefluxing megaureter. Excretory urogram in a female with a history of a febrile UTI. The right side is normal. The left side reveals hydroureteronephrosis with predominant dilation of the distal ureter. Note the characteristic appearance of the distal ureter. There was no vesicoureteral reflux. The diagnosis of obstruction was confirmed by diuretic renography.

developed, and the urethra may be narrowed. When no obstruction is present, the goal of treatment is the prevention of UTI with antibiotic prophylaxis. When obstruction of the ureters or urethra is demonstrated, temporary drainage procedures, such as a vesicostomy, can help to preserve renal function until the child is old enough for surgical reconstruction. Some children with prune-belly syndrome have been found to have classic or atypical PUVs. UTIs occur often and should be treated promptly. Correction of the undescended testes by orchidopexy can be difficult in these children because the testes are located high in the abdomen and surgery is best accomplished in the first 6 months of life. Reconstruction of the abdominal wall offers cosmetic and functional benefits.

The prognosis depends on the degree of pulmonary hypoplasia and renal dysplasia. One third of children with prune-belly syndrome are stillborn or die in the first few months of life because of pulmonary hypoplasia. As many as 30% of the long-term survivors develop end-stage renal disease from dysplasia or complications of infection or reflux and eventually require renal transplantation. Renal transplantation in these children offers good results.

Megacystis-microcolon-intestinal hypoperistalsis syndrome manifests with a dilated unobstructed bladder in the context of the more dominant gastrointestinal manifestations of intestinal pseudoobstruction (see Table 378.11 and Figs. 378.6 and 378.7). The abdominal muscles are normal, but abdominal distention is prominent. Associated pathogenic gene variants include *ACTG2* (~45%) as well as *MYH11*, *LOMD1*, *MYL9*, and *MYLK*; ~20% are unknown. Hydronephrosis is common, and most patients are female.

Bladder Neck Obstruction

Bladder neck obstruction usually is secondary to ectopic ureterocele, bladder calculi, or a tumor of the prostate (rhabdomyosarcoma). The manifestations include difficulty voiding, urinary retention, UTI, and bladder distention with overflow incontinence. Apparent bladder neck obstruction is common in cases of PUVs, but it seldom has any functional significance. Primary bladder neck obstruction is extremely rare.

Posterior Urethral Valves

The most common cause of severe obstructive uropathy in children is PUVs, affecting 1 in 8,000 males. The urethral valves are tissue leaflets fanning distally from the prostatic urethra to the external urinary sphincter. A slitlike opening usually separates the leaflets. Valves are of unclear embryologic origin and cause varying degrees of obstruction. Approximately 30% of patients experience end-stage renal disease or chronic renal insufficiency. The prostatic urethra dilates, and the bladder muscle undergoes hypertrophy. VUR occurs in 50% of patients, and distal ureteral obstruction can result from a chronically distended bladder or bladder muscle hypertrophy. Renal changes range from mild hydronephrosis to severe renal dysplasia; their severity depends on the severity of the obstruction and its time of onset during fetal development. As in other cases of obstruction or renal dysplasia, there may be oligohydramnios and pulmonary hypoplasia.

Affected males with PUVs often are discovered prenatally when maternal US reveals bilateral hydronephrosis, a distended bladder, and, if the obstruction is severe, oligohydramnios. Prenatal bladder decompression by percutaneous vesicoamniotic shunt or open fetal surgery has been reported. Experimental and clinical evidence of the possible benefits of fetal intervention is lacking, and few affected fetuses are candidates. Prenatally diagnosed PUVs, particularly when discovered in the second trimester, carry a poorer prognosis than those detected in the third trimester following a normal second-trimester fetal US. In the male neonate, PUVs are suspected when there is a palpably distended bladder and the urinary stream is weak. If the obstruction is severe and goes unrecognized during the neonatal period, infants can present later in childhood with failure to thrive because of uremia or sepsis caused by infection in the obstructed urinary tract. With lesser degrees of obstruction, children present later in life with difficulty in achieving diurnal urinary continence or with UTI. The diagnosis is established with a VCUG (Fig. 577.14) or by perineal US.

After the diagnosis is established, renal function and the anatomy of the upper urinary tract should be carefully evaluated. In the healthy neonate, a small polyethylene feeding tube (No. 5 or No. 8 French) is inserted in the bladder and left for several days. Passing the feeding tube may be difficult because the tip of the tube can coil in the prostatic

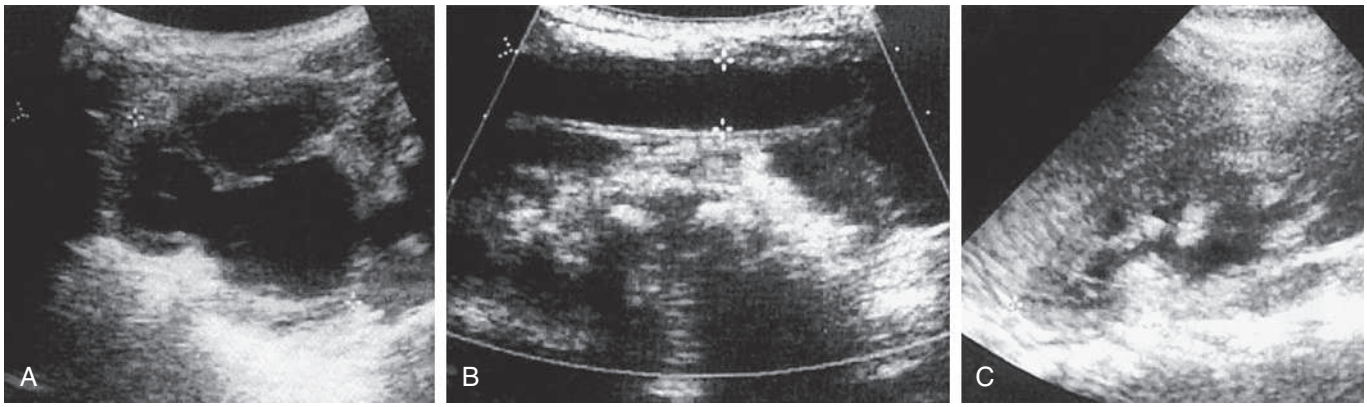


Fig. 577.12 Neonate with primary nonrefluxing megaureter. **A,** Renal US shows grade 4 hydronephrosis. **B,** Dilated ureter. Renal scan showed equal function with the contralateral kidney and satisfactory drainage with diuresis stimulation. **C,** Follow-up US at 10 mo shows complete resolution of hydronephrosis.

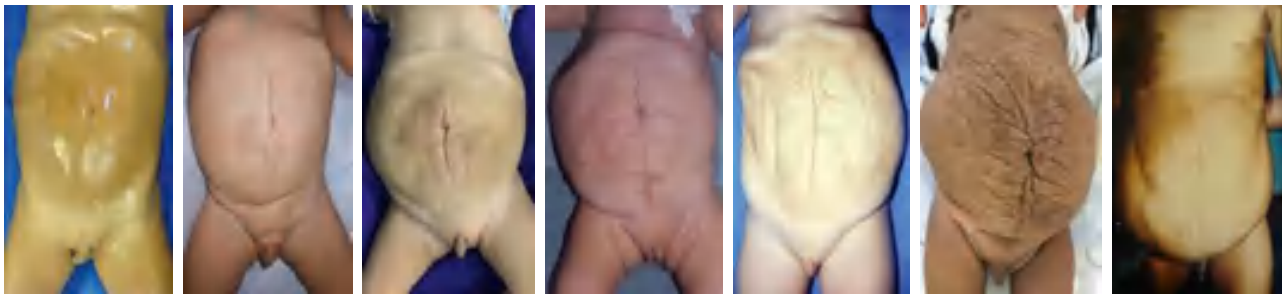


Fig. 577.13 Abdominal wall features of prune-belly syndrome, with increasing flaccidity and cutaneous wrinkles, including pot-belly appearance in older age. *(From Lopes RI, Baker LA, Dénes FT. Modern management of and update on prune belly syndrome. J Pediatr Urol. 2021;17:548–554. Fig. 1.)*

urethra. A sign of this problem is that urine drains around the catheter rather than through it. A Foley (balloon) catheter *should not be used*, because the balloon can cause severe bladder spasm, which can produce severe ureteral obstruction.

If the serum creatinine level remains normal or returns to normal, treatment consists of transurethral ablation of the valve leaflets, which is performed endoscopically under general anesthesia. If the urethra is too small for transurethral ablation, temporary vesicostomy is preferred, in which the dome of the bladder is exteriorized on the lower abdominal wall. When the child is older, the valves may be ablated and the vesicostomy closed.

If the serum creatinine level remains high or increases despite bladder drainage by a small catheter, secondary ureteral obstruction, irreversible renal damage, or renal dysplasia should be suspected. In such cases, a vesicostomy should be considered. Cutaneous pyelostomy rarely affords better drainage compared with cutaneous vesicostomy, and the latter also allows continued bladder growth and gradual improvement in bladder wall compliance.

In the septic and uremic infant, lifesaving measures must include prompt correction of the electrolyte imbalance and control of the infection by appropriate antibiotics. Drainage of the upper tracts by percutaneous nephrostomy and hemodialysis may be necessary. After the patient's condition becomes stable, evaluation and treatment may be undertaken. PUVs are diagnosed in some older males because of a poor stream, diurnal incontinence, or a UTI; these males are treated by primary valve ablation.

Favorable prognostic factors include a normal prenatal US between 18 and 24 weeks of gestation, a serum creatinine level <0.8-1.0 mg/dL after bladder decompression, and visualization of the corticomedullary junction on renal sonography. In several situations, a "popoff valve" can occur during urinary tract development, which preserves the integrity of one or both kidneys. For example, 15% of males with PUVs have unilateral reflux into a nonfunctioning dysplastic kidney, termed the **VURD syndrome** (valves, unilateral reflux, dysplasia). In these males, the high bladder pressure is dissipated into the nonfunctioning kidney, allowing normal development of the contralateral kidney. In newborn males with urinary ascites, the urine leaks out from the obstructed collecting system through the renal fornices, allowing normal development of the kidneys. Unfavorable prognostic factors include the presence of oligohydramnios in utero, identification of hydronephrosis before 24 weeks of gestation, a serum creatinine level >1.0 mg/dL after bladder decompression, identification of cortical cysts in both kidneys, and persistence of diurnal incontinence beyond 5 years of age.

The prognosis in the newborn is related to the child's degree of pulmonary hypoplasia and potential for recovery of renal function. Severely affected infants often are stillborn. Of those who survive the neonatal period, approximately 30% eventually require kidney transplantation, and 15% have renal insufficiency. In some series, kidney transplantation in children with PUVs has a lower success rate than does transplantation in children with normal bladders, presumably because of the adverse influence of altered bladder function on graft function and survival.

After valve ablation, antimicrobial prophylaxis is beneficial in preventing UTI, because hydronephrosis to some degree often persists for many years. These males should be evaluated annually with a renal US, physical examination including assessment of somatic growth and blood pressure, urinalysis, and determination of serum levels of electrolytes. Many individuals have significant polyuria resulting from a concentrating defect secondary to prolonged obstructive uropathy. If these children acquire a systemic illness with vomiting and/or diarrhea, urine output cannot be used to assess their hydration status. They

Table 577.6 The PBS RUBACE Severity Scoring Rubric

Eagle-Barrett syndrome PBS triad ("RUBAC") Max score: 16					Extra-genitourinary manifestations ("E") Max score: 15				
No subcategory points are awarded for normal anatomy with absent pathology					No subcategory points are awarded for normal anatomy with absent pathology				
Renal Max score: 6	**Ureteral Max score: 3**	**Bladder/outlet Max score: 3**	**Abdominal wall Max score: 2**	**Cryptorchidism Max score: 2**	**Neurologic Max score: 3**	**Cardiac Max score: 3**	**Gastrointestinal Max score: 3**	**Musculoskeletal Max score: 3**	**Respiratory Max score: 2**
1 pt: G1-G2: Structural damage (dilation, dysplasia, scarring) with preserved GFR ≥ 60	**1 pt**: Low grade or absent VUR, or distal ureter 4–10mm	**1 pt**: Urotherapy required to empty bladder, or bladder size is 100–200% of normal	**1 pt**: Can do "sit-up" exercise before or after abdomino-plasty, musculature mostly intact, minimal laxity, or mild/nonconvincing prune appearance	**1 pt**: History of or current unilateral or palpable undescended testicle(s), or patient is female		**1 pt**: Congenital septal defects (PDA, ASD, VSD) which are spontaneously resolved	**1 pt**: Mild to moderate constipation, managed with diet or laxatives	**1 pt**: Mild facies, abnormally shaped fingers or toes (no loss of function), or rib flaring	**1 pt**: Minimal respiratory support at birth, some difficulty coughing, mild intermittent asthma, or mild reactive airway disease
2 pts: G3a-b: Kidney damage with decreased GFR 30–59 **3 pts**: G4: Severe loss of kidney function with GFR 15–29	**2 pts**: Persistent high grade VUR (no surgery), s/p lower tract ureteral reconstruction, or distal ureter 1–2 cm	**2 pts**: Urethral-catheterization or pharm required to empty, bladder size >200% normal, or patient takes antibiotic prophylaxis for recurrent UTI	**2 pts**: Severe abdominal laxity with obvious thinning of abdominal wall, classic prune appearance, or s/p abdominoplasty + cannot do a "sit-up"	**2 pts**: History of or current bilateral nonpalpable testes		**2 pts**: Small septal defects which are not spontaneously resolved, minimal L to R shunting, or PDA requiring surgical management	**2 pts**: MACE/cecostomy required, or malrotation s/p Ladd's	**2 pts**: Scoliosis, hip dysplasia, club or rockerbottom foot, genu valgum, pectus excavatum or carinum	**2 pts**: Persistent/ moderate asthma, frequent respiratory tract infections (≥3/year), or ≥2 hospitalizations for pneumonia
					PBS-plus or congenital/genetic syndrome or association				
4 pts: Renal failure with GFR <15, or on dialysis or s/p renal transplant **Additional points for young age:** If patient is <2 years, add +2 pts and if patient is <13 years, add +1 pt	**3 pts**: Persistent high grade VUR despite surgery, distal ureter 2+ cm girth, or current diverting ureterostomy or nephrostomy	**3 pts**: Current surgical diversion (e.g., s/p tube, vesicostomy, APV), urethral atresia, or megalourethra requiring repair			**3 pts**: Seizures, tethered cord, spina bifida, hearing loss, intellectual delay, autism, or severe neurologic condition not otherwise specified	**3 pts**: Severe congenital or cyanotic heart disease-Tetralogy of Fallot, left-sided obstructive lesions, reversed shunt, CHF or severe cardiologic conditions not otherwise specified	**3 pts**: Required surgical bowel diversion (e.g., imperforate anus, anal atresia), gastrointestinal malignancy (e.g., hepatoblastoma), or severe GI condition not otherwise specified	**3 pts**: Arthrogryposis, muscular dystrophy, or severe musculoskeletal malformation not otherwise specified	**3 pts**: Ventilator-dependent >1 week, tracheostomy, history of pneumothorax, or severe asthma
Total triad RUBAC score: _____					**Total E score: _____**				
Total triad RUBAC score _____ + Total E score _____ = Total RUBACE score _____									

PBS, Prune-belly syndrome; RUBACE, renal-ureter-bladder-abdominal wall-cryptorchidism-extra GU anomalies.
From Wong DG, Arevalo MK, Passoni NM, et al. Phenotypic severity scoring system and categorization for prune belly syndrome: application to a pilot cohort of 50 living patients. *BJU Int.* 2019;123:130–139. Table 1.

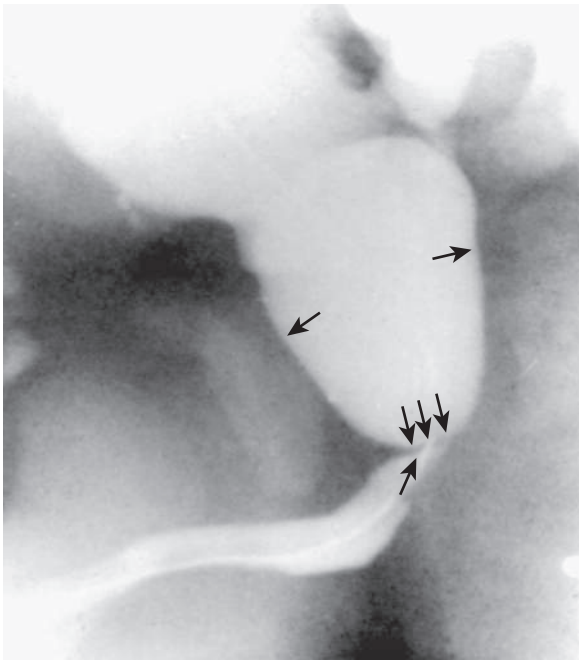


Fig. 577.14 VCUG in an infant with posterior urethral values. Note the dilation of the prostatic urethra and the transverse linear filling defect corresponding to the valves *(arrows)*.

can become dehydrated quickly, and there should be a low threshold for hospital admission for intravenous rehydration. Some of these patients have renal tubular acidosis, requiring oral bicarbonate therapy. If there is any significant degree of renal dysfunction, growth impairment, or hypertension, the child should be followed closely by a pediatric nephrologist. When VUR is present, expectant treatment and prophylactic doses of antibacterial drugs are advisable. If breakthrough UTI occurs, surgical correction should be undertaken.

After treatment, males with PUVs often do not achieve diurnal urinary continence as early as other males. Incontinence can result from a combination of factors, including uninhibited bladder contractions, poor bladder compliance, bladder atonia, bladder neck dyssynergia, or polyuria. Often these males require urodynamic evaluation with urodynamics or videourodynamics to plan therapy. Individuals with a poorly compliant bladder are at significant risk for ongoing renal damage, even in the absence of infection. Overnight catheter drainage has been shown to be beneficial in males with polyuria and can help preserve renal function. Urinary incontinence usually improves with age, particularly after puberty. Meticulous attention to bladder compliance, emptying, and infection can improve results in the future.

Urethral Atresia

The most severe form of obstructive uropathy in males is urethral atresia, a rare condition. In utero there is a distended bladder, bilateral hydroureteronephrosis, and oligohydramnios. In most cases, these infants are stillborn or succumb to pulmonary hypoplasia. Rare males with prune-belly syndrome also have urethral atresia. If the urachus is patent, oligohydramnios is unlikely, and the infant usually survives.

Urethral reconstruction is difficult, and most patients are managed with continent urinary diversion.

Urethral Hypoplasia

Urethral hypoplasia is a rare form of obstructive uropathy in males that is less severe than urethral atresia. In urethral hypoplasia, the urethral lumen is extremely small. Neonates with urethral hypoplasia typically have bilateral hydronephrosis and a distended bladder. Passage of a small pediatric feeding tube through the urethra is difficult or impossible. Usually a cutaneous vesicostomy must be performed to relieve upper urinary tract obstruction, and the severity of renal insufficiency is variable. The most severely affected males have end-stage renal disease. Treatment includes urethral reconstruction, gradual urethral dilation, or continent urinary diversion.

Urethral Stricture

Urethral strictures in males usually result from urethral trauma, either iatrogenic (catheterization, endoscopic procedures, previous urethral reconstruction) or accidental (straddle injuries, pelvic fractures). Because these lesions can develop gradually, the decrease in force of the urinary stream is seldom noticed by the child or the parents. More commonly, the obstruction causes symptoms of bladder instability, hematuria, or dysuria. Catheterization of the bladder usually is impossible. The diagnosis is made by a **retrograde urethrogram,** in which contrast is injected toward the bladder through a catheter inserted into the distal urethra. US also has been used to diagnose urethral strictures. Endoscopy is confirmatory. Endoscopic treatment of short strictures by direct vision urethrotomy is often successful initially and results in a profoundly improved urinary stream, but strictures are prone to recur. Longer strictures surrounded by periurethral fibrosis often require urethroplasty. Repeated endoscopic procedures should be avoided as they cause additional urethral damage. Noninvasive measurement of the urinary flow rate and pattern is useful for diagnosis and follow-up.

In females, true urethral strictures are rare because the female urethra is protected from trauma, particularly in childhood.

Anterior Urethral Valves and Urethral Diverticula in the Male

Anterior urethral valves are rare. The obstruction is not obstructing valve leaflets, as occurs in the posterior urethra. Rather, it is a urethral diverticulum in the penile urethra that expands during voiding. Distal extension of the diverticulum causes extrinsic compression of the distal penile urethra, causing urethral obstruction. There is usually a soft mass on the ventral surface of the penis at the penoscrotal junction. In addition, the urinary stream is typically weak, and the physical findings associated with PUVs are often present. The diverticulum may be small and minimally obstructive or, in other cases, may be severely obstructive and cause renal insufficiency. The diagnosis is suspected on physical examination and is confirmed by VCUG. Treatment involves open excision of the diverticulum or transurethral excision of the distal urethral cusp. Urethral diverticula occasionally occur after extensive hypospadias repair.

Fusiform dilation of the urethra or megalourethra can result from underdevelopment of the corpus spongiosum and support structures of the urethra. This condition is commonly associated with prune-belly syndrome.

Male Urethral Meatal Stenosis

See Chapter 581 for information on urethral meatal stenosis in males.

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Chapter 578

Anomalies of the Bladder

Heather N. Di Carlo and Chad B. Crigger

BLADDER EXSTROPHY

Exstrophy of the urinary bladder occurs in approximately 1 in 35,000-40,000 births with a male:female ratio of 2:1. The severity ranges from simple **epispadias** (in males) to complete exstrophy of the cloaca involving exposure of the entire hindgut and the bladder **(cloacal exstrophy)**.

Considering the range of defects associated with exstrophy, prenatal diagnosis is challenging. Accurately diagnosing exstrophy (and its subtypes) is paramount in properly counseling families. Proper prenatal diagnosis allows for planning that may optimize postnatal medical and surgical management. Classically, the diagnosis was suspected on prenatal ultrasound. For instances in which the diagnosis remains uncertain, as for midline abdominal defects such as exstrophy versus gastroschisis or omphalocele, fetal magnetic resonance imaging (fMRI) may help elucidate the correct diagnosis.

Clinical Manifestations

Anomalies of the bladder are hypothesized to result when the mesoderm fails to invade the cephalad extension of the cloacal membrane; the timing and extent of this failure determines the degree of the anomaly. In classic bladder exstrophy (Fig. 578.1), the bladder protrudes from the abdominal wall, and its mucosa is exposed. The umbilicus is displaced downward, the pubic rami are widely separated in the midline, and the rectus muscles are separated. In males, there is complete epispadias with dorsal chordee, and the overall penile length is approximately half that of unaffected males. The scrotum typically is separated slightly from the penis and is wide and shallow. Undescended testes and inguinal hernias are common. Females may also have epispadias, with separation of the two halves of the clitoris and wide separation of the labia. The anus is displaced anteriorly in both sexes, and there may be rectal prolapse. The pubic rami are widely separated.

The consequences of untreated bladder exstrophy are total urinary incontinence and an increased incidence of bladder cancer, usually adenocarcinoma. The external and internal genital deformities cause sexual disability in both sexes, particularly in males. The wide separation of the pubic rami causes a characteristic broad-based gait but no significant lasting disability. In classic bladder exstrophy, the upper urinary tracts usually are normal at birth.

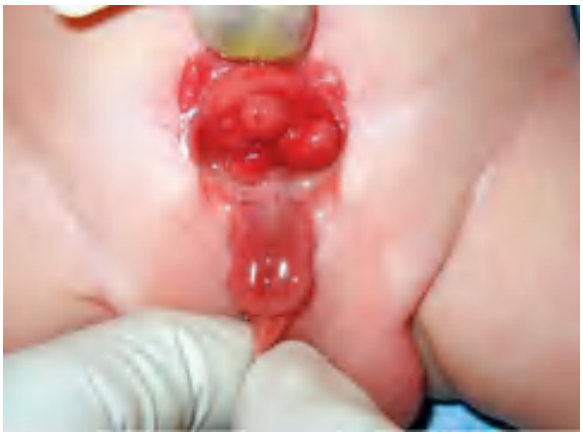

Fig. 578.1 Classic bladder exstrophy in a newborn male. The bladder is exposed in the midline, the umbilical cord is displaced caudad, the penis is epispadiac, and the scrotum is broad.

Treatment

Management of bladder exstrophy should start at birth. The bladder should be covered with plastic wrap to keep the bladder mucosa moist. Saline may be gently irrigated as needed to moisten the bladder template. *Application of gauze or petroleum-gauze to the bladder mucosa should be avoided, because significant inflammation will result.* The infant should be transferred promptly to a center with pediatric urology and pediatric anesthetic support for newborns with complex anomalies. These children are prone to *latex allergy,* and latex precautions should be practiced from birth, both in the nursery and in the operating room.

There are two surgical approaches: staged reconstruction and total single-stage reconstruction. Most babies also undergo bilateral iliac osteotomy, which allows the pubic symphysis to be approximated, which supports the bladder closure. In a staged reconstruction, the initial stage is bladder closure, the second stage (in males) is epispadias repair, and the final stage is bladder neck reconstruction. The single-stage reconstruction attempts to reconstruct the entire malformation in a single procedure. When this operation is performed in the newborn, there is an increased risk of intraoperative penile injury and postoperative hydronephrosis compared with the staged reconstruction. The complication rate is high with both approaches, and there is no consensus on which is better.

Although bladder closure within the first 48 hours of life has been the historical standard, many centers of excellence now defer the procedure until 1-2 weeks of life to ensure that the appropriate multidisciplinary surgical and anesthetic teams are available. During bladder exstrophy closure, the abdominal wall is mobilized and the pubic rami are brought together in the midline following pelvic osteotomy. Early bladder closure can be performed in almost all neonates with classic bladder exstrophy. Treatment should be deferred in select situations including when surgical therapy would be excessively risky or complex, such as a premature baby, or if performed by inexperienced surgeons. In the staged approach, in males, epispadias repair usually is performed around age 1 or 2 years. At this point the child has total urinary incontinence because there is no functional external urinary sphincter. Most infants with bladder exstrophy have vesicoureteral reflux and should receive antibiotic prophylaxis. Typically, the bladder capacity is monitored every 12-24 months using cystoscopy with cystogram under anesthesia. The final stage of reconstruction involves creation of a sphincter muscle for bladder control and correction of vesicoureteral reflux. This is usually performed when the child is 3-6 years old with a bladder capacity of at least 80-90 mL, and the child must have gained rectal sphincter control.

Total single-stage reconstruction includes newborn closure of the bladder and bladder neck narrowing, abdominal wall closure, and, in males, correction of epispadias using a technique of penile disassembly. This involves separating the two corpora cavernosa and the midline urethra into three parts via radical mobilization. Postoperatively, the infant's upper urinary tract is monitored closely for possible development of hydronephrosis and infection. Comparison of outcomes between the multistage and single-stage approaches is ongoing.

At puberty pubic hair is often distributed to the sides of the external genitals. A monsplasty can be performed during adolescence to provide a normal escutcheon.

Long-Term Prognosis

Long-term management of individuals born with bladder exstrophy includes monitoring the upper urinary tract appearance and function for any deterioration and infection, as well as assessing continence. As these patients age, erectile function is assessed in males, and, later on in adults, sexual function and fertility are evaluated.

The previously described plan of treatment has yielded a continence rate of 60–70% in a few centers, with <15% risk of deterioration of the upper urinary tract. This continence rate reflects not only successful reconstruction but also the quality and size of the bladder. From a functional standpoint, the reconstructed bladder neck does not relax during voiding as in a normal child; instead the patient must void by assisted techniques such as the Valsalva maneuver or Credé maneuver.

Children who remain incontinent for more than 1 year after bladder neck reconstruction or those who are ineligible for bladder neck reconstruction because of small bladder capacity are candidates for an alternative reconstructive procedure to achieve dryness. In select cases, cystoscopic injection of bulking agents such as dextranomer or polydimethylsiloxane microspheres into the bladder neck can provide sufficient bladder neck coaptation and resistance to establish continence. Alternatively, if the child is not a candidate for endoscopic therapy, options include:

- Augmentation cystoplasty, in which the bladder is enlarged with a patch of small or large bowel to increase its capacity.
- Creation of a neobladder out of a small or large bowel segment with placement of a continent abdominal stoma through which clean, intermittent catheterization can be performed.
- Placement of an artificial urinary sphincter, with possible combined augmentation cystoplasty.
- Ureterosigmoidostomy, in which the ureters are detached from the bladder and sutured to the sigmoid colon; individuals void urine and stool from the rectum and rely on their anal sphincter for continence. This approach does not require many resources in surgical technique or long-term care (such as ostomy supplies).
- Mainz II procedure, in which the sigmoid colon is reconfigured into a "bladder" into which the ureters are connected; the patient voids 3-6 times daily through the rectum, and the stool tends to be more solid.

Ureterosigmoidostomy carries a significant risk of chronic pyelonephritis (see Chapter 575), upper urinary tract damage, metabolic acidosis resulting from absorption of hydrogen ion and chloride in the intestine, and at least a 15–22% long-term risk of colon carcinoma. Patients from less-developed countries often undergo the Mainz II procedure because the continence rate is high and pyelonephritis and upper tract changes are relatively uncommon.

Late follow-up has shown that although adult males with exstrophy have a penis that is half the normal length, they usually experience satisfactory sexual function. Fertility has been low, possibly because of iatrogenic injury to the secondary sexual organs during reconstruction. With artificial reproductive technology, nearly all affected men can be fertile. In adult females, fertility is not affected, but uterine prolapse during pregnancy is a problem. In adult females who have undergone a continent urinary diversion, delivery by cesarean section is usually necessary.

OTHER EXSTROPHY ANOMALIES

More rarely, children have a more severe form of exstrophy, cloacal exstrophy, which occurs in 1 in 400,000 live births. In addition to an exposed bladder, gastrointestinal manifestations typically include omphalocele, an imperforate anus, and a short bowel, resulting in short bowel syndrome (see Chapter 385.6). It is the most devastating anomaly managed by pediatric urologists. Approximately 50% of patients have an upper urinary tract anomaly, and 50% have spina bifida (see Chapter 631.2). Children with cloacal exstrophy do not achieve normal urine or stool continence. Reconstructive techniques result in a satisfactory outcome in most patients with permanent urinary diversion (either ileal conduit or continent urinary diversion) and a colostomy. Because the penis in males with cloacal exstrophy usually is diminutive, genital reconstruction in males with cloacal exstrophy has been unsatisfactory. Until recently, many specialists recommended assigning a female gender to such infants, but currently there is debate as to whether these children, who have a 46,XY karyotype and brain androgen imprinting in utero, can have a satisfactory female gender identity (see Chapter 153). Decisions regarding gender assignment should be made jointly by the physicians caring for the infant (surgical team, pediatric endocrinologist, child psychiatrist, and ethicist) and the family. Current practice by pediatric urologists is to reconstruct genitalia in a manner congruent with the genotype when at all possible, and after extensive counseling with the patient's family.

Epispadias is at the less severe end of the spectrum of exstrophy anomalies, affecting approximately 1 in 117,000 males and 1 in 480,000 females. In males, the diagnosis is obvious because the prepuce is distributed primarily on the ventral aspect of the penile shaft and the urethral meatus is on the dorsum of the penis. Distal epispadias in males (Fig. 578.2) usually is associated with normal urinary control and normal upper urinary tracts and should be repaired by 6-12 months of age. In females, the clitoris is bifid, and the urethra is split dorsally (Fig. 578.3). In more severely affected males and in all females with

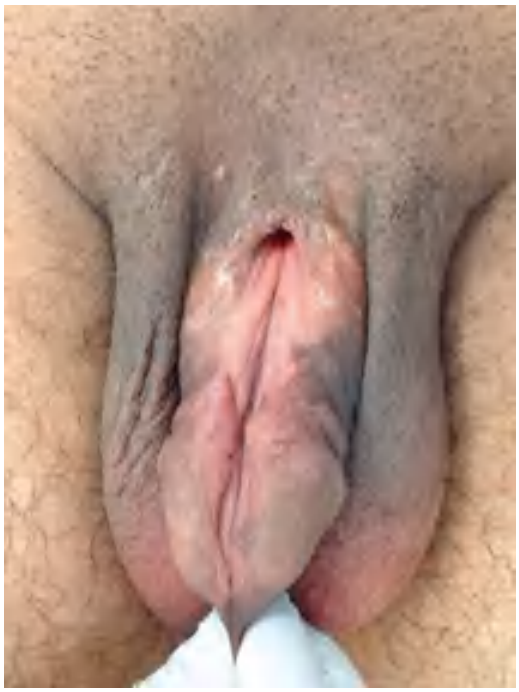

Fig. 578.2 Adolescent male with penopubic epispadias.

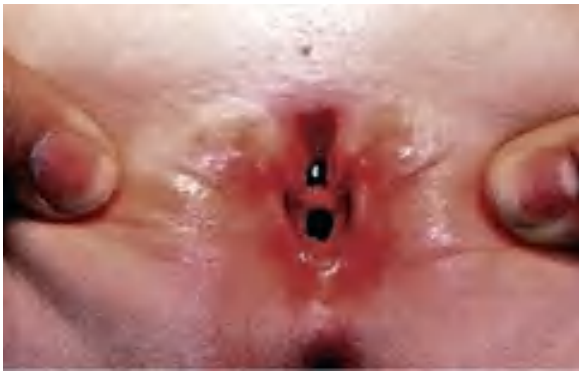

Fig. 578.3 Female with complete epispadias. *(From Gearhart JP, Rink RC, Mouriquand PDE, eds. Pediatric Urology, 2nd ed. Philadelphia: Saunders; 2010.)*

epispadias, there is total urinary incontinence because the sphincter is incompletely formed along with a wide separation of the pubic rami. These children require surgical reconstruction of the bladder neck, similar to the final management stage in children with classic bladder exstrophy.

BLADDER DIVERTICULA

Bladder diverticula develop as herniations of the bladder mucosa between defects of bladder smooth muscle fibers. Primary bladder diverticula usually develop at the ureterovesical junction and may be associated with vesicoureteral reflux, because the diverticulum interferes with the normal flap-valve attachment between the ureter and bladder. In rare circumstances, the diverticulum is so large that it interferes with normal micturition by obstructing the bladder neck. Bladder diverticula also commonly are associated with distal urethral obstructions such as posterior urethral valves or neurogenic bladder dysfunction. They occur commonly in children with connective tissue disorders, including Williams syndrome, Ehlers-Danlos syndrome, and Menkes syndrome (Fig. 578.4). Small diverticula require no treatment other than that of the primary disease, whereas large diverticula can contribute to inefficient voiding, residual urine, urinary stasis, and urinary tract infections and should be excised.

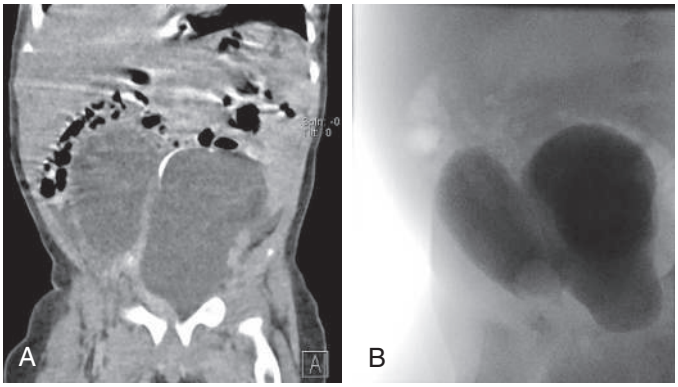

Fig. 578.4 Six-mo-old male with abdominal mass. Ultrasound showed a large fluid-filled mass and normal kidneys. **A,** CT scan shows large bladder diverticulum on right side with ureter coursing between the diverticulum and the bladder. **B,** Voiding cystourethrogram demonstrates no reflux and large diverticulum on left side. Managed with diverticulectomy.

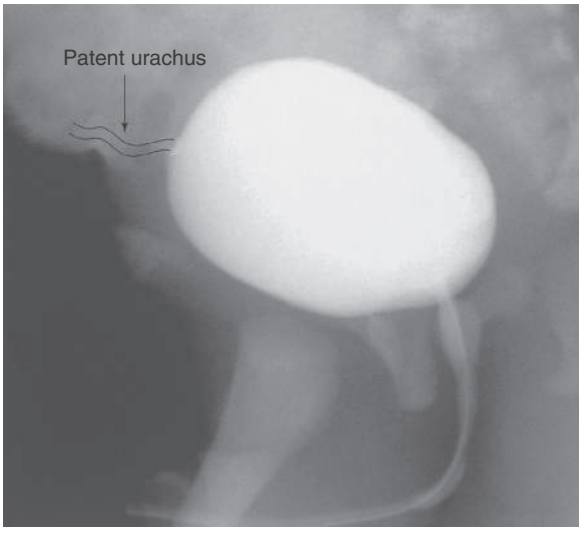

Fig. 578.5 Patent urachus. Vesicourethrogram image of patent urachus in a newborn. Retrograde contrast filling of patent canal with contrast pooling in umbilicus. *(From Partin AW, Dmochowski RR, Kavoussi LR, Peters C., eds. Campbell-Walsh Urology, 12th ed. Philadelphia: Elsevier; 2021. Fig. 30-7.)*

URACHAL ANOMALIES

The urachus is an embryologic canal connecting the dome of the fetal bladder with the allantois, a structure that contributes to the formation of the umbilical cord. The lumen of the urachus is normally obliterated during embryonic development, transforming the urachus into a solid cord. Urachal abnormalities are more common in males than in females. A **patent urachus** can occur as an isolated anomaly, or it may be associated with prune-belly syndrome or posterior urethral valves (see Chapter 577; Fig. 578.5). A patent urachus results in continuous urinary drainage from the umbilicus and treatment involves excising the tract. Another urachal anomaly is the **urachal cyst,** which can become infected. Typical symptoms and physical findings include suprapubic pain, fever, irritative voiding symptoms, and an infraumbilical mass, which can be erythematous. Diagnosis is made by ultrasonography or CT (Fig. 578.6). Treatment is intravenous antibiotic therapy and drainage and excision. Other urachal anomalies include the **vesicourachal diverticulum,** which is a diverticulum of the bladder dome, and **umbilical-urachal sinus,** which is a blind external sinus that opens at the umbilicus. These lesions should be excised.

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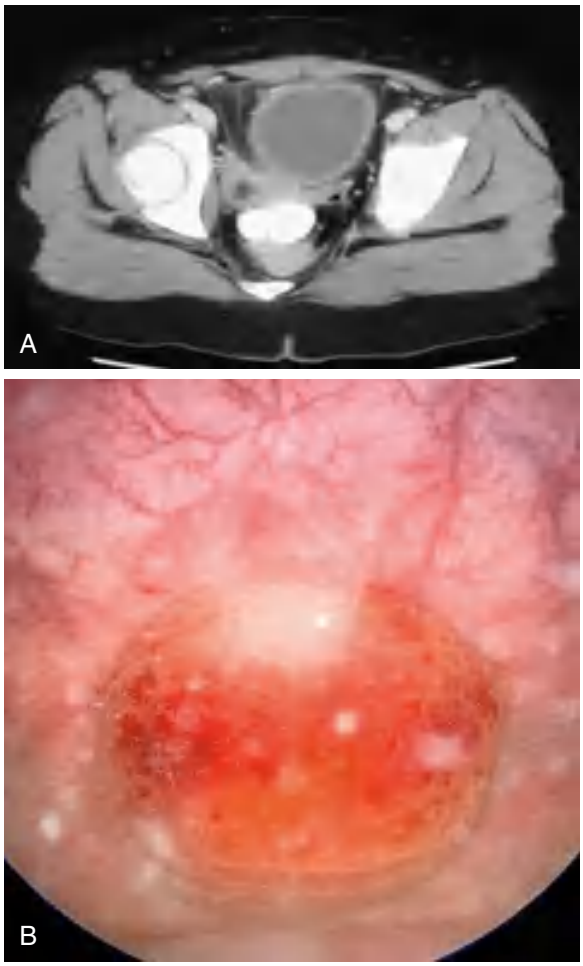

Fig. 578.6 A, CT scan demonstrating infected urachal abscess in an 8-yr-old child. The condition was managed by drainage and excision. B, Cystoscopic view of 10-yr-old child with new-onset daytime frequency and incontinence secondary to infected urachal cyst.

Chapter 579

Neuropathic Bladder

Heather N. Di Carlo and Chad B. Crigger

Neuropathic bladder dysfunction in children is usually congenital, generally resulting from neural tube defects or other spinal abnormalities (see Chapter 754). Acquired diseases and traumatic lesions of the spinal cord are less common (see Chapter 751). Central nervous system tumors, sacrococcygeal teratoma, spinal abnormalities associated with imperforate anus (see Chapter 392), and spinal cord trauma also can result in abnormal innervation of the bladder and/or sphincter (Table 579.1).

NEURAL TUBE DEFECTS

Neural tube defects, resulting from failure of the neural tube to close spontaneously between the third and fourth week in utero, result in abnormalities of the vertebral column that affect spinal cord function, including **spina bifida occulta**, **myelomeningocele,** and **meningocele**

Table 579.1 Causes of Neuromuscular Dysfunction of the Lower Urinary Tract

CONGENITAL
Neural tube defect
Occult forms of neural tube defect (lipomeningocele and other spinal dysraphisms)
Sacral agenesis
Anorectal malformations
ACQUIRED
Extensive pelvic surgery
Central nervous system disorders
Cerebral palsy
Conditions of the brain (tumors, infarcts, encephalopathies)
Spinal cord insults
Trauma
Transverse myelitis

From Partin AW, Dmochowski RR, Kavoussi LR, Peters CW, eds. *Campbell-Walsh Urology*, 12th ed. Philadelphia: Elsevier; 2021: Box 34-1.

(see Chapters 631.2, 631.3, and 631.4). Specialized medical centers in the United States have performed antenatal myelomeningocele closure. Long-term results from one large clinical trial of **in utero closure** have not shown a definite improvement in lower urinary tract function, although some children have demonstrated nearly normal bladder function. Overall, this trial has demonstrated a significant reduction in the need for ventriculoperitoneal shunting and improved performance on measures of self-care, motor function, and mobility.

Clinical Manifestations and Diagnosis

The most important urologic consequences of neuropathic bladder dysfunction associated with neural tube defects are urinary incontinence (see Chapter 580), urinary tract infections (UTIs; see Chapter 575), and hydronephrosis from vesicoureteral reflux (see Chapter 576) or detrusor-sphincter dyssynergia (see Chapter 580). Pyelonephritis and renal functional deterioration (see Chapter 575) are common causes of premature death in affected patients.

In the neonate, renal ultrasonography, assessment of postvoiding residual urine volumes, and a voiding cystourethrogram are performed after closure of the myelomeningocele as approximately 10–15% of newborns with myelomeningocele have hydronephrosis, and renal malformations are common; 25% have vesicoureteral reflux. A **urodynamic** study also should be performed. In this study, the bladder is filled with saline, and the bladder volume, bladder pressure, abdominal pressure, and sphincter tone are measured until the patient voids. During bladder filling, the bladder might show (1) uninhibited (premature) contractions (termed hyperreflexia) at low volumes, (2) normal bladder volume with contraction at an appropriate volume, or (3) atonia (lack of bladder contraction). Bladder compliance or elasticity also may be abnormal (i.e., abnormally high bladder pressure during bladder filling). The sphincter can show (1) normal tonicity with relaxation during bladder contraction, (2) reduced or absent tonicity, or (3) normal or increased tonicity that increases significantly during a bladder contraction (termed **detrusor-sphincter dyssynergia**; Fig. 579.1).

Renal Damage

Renal damage usually results from detrusor-sphincter dyssynergia. This dyssynergia causes functional obstruction of the bladder outlet, leading to bladder muscle hypertrophy and trabeculation, high intravesical pressure, and transmission of this high pressure into the upper urinary tracts, causing hydronephrosis (Fig. 579.2). Vesicoureteral reflux and UTI compound this problem, but severe hydronephrosis can result without reflux. Treatment includes reduction of bladder pressure with anticholinergic drugs (e.g., oxybutynin, 0.2 mg/kg/dose up to three times per day) and **clean intermittent catheterization** every 3-4 hours. If the child has vesicoureteral reflux or UTI, antimicrobial prophylaxis also is prescribed.

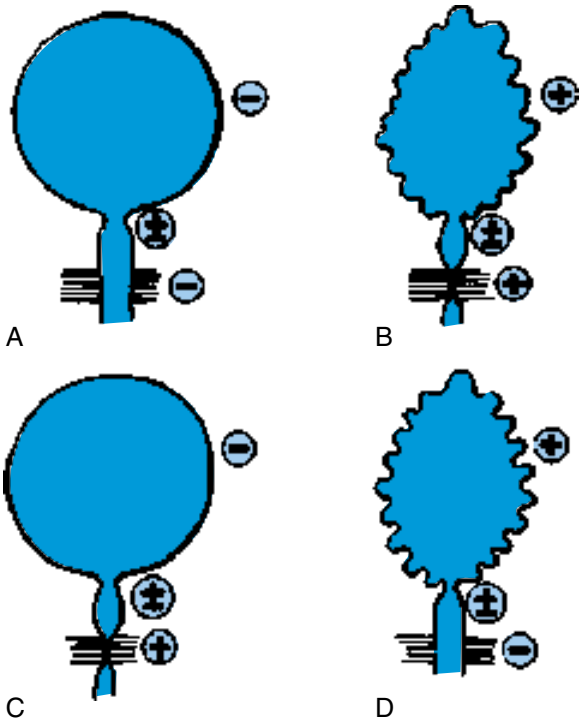

Fig. 579.1 Grouping of neuropathic bladder dysfunction according to the innervation, tonicity, and coordination of the detrusor and sphincters described by Guzman. This grouping is based on data from imaging studies, cystometrography, and electromyography of the sphincters. Patients in group B are at risk of developing reflux and hydronephrosis. For guidance in the treatment of incontinence, group A patients benefit from procedures that increase outlet resistance, group B patients from anticholinergics or bladder augmentation surgery, and group C patients from intermittent catheterization. Group D patients require both increased outlet resistance and pharmacologic or surgical bladder enlargement. Most patients require intermittent catheterization to empty. *(Modified from Gonzalez R. Urinary incontinence. In Kelalis PK, King LR, Belman AB, eds. Clinical Pediatric Urology. Philadelphia: Saunders; 1992. p. 387.)*

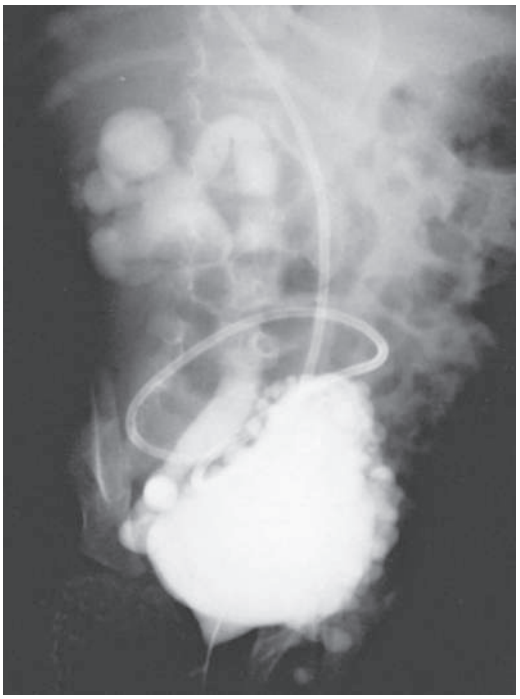

Fig. 579.2 Voiding cystourethrogram in an infant with myelodysplasia shows a severely trabeculated bladder with multiple diverticula and grade V (out of V) right vesicoureteral reflux. Evaluation showed severe detrusor-sphincter dyssynergia.

Temporary urinary diversion by cutaneous vesicostomy is an alternative in the newborn or infant with severe reflux, if intermittent catheterization is difficult, or if anticholinergic medications are not well tolerated. Another option for treating the severely trabeculated bladder is transurethral injection of botulinum toxin (Botox) into the detrusor muscle, which reduces bladder hypertonicity for approximately 6 months and often needs to be repeated. A different approach in these children is to temporarily inactivate the tight sphincter by urethral overdilation or transurethral injection of botulinum toxin into the sphincter. In children with upper tract changes, continuous overnight bladder drainage allows significant bladder relaxation and can reduce bladder wall thickening and lessen hydronephrosis.

Clean intermittent catheterization and anticholinergic therapy cure reflux in up to 80% of children with grade I or II reflux. Children with more severe reflux often require subureteral endoscopic injection therapy (see Chapter 576) or open antireflux surgery followed by intermittent catheterization and anticholinergic drugs. In older children with myelomeningocele with high-grade reflux, UTI, and hydronephrosis, augmentation enterocystoplasty (enlarging the bladder with a patch of intestine) with intermittent catheterization may be necessary. This intervention allows a normal-capacity bladder with low bladder pressure and effective drainage of the bladder.

Urinary Incontinence

Incontinence in the child with neuropathic bladder can result from total or partial denervation of the sphincter, bladder hyperreflexia, poor bladder compliance, chronic urinary retention, or a combination of these factors.

Incontinence is often addressed at 4-5 years of age and is tailored to the individual child. Nearly all children require clean intermittent catheterization to stay dry. This technique allows efficient bladder emptying with minimal risk of symptomatic UTI. *The urinary tract should be reevaluated with renal ultrasonography, a voiding cystourethrogram, and a urodynamic study (including bladder capacity) prior to initiation of an intermittent catheterization regimen*. If the external sphincter tone is sufficient and the bladder has adequate compliance, intermittent catheterization every 3-4 hours is often successful in keeping the child socially dry. If there are unstable bladder contractions, an anticholinergic medication such as oxybutynin chloride, hyoscyamine, or tolterodine is prescribed to increase bladder capacity. If there is sphincteric incompetence, α-adrenergic medications are prescribed to enhance outlet resistance. Bacteriuria is seen in up to 50% of children using intermittent self-catheterization, but it seldom causes symptoms. In the absence of reflux, there seems to be little cause for concern. Performing intermittent catheterization with a new catheter (hydrophilic or standard silicone) each time is also quite effective in preventing bacteriuria and avoids the need for antibiotic prophylaxis. With this treatment plan, 40–85% of patients are dry, depending on the definition of continence; some children wear a pad in their underwear or a diaper for security but feel that they are dry.

If there is persistent incontinence despite medical therapy, reconstructive urinary tract surgery nearly always provides complete or satisfactory continence. If urethral resistance is low, bladder neck reconstructive procedures such as a periurethral sling are often successful. Alternatively, implantation of an artificial sphincter is usually successful. This sphincter consists of an inflatable cuff that is placed around the bladder neck, a pressure-regulating balloon implanted in the extraperitoneal space, and a pump mechanism that is implanted in the scrotum of boys and in the labia majora of girls. Squeezing the pump 3-4 times moves the fluid out of the inflatable urethral cuff, and then the cuff slowly refills over the next 2-3 minutes.

If the bladder capacity or bladder compliance is low, or if there are persistent uninhibited contractions despite anticholinergic therapy, enlargement of the bladder with a patch of small or large intestine,

termed augmentation cystoplasty or **enterocystoplasty**, is effective. These patients still need to perform clean intermittent catheterization. If urethral catheterization is difficult, a continent urinary stoma may be incorporated into the urinary tract reconstruction. A common method is the **Mitrofanoff procedure** (appendicovesicostomy), in which the appendix is isolated from the cecum on its vascular pedicle and is interposed between the bladder and abdominal wall to allow intermittent catheterization through a dry stoma. An ileal conduit with a bag on the abdominal wall is rarely used.

Complications of Augmentation Cystoplasty

Urinary Tract Infection

The urine may be colonized with gram-negative bacteria, and attempts to sterilize the urine for prolonged periods usually fail. There is no evidence that chronic bacteriuria in patients who have had enterocystoplasty is associated with renal damage; therefore only symptomatic UTIs should be treated.

Metabolic Acidosis

The enteric mucosal surface in contact with the urine absorbs ammonium, chloride, and hydrogen ions and loses potassium. *Hyperchloremic metabolic acidosis can result, possibly requiring medical treatment* (see Chapter 73). Chronic acidosis can compromise skeletal growth. This condition is common with colocystoplasty but is uncommon with ileocystoplasty. Metabolic acidosis is also common in patients with compromised renal function. To overcome this limitation of enterocystoplasty in patients with chronic renal insufficiency, a composite augmentation using the stomach and a small or large bowel gastric segment can be used. The stomach secretes chloride and hydrogen ions; thus preexisting metabolic acidosis remains stable or improves. However, augmentation with a gastric segment remains rare.

Spontaneous Perforation

Perforation of the augmented bladder is a life-threatening complication that results most often from acute or chronic overdistention of the augmented bladder. Patients with this complication typically present with severe abdominal pain and signs of peritonitis. Prompt diagnosis and treatment with exploratory laparotomy and bladder closure are necessary. Meticulous adherence to the prescribed program of intermittent catheterization to avoid bladder overdistention is important.

Bladder Calculi

Bladder calculi have developed in as many as 70% of children followed for 10 years after enterocystoplasty. The calculi develop in response to mucus that accumulates in the bladder and serves as a nidus for stone formation. This complication can be prevented by daily irrigation of the bladder with sterile saline.

Malignant Neoplasm

Invasive transitional cell carcinoma has been reported in nearly 4.6% of patients undergoing enterocystoplasty (compared with a 2.6% risk in spina bifida patients without enterocystoplasty). The pathogenesis is uncertain, but there is speculation that it is related to bacteriuria and the bowel-bladder contact. The risk is highest following gastrocystoplasty. The risk increases 10 years following enterocystoplasty. Although there are no formal guidelines or recommendations regarding screening, it seems appropriate to advise yearly endoscopic examinations or urine cytologic studies beginning in the tenth postoperative year.

ASSOCIATED DISORDERS

Constipation

Many patients with spina bifida also have bowel problems with constipation, and a vigorous bowel regimen is important. Some benefit from the **Malone antegrade continence enema (MACE) procedure**, in which the appendix is brought out to the skin to allow a catheter to be inserted into the cecum for antegrade enema. The stoma is continent, and an antegrade enema can be performed with tap water each day. This form of management allows the patient to be continent of stool and be more self-sufficient. An alternative to the MACE procedure is a percutaneous cecostomy, in which a button is placed into the cecum to allow an antegrade flush. The MACE and percutaneous cecostomy procedures can be performed laparoscopically.

Latex Allergy

Latex allergy is a very serious problem encountered by as many as half of patients with spina bifida and other urologic conditions who require clean intermittent catheterization and urinary tract reconstructive procedures. This immunoglobulin E–mediated allergy is acquired and is secondary to repeated exposure to the latex allergen. Latex allergy can manifest as watery eyes, sneezing, itching, hives, or anaphylaxis when blowing up a balloon or if an examiner is using latex gloves. Intraoperatively, a sensitized patient can experience anaphylactic shock. A latex-free environment should be provided for all children with spina bifida in the office, during hospitalization, and during operative procedures. Affected children also should wear a medical alert bracelet.

Occult Spinal Dysraphism

Approximately 1 in 4,000 patients have occult spinal dysraphism, a category that includes lipomeningocele, intradural lipoma, diastematomyelia, tight filum terminale, dermoid cyst-sinus, aberrant nerve roots, anterior sacral meningocele, and cauda equina tumor. More than 90% of patients have a cutaneous abnormality overlying the lower spine, including a **sacral dimple**, tuft of hair, dermal vascular malformation, or subcutaneous lipoma (Fig. 579.3). Often these children have high-arched feet, discrepancy in muscle size and strength between the legs,

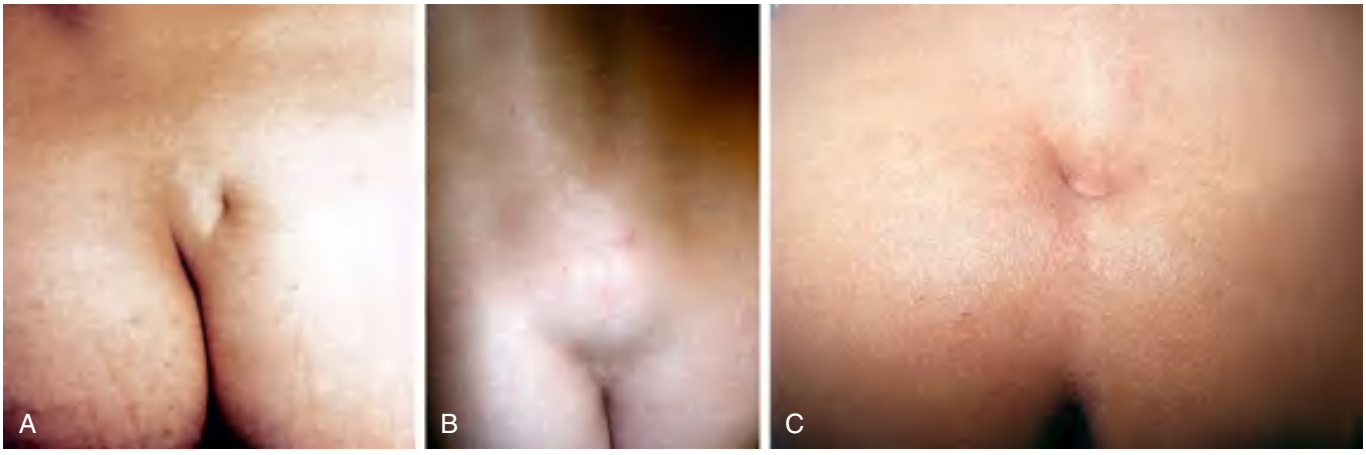

Fig. 579.3 A, Buttocks of teenage boy with tethered cord secondary to lipomeningocele. Note sacral dimple and deviation of gluteal fold to the left. B, Fat deposit over sacrum in girl with tethered cord secondary to lipomeningocele. C, Deep sacral pit in child with neuropathic bladder.

and a gait abnormality. Newborns and young infants often have a normal neurologic examination. Older children often have absent perineal sensation and back pain. Lower urinary tract function is abnormal in 40% of patients, including incontinence, recurrent UTI, and fecal soiling. The likelihood of a normal examination is inversely related to the child's age at surgical correction of the spinal lesion. In infants with abnormal urodynamics, 60% revert to normal; in older children, only 27% become normal. Management of the urinary tract in other children is similar to that described earlier for neural tube defects.

Sacral Agenesis

Sacral agenesis is defined as the absence of part or all of two or more lower vertebral bodies. *This condition is more common in the offspring of women with diabetes.* These children have a flattened buttock and a low, short gluteal cleft but usually have no orthopedic deformity, although some have high-arched feet. Palpation of the coccygeal area detects the absent vertebrae. Approximately 20% of cases are undetected until the age of 3-4 years; many are diagnosed after unsuccessful toilet training. Urodynamic studies in these children show a variety of patterns, and most need clean intermittent catheterization and pharmacotherapy to stay dry.

Imperforate Anus

Approximately 30–45% of children with a high imperforate anus have a neuropathic bladder, often because of sacral agenesis. Newborns with imperforate anus should undergo a spinal ultrasound during their initial evaluation, and if these children have difficulty with toilet training, complete urologic evaluation with upper and lower urinary tract imaging and urodynamics should be performed (see Chapter 392).

Cerebral Palsy

Children with cerebral palsy (see Chapter 638.1) often have reasonable bladder control. However, they achieve continence at a later age than unaffected children. Overall, 25–50% are incontinent, and the risk is directly related to the severity of physical impairment. Their upper urinary tracts are usually normal. Urodynamic studies have shown that most have uninhibited bladder contractions. Timed voiding and anticholinergic therapy are usually effective. Upper urinary tract deterioration is uncommon, and clean intermittent catheterization is rarely necessary.

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Chapter 580

Enuresis and Voiding Dysfunction

Heather N. Di Carlo and Chad B. Crigger

NORMAL VOIDING AND TOILET TRAINING

Fetal voiding occurs by reflex bladder contraction in concert with simultaneous contraction of the bladder and relaxation of the sphincter. Urine storage results from sympathetic and pudendal nerve-mediated inhibition of detrusor contractile activity accompanied by closure of the bladder neck and proximal urethra with increased activity of the external sphincter. The infant has coordinated reflex voiding as often as 15-20 times/day. Over time, bladder capacity increases. In children up to the age of 14 years, the mean bladder capacity in milliliters is equal to the ([age (in years) + 2] times 30) (e.g., the bladder capacity of a 6 year old should be [6 + 2] × 30 or 240 mL).

At 2-4 years, the child is developmentally ready to begin toilet training. To achieve conscious bladder control, several conditions must be present: awareness of bladder filling, cortical inhibition (suprapontine modulation) of reflex (unstable) bladder contractions, ability to consciously tighten the external sphincter to prevent incontinence, normal bladder growth, and motivation by the child to stay dry. The transitional phase of voiding refers to the period when children are acquiring bladder control. *Females typically acquire bladder control before males, and bowel control typically is achieved before bladder control.*

DIURNAL INCONTINENCE

Daytime incontinence not secondary to neurologic abnormalities is common in children. At 5 years of age, 95% have been dry during the day at some time and 92% are dry consistently. At 7 years of age, 96% are dry, although 15% have significant **urgency** at times. At 12 years, 99% are dry consistently during the day. The most common causes of daytime incontinence are **overactive bladder (urge incontinence)** and bladder-bowel dysfunction (BBD). Table 580.1 lists the causes of diurnal incontinence in children; Table 580.2 categorizes four types of voiding dysfunction.

The patient history should assess the pattern of incontinence, including the frequency of voiding, frequency of day and night urinary leakage, volume of urine lost during incontinent episodes, whether the incontinence is associated with urgency or giggling, whether it occurs after voiding, and whether the incontinence is continuous. In addition, whether the patient has a strong continuous urinary stream and sensation of incomplete bladder emptying should be assessed. A diary of when the child voids and whether the child is wet or dry is helpful. Other urologic problems, such as urinary tract infections (UTIs), vesicoureteral reflux, neurologic disorders, or a family history of renal duplication anomalies, should be assessed. Bowel habits also should be evaluated because incontinence is common in children with constipation and/or encopresis. Diurnal incontinence can occur in children with a history of sexual abuse or following bullying. Physical examination is directed at identifying signs of organic causes of incontinence. Short stature, hypertension, enlarged kidneys and/or bladder, constipation, labial adhesion, ureteral ectopy, back or sacral anomalies (see Fig. 579.4), and neurologic abnormalities should be documented.

Assessment tools include urinalysis, with culture if indicated; bladder diary (recorded times and volumes voided, whether wet or dry); postvoid residual urine volume (generally obtained by bladder scan); and the **Dysfunctional Voiding Symptom Score** (Fig. 580.1). An alternative to the Dysfunctional Voiding Symptom Score is the **Vancouver Nonneurogenic Lower Urinary Tract Dysfunction/Dysfunctional Elimination Syndrome** questionnaire. This questionnaire is a validated tool that consists of 14 questions scored on a 5-point Likert scale to assess lower urinary tract and bowel dysfunction. In most cases, a

Table 580.1 Causes of Urinary Incontinence in Childhood

Overactive bladder (urge incontinence or diurnal urge syndrome)
Infrequent voiding (underactive bladder)
Voiding postponement
Detrusor-sphincter discoordination
Nonneurogenic neurogenic bladder (Hinman syndrome)
Vaginal voiding
Giggle incontinence
Cystitis
Bladder outlet obstruction (posterior urethral valves)
Ectopic ureter and fistula
Sphincter abnormality (epispadias, exstrophy; urogenital sinus abnormality)
Neuropathic
Overflow incontinence
Traumatic
Iatrogenic
Behavioral
Combinations

Table 580.2 Symptoms and Signs of Four Main Subtypes of Lower Urinary Tract Dysfunction

	SYMPTOMS	SIGNS
Overactive bladder	(Cystometric) detrusor overactivity, frequency, voiding urgency, incontinence, constipation, enuresis	Holding maneuvers, normal flow pattern, thick bladder wall, low-volume voids
Dysfunctional voiding	Failure to relax the sphincter during voiding, normal micturition frequency, incontinence, constipation, urinary tract infections, enuresis	Post-void residue, staccato or interrupted flow pattern, normal frequency of voids
Underactive bladder	(Cystometric) weak detrusor contractions, low micturition frequency incontinence, constipation, urinary tract infections	Post-void residue, staccato or interrupted flow pattern, frequent large volume voids
Voiding postponement	Low micturition frequency, incontinence	Normal flow pattern

Classification of daytime lower urinary tract dysfunction, assessment, and documentation should be based on the following parameters: incontinence (presence or absence and symptom frequency), voiding frequency, voiding urgency, voided volumes, and fluid intake.
From Nieuwhof-Leppink AJ, Schroeder RPJ, van de Putte EM, et al. Daytime urinary incontinence in children and adolescents. *Lancet Child Adolesc Health.* 2019;3:492–500.

Patient name:
Hospital number:
Reason for referral:
Date:

Over the last month	Almost never	Less than half the time	About half the time	Almost every time	Not available
1. I have had wet clothes or wet underwear during the day.	0	1	2	3	NA
2. When I wet myself, my underwear is soaked.	0	1	2	3	NA
3. I miss having a bowel movement every day.	0	1	2	3	NA
4. I have to push for my bowel movements to come out.	0	1	2	3	NA
5. I only go to the bathroom one or two times each day.	0	1	2	3	NA
6. I can hold onto my pee by crossing my legs, squatting or doing the "pee dance."	0	1	2	3	NA
7. When I have to pee, I cannot wait.	0	1	2	3	NA
8. I have to push to pee.	0	1	2	3	NA
9. When I pee it hurts.	0	1	2	3	NA
10. Parents to answer. Has your child experienced something stressful like the example below?	No (0)			Yes (3)	
Total*					

- New baby.
- New home.
- New school.
- School problems.
- Abuse (sexual/physical).
- Home problems (divorce/death).
- Special events (birthday).
- Accident/injury.
- Others.

*Females with a score ≥6 and males with a score ≥9 are most likely to have dysfunctional voiding.

Fig. 580.1 Dysfunctional Voiding Symptom Score questionnaire. *(From Farhat W, Bagli DJ, Capolicchio G, et al. The dysfunctional voiding scoring system: quantitative standardization of dysfunctional voiding symptoms in children. J Urol. 2000;164:1011–1015.)*

uroflow study with electromyography (noninvasive assessment of urinary flow pattern and measurement of external sphincter activity) is indicated. Another item that may be useful in children older than age 5 years is the **Pediatric Symptom Checklist (PSC)**, a brief screening questionnaire that may reveal psychosocial stressors contributing to incontinence (see Chapter 32).

Bowel function should also be assessed. The **Bristol Stool Form Score** (Fig. 580.2) should be recorded. In addition, the clinician should utilize the Rome III diagnostic criteria, which classify functional gastrointestinal disorders that do not have underlying structural or tissue-based causes. Children 4 years of age or older are diagnosed as being constipated if they fulfill two or more of the following criteria over a period of 2 months: two or fewer defecations in the toilet per week, at least one episode of fecal incontinence per week, a history of retentive posturing or excessive volitional stool retention, a history of painful or hard bowel movements, the presence of a large fecal mass in the rectum, and a history of large-diameter stools that obstruct the toilet.

Imaging (renal-bladder ultrasound with or without a voiding cystourethrogram) is indicated in children with diurnal incontinence who have significant physical findings, those who have a family history of urinary tract anomalies or UTIs, and those who do not respond to therapy appropriately. Urodynamics should be performed if there is evidence of neurologic disease and may be helpful if empirical therapy is ineffective. *If there is any evidence of a neurologic disorder or if there is a sacral abnormality on physical examination, an MRI of the lower spine should be obtained.*

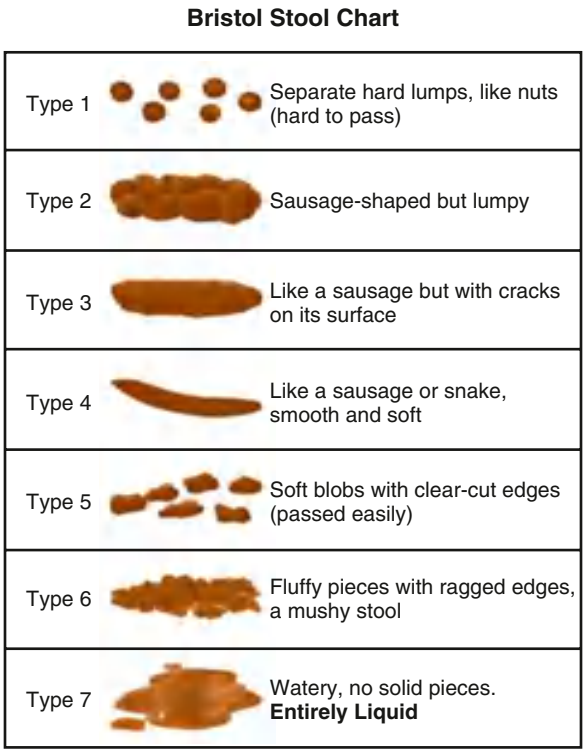

Fig. 580.2 Bristol Stool Chart for evaluating bowel function.

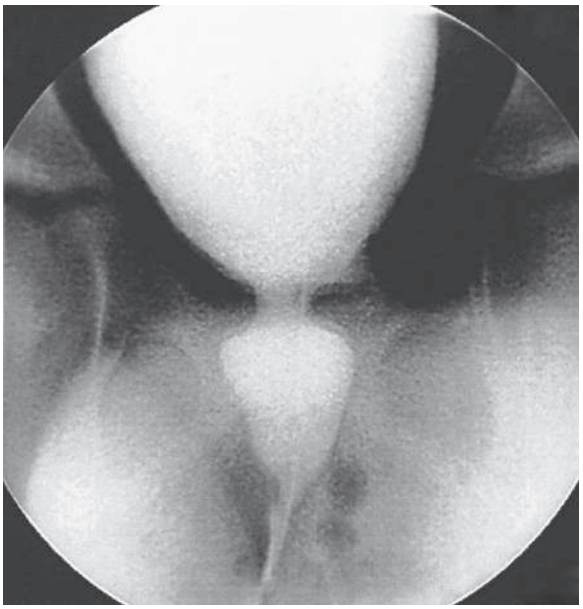

Fig. 580.3 Spinning-top deformity. Voiding cystourethrogram demonstrating dilation of the urethra with distal urethral narrowing and contraction of the bladder neck.

OVERACTIVE BLADDER (DIURNAL URGE SYNDROME)

Children with an overactive bladder typically exhibit urinary frequency, urgency, and urge incontinence. Often a female will squat down on her foot to try to prevent incontinence (termed *Vincent's curtsy*). The bladder in these children is functionally, but not anatomically, smaller than normal and exhibits strong uninhibited contractions. Approximately 25% of children with nocturnal enuresis also have symptoms of an overactive bladder. Many children indicate they do not feel the need to urinate, even just before they are incontinent. In females, a history of recurrent UTI is common, but incontinence can persist long after infections are brought under control. It is unclear if the voiding dysfunction is a sequela of the UTIs or if the voiding dysfunction predisposes to recurrent UTIs. In some females, voiding cystourethrography shows a dilated urethra (**spinning-top deformity**; Fig. 580.3) and narrowed bladder neck with bladder wall hypertrophy. The urethral finding results from inadequate relaxation of the external urinary sphincter.

The overactive bladder nearly always resolves, but the time to resolution is highly variable, occasionally not until the teenage years. Initial therapy is timed voiding, every 1.5-2 hours. Treatment of constipation and UTIs is important. Another treatment is **biofeedback**, in which children are taught pelvic floor exercises **(Kegel exercises),** because daily performance of these exercises can reduce or eliminate unstable bladder contractions. Biofeedback often consists of 8-10 1-hour sessions and may include participation with animated computer games. Biofeedback also may include periodic uroflow studies with sphincter electromyography to be certain that the pelvic floor relaxes during voiding, and assessment of postvoid residual urine volume by sonography. **Anticholinergic** therapy often is helpful if bowel function is normal. **Oxybutynin chloride** and **tolterodine** are the only U.S. Food and Drug Administration (FDA)-approved medications in children, but hyoscyamine, trospium, solifenacin, and mirabegron have also demonstrated safety in this population; these medications reduce bladder overactivity and may help the child achieve dryness. Adequate hydration should be emphasized to combat constipation as oxybutynin can induce constipation in some patients. Treatment with an α-adrenergic blocker such as terazosin or doxazosin can aid in bladder emptying by promoting bladder neck relaxation; these medications also have mild anticholinergic properties. If pharmacologic therapy is successful, the dosage should be tapered periodically to determine its continued need. Children who do not respond to therapy should be evaluated with urodynamic studies to rule out other possible forms of bladder or sphincter dysfunction. In refractory cases, other procedures such as **sacral neuromodulation** (InterStim), percutaneous tibial nerve stimulation, and intravesical botulinum toxin injection have been effective in children.

If the child has constipation based on the criteria described earlier, treatment generally is initiated with polyethylene glycol powder, which has been shown to be safe in children and is generally more effective than other laxative preparations (see Chapter 378.3).

NONNEUROGENIC NEUROGENIC BLADDER (HINMAN SYNDROME)

Hinman syndrome is a very serious but uncommon disorder involving failure of the external sphincter to relax during voiding in children without neurologic abnormalities. Children with this syndrome, also called **nonneurogenic neurogenic bladder**, typically exhibit a staccato stream, day and night wetting, recurrent UTIs, constipation, and encopresis. Evaluation of affected children often reveals vesicoureteral reflux, a trabeculated bladder, and a decreased urinary flow rate with an intermittent pattern (Fig. 580.4). In severe cases, hydronephrosis, renal insufficiency, and end-stage renal disease can occur. The pathogenesis of this syndrome is thought to involve learning abnormal voiding habits during toilet training; the syndrome is rarely seen in infants. Urodynamic studies and MRI of the spine are indicated to rule out a neurologic cause for the bladder dysfunction.

The treatment usually is complex and can include anticholinergic and α-adrenergic blocker therapy, timed voiding, treatment of constipation, behavioral modification, and encouragement of relaxation during voiding. Biofeedback has been used successfully in older children to teach relaxation of the external sphincter. Botulinum toxin injection into the external sphincter can provide temporary sphincteric paralysis and thereby reduce outlet resistance. In severe cases, intermittent catheterization is necessary to ensure bladder emptying. In selected patients, external urinary diversion is necessary to protect the upper urinary tract. These children require long-term treatment and careful follow-up.

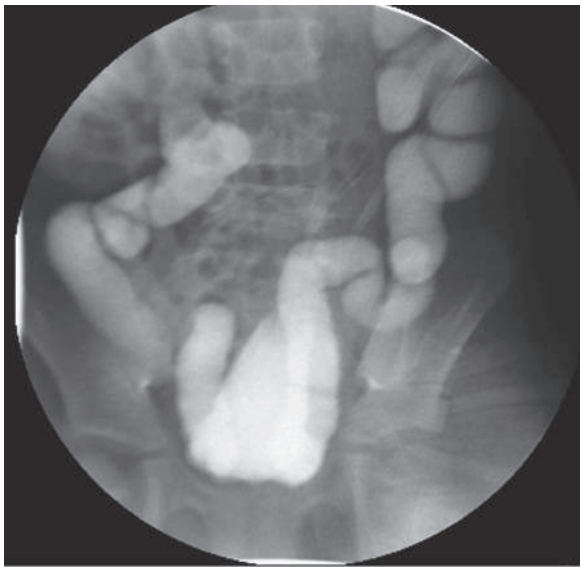

Fig. 580.4 Voiding cystourethrogram demonstrating severe bladder trabeculation and vesicoureteral reflux in a 12-yr-old male with Hinman syndrome. The patient presented with day and night incontinence, had chronic renal failure, and underwent kidney transplantation.

INFREQUENT VOIDING (UNDERACTIVE BLADDER)

Infrequent voiding is a common disorder of micturition. Affected children, usually females, often void only 1-2 times a day rather than the normal 4-7 times. Poor detrusor contraction strength and/or duration lead to bladder overdistention and prolonged retention of urine and ultimately bacterial growth that can lead to recurrent UTIs. Some of these children are constipated. Some also have occasional episodes of incontinence from overflow or urgency. The disorder is behavioral. If the child has UTIs, treatment includes antibacterial prophylaxis and encouragement of frequent voiding and complete emptying of the bladder by double voiding until a normal pattern of micturition is reestablished.

VAGINAL VOIDING

In females with vaginal voiding, incontinence typically occurs after urination after the female stands up. The volume is usually minimal, about 5-10 mL, and characterized as dribbling. One of the most common causes is **labial adhesion** (Fig. 580.5). This lesion, typically seen in young females, can be managed either by topical application of estrogen or steroid cream to the adhesion or manual separation (this should only be done after ensuring adequate anesthesia and potentially sedation; see Chapter 586). Some females experience vaginal voiding because they do not separate their legs widely during urination. These females typically are overweight and/or do not pull their underwear down to their ankles when they urinate. Management involves encouraging the female to separate the legs as widely as possible during urination. The most effective way to do this is to have the child sit backward on the toilet seat during micturition.

OTHER CAUSES OF INCONTINENCE IN FEMALES

Ureteral ectopia, usually associated with a duplicated collecting system in females, refers to a ureter that drains outside the bladder, often into the vagina or distal urethra. It can produce urinary incontinence characterized by constant urinary dribbling all day, even though the child voids regularly. Sometimes the urine production from the renal segment drained by the ectopic ureter is small, and urinary drainage is confused with watery vaginal discharge. Children with a history of vaginal discharge or incontinence and an abnormal voiding pattern require careful study. The ectopic orifice is usually difficult to find. On ultrasonography or intravenous urography, one may suspect duplication of the collecting system (Fig. 580.6), but the upper collecting system drained by the ectopic ureter usually has poor or delayed function.

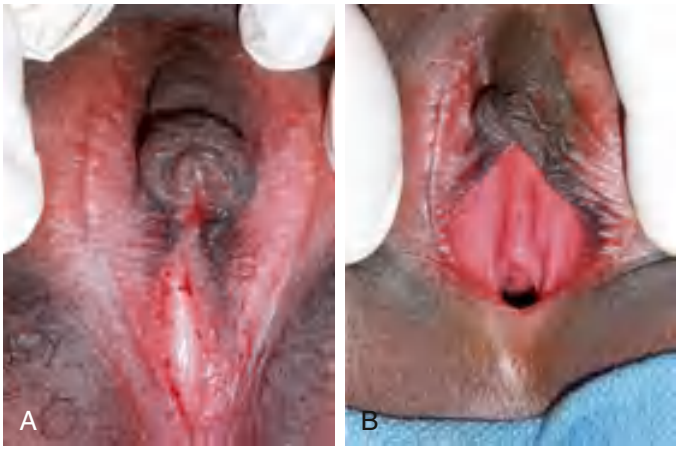

Fig. 580.5 A, Labial adhesion. Note the inability to visualize the urethral meatus and vagina. B, Normal female external genitals following lysis of labial adhesion.

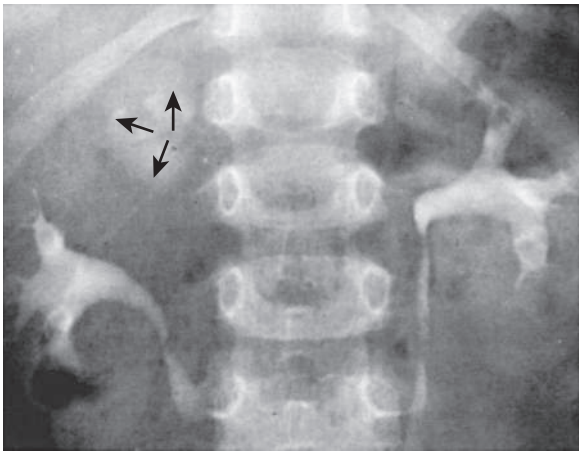

Fig. 580.6 Duplication of the right collecting system with ectopic ureter. Excretory urogram in a female presenting with a normal voiding pattern and constant urinary dribbling. The left kidney is normal, and the right side, well visualized, is the lower collecting system of a duplicated kidney. On the upper pole opposite the first and second vertebral bodies, note the accumulation of contrast material *(arrows)* corresponding with a poorly functioning upper pole drained by a ureter opening in the vestibule.

CT scanning of the kidneys or an MR urogram should demonstrate subtle duplication anomalies. Examination under anesthesia for an ectopic ureteral orifice in the vestibule or the vagina may be necessary (Fig. 580.7). Treatment in these cases is either partial nephrectomy, with removal of the upper pole segment of the duplicated kidney and its ureter down to the pelvic brim, or ipsilateral ureteroureterostomy, in which the upper pole ectopic ureter is anastomosed to the normally positioned lower pole ureter. These procedures often are performed by minimally invasive laparoscopy with or without robotic assistance.

Giggle incontinence typically affects females 7-15 years of age. The incontinence occurs suddenly during giggling, and the entire bladder volume is lost. The pathogenesis is thought to be sudden relaxation of the urinary sphincter. Anticholinergic medication and timed voiding occasionally are effective. The most effective treatment is low-dose methylphenidate, which seems to stabilize the external sphincter.

Total incontinence in females may be secondary to **epispadias** (see Fig. 578.2). This condition, which affects only 1 in 480,000 females, is characterized by separation of the pubic symphysis, separation of the right and left sides of the clitoris, and a patulous urethra. Treatment is bladder neck reconstruction; an alternative surgical therapy is

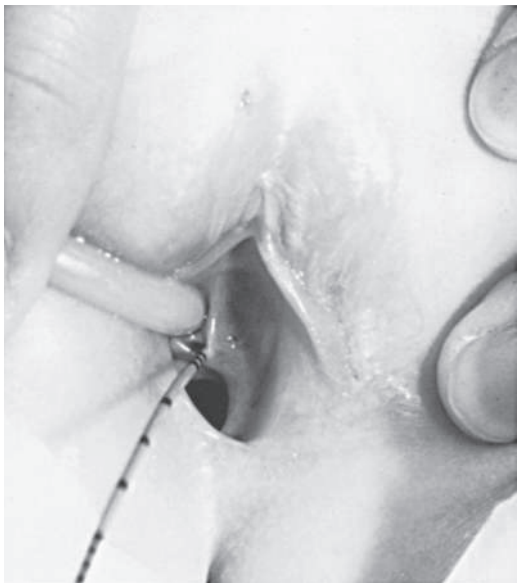

Fig. 580.7 An ectopic ureter entering the vestibule next to the urethral meatus. The thin ureteral catheter with transverse marks has been introduced into this ectopic ureter. This female had a normal voiding pattern and constant urinary dribbling.

Table 580.3 Nocturnal Enuresis

CAUSES
Delayed maturation of the cortical mechanisms that allow voluntary control of the micturition reflex
Defective sleep arousal
Reduced antidiuretic hormone production at night, resulting in an increased urine output (nocturnal polyuria)
Genetic factors, with chromosomes 12 and 13q the likely sites of the gene for enuresis
Bladder factors (lack of inhibition, reduced capacity, overactive)
Constipation
Organic factors, such as urinary tract infection, obstructive uropathy, or sickle cell anemia nephropathy
Sleep disorders
Sleep-disordered breathing secondary to enlarged adenoids
Psychologic factors more often implicated in secondary enuresis
OTHER FEATURES
Enuresis can occur in any stage of sleep (but usually non–rapid eye movement sleep)
All children are most difficult to arouse in the first third of the night and easiest to awaken in the last third, but enuretic children are more difficult to arouse than those with normal bladder control
Enuretic children often are described as "soaking the bed"
Family history in enuretic children often positive for enuresis
Risk increased with developmental delay, attention-deficit/hyperactivity disorder, autism spectrum disorders

placement of an artificial urinary sphincter to repair the incompetent urethra.

A short, incompetent urethra may be associated with certain urogenital sinus malformations. The diagnosis of these malformations requires a high index of suspicion and a careful physical examination of all incontinent females. In these cases, urethral and vaginal reconstruction often restores continence.

VOIDING DISORDERS WITHOUT INCONTINENCE

Some children have abrupt onset of severe urinary frequency, voiding as often as every 10-15 minutes during the day, without dysuria, UTI, daytime incontinence, or nocturia. The most common age for these symptoms to occur is 4-6 years, after the child is toilet trained; males are more often affected. This condition is termed the **daytime frequency syndrome of childhood,** or **pollakiuria**. The condition is functional without associated anatomic problems. Often the symptoms occur just before a child starts kindergarten or if the child is having emotional family stress-related problems. These children should be checked for UTIs, and the clinician should ascertain that the child is emptying the bladder satisfactorily. Another contributing cause is constipation. Occasionally, pinworms cause these symptoms. The condition is self-limited, and symptoms generally resolve within 2-3 months. Anticholinergic therapy is rarely effective.

Some children have **dysuria-hematuria syndrome,** in which the child has dysuria without UTI but with microscopic or total gross hematuria (blood throughout the stream). This condition affects children who are toilet-trained and is often secondary to hypercalciuria. A 24-hour urine sample should be obtained and calcium and creatinine excretion assessed. A 24-hour calcium excretion of >4 mg/kg is abnormal and deserves treatment with thiazides, because some of these children are at risk for urolithiasis. **Terminal hematuria** (blood at the end of the stream) occurs in males and typically is secondary to BBD or urethral meatal stenosis. Cystoscopy is not indicated, and the condition usually resolves with treatment for constipation.

NOCTURNAL ENURESIS

By 5 years of age, 90–95% of children are nearly completely continent during the day, and 80–85% are continent at night. Nocturnal enuresis refers to the occurrence of involuntary voiding at night after 5 years old, the age when volitional control of micturition is expected. Enuresis may be **primary** (estimated 75–90% of children with enuresis; nocturnal urinary control never achieved) or **secondary** (10–25%; the child was dry at night for at least a few months and then enuresis developed). Overall, 75% of children with enuresis are wet only at night, and 25% are incontinent day and night. This distinction is important, because children with both forms are more likely to have an abnormality of the urinary tract. *Monosymptomatic enuresis* is more common than *polysymptomatic enuresis* (associated urgency, hesitancy, frequency, daytime incontinence).

Epidemiology

Approximately 60% of children with nocturnal enuresis are males. The family history is positive in 50% of cases. Although primary nocturnal enuresis may be polygenetic, candidate genes have been localized to chromosomes 6, 12, and 13. If one parent was enuretic, each child has a 44% risk of enuresis; if both parents were enuretic, each child has a 77% likelihood of enuresis. Nocturnal enuresis without overt daytime voiding symptoms affects up to 20% of children at the age of 5 years; it ceases spontaneously in approximately 15% of involved children every year thereafter. Its frequency among adults is <1%.

Pathogenesis

The pathogenesis of primary nocturnal enuresis (normal daytime voiding habits) is multifactorial (Table 580.3).

Clinical Manifestations and Diagnosis

A careful history should be obtained, especially with respect to fluid intake at night and the pattern of nocturnal enuresis. Children with diabetes insipidus (see Chapter 596), diabetes mellitus (see Chapter 629), and chronic renal disease (see Chapter 572) can have a high obligatory urinary output and a compensatory polydipsia. The family should be asked whether the child snores loudly at night. Many children with enuresis sleepwalk or talk in their sleep. A complete physical examination should include palpation of the abdomen and possibly a rectal examination after voiding to assess the possibility of a chronically distended bladder and constipation. The child with nocturnal enuresis should be examined carefully for neurologic and spinal abnormalities. There is an increased incidence of bacteriuria in enuretic females, and, if found, it should be investigated and treated (see Chapter 575), although this does not always lead to resolution of bed-wetting. A urine sample should be obtained after an overnight fast and evaluated

for specific gravity or osmolality to exclude polyuria as a cause of frequency and incontinence and to ascertain that the concentrating ability is normal. The absence of glycosuria should be confirmed. If there are no daytime symptoms, the physical examination and urinalysis are normal, and the urine culture is negative, further evaluation for urinary tract pathology generally is not warranted. A renal ultrasound is reasonable in an older child with enuresis or in children who do not respond appropriately to therapy.

Treatment

The best approach to treatment is to reassure the child and parents that the condition is self-limited and to avoid punitive measures that can affect the child's psychologic development adversely. Fluid intake should be restricted to 2 oz after 6 or 7 PM. The parents should be certain that the child voids at bedtime. Avoiding extraneous sugar and caffeine after 5 PM is also beneficial. If the child snores and the adenoids are enlarged, referral to an otolaryngologist should be considered, because adenoidectomy can cure the enuresis in some cases.

Active treatment should be avoided in children younger than 6 years of age, because enuresis is extremely common in younger children. Treatment is more likely to be successful in children approaching puberty compared with younger children. In addition, treatment is most likely to be effective in children who are motivated to stay dry and is less successful in children who are overweight. Treatment should be viewed as a facilitator that requires active participation by the child (e.g., a coach and an athlete).

The simplest initial measure is **motivational therapy** and includes a star chart for dry nights. Waking children a few hours after they go to sleep to have them void often allows them to awaken dry, although this measure is not curative. Some have recommended that children try holding their urine for longer periods during the day, but there is no evidence that this approach is beneficial. **Conditioning therapy** involves use of a loud auditory or vibratory alarm attached to a moisture sensor in the underwear. The alarm activates when voiding occurs and is intended to awaken children and alert them to void. This form of therapy has a reported success of 30–60%, although the relapse rate is significant. Often the auditory alarm wakes up other family members and not the enuretic child; persistent use of the alarm for several months often is necessary to determine whether this treatment is effective. Conditioning therapy tends to be most effective in older children. Another form of therapy to which some children respond is self-hypnosis. The primary role of psychologic therapy is to help the child deal with enuresis psychologically and help motivate the child to void at night if he or she awakens with a full bladder.

Pharmacologic therapy is intended to treat the symptom of enuresis and thus is regarded as second line and is not curative. Direct comparisons of the moisture alarm with pharmacologic therapy favor the former because of lower relapse rates, although initial response rates are equivalent.

One form of pharmacologic treatment is **desmopressin acetate,** a synthetic analog of antidiuretic hormone that reduces urine production overnight. This medication is FDA-approved in children and is available as a tablet, with a dosage of 0.2-0.6 mg orally 2 hours before bedtime. A nasal spray formulation is available but is no longer recommended for nocturnal enuresis due to increased risk of hyponatremia and convulsions. Hyponatremia has not been reported in children using oral tablets. Fluid restriction at night is important, and the drug should not be used if the child has a systemic illness with vomiting or diarrhea or if the child has polydipsia. Desmopressin acetate is effective in as many as 40% of children and is most effective in those approaching puberty. If effective, it should be used for 3-6 months, and then an attempt should be made to taper the dosage. Some families use it intermittently (sleepovers, school trips, vacations) with success. If tapering results in recurrent enuresis, the child should return to the higher dosage. Few adverse events have been reported with the long-term use of desmopressin acetate.

For therapy-resistant enuresis or children with symptoms of an overactive bladder, anticholinergic therapy is indicated. Oxybutynin 5 mg or tolterodine 2 mg at bedtime is often prescribed. If the medication is ineffective, the dosage may be doubled. The clinician should monitor constipation as a potential side effect.

A third-line treatment is **imipramine,** which is a tricyclic antidepressant. This medication has mild anticholinergic and α-adrenergic effects, reduces the urine output slightly, and might alter the sleep pattern. The dosage of imipramine is 25 mg in children age 6-8 years, 50 mg in children age 9-12 years, and 75 mg in teenagers. Reported success rates are 30–60%. Side effects include anxiety, insomnia, dry mouth, and heart rhythm changes. If there is any history of palpitations or syncope in the child, or sudden cardiac death or unstable arrhythmia in the family, long QT syndrome in the patient needs to be excluded prior to prescribing imipramine. The drug is one of the most common causes of poisoning by prescription medication, so it is also important to emphasize safe storage.

In unsuccessful cases, combining therapies often is effective. Alarm therapy plus desmopressin is more successful than either alone. The combination of oxybutynin chloride and desmopressin is more successful than a single agent. Desmopressin and imipramine also may be combined.

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Chapter 581

Anomalies of the Penis and Urethra

Heather N. Di Carlo and Chad B. Crigger

HYPOSPADIAS

Hypospadias is a urethral opening on the ventral surface of the penile shaft affecting 1 in 200 male newborns. Typically an isolated defect, its incidence is increased in many males with chromosomal abnormalities, anorectal malformation, and congenital heart disease. Usually, there is incomplete development of the prepuce, called a **dorsal hood,** in which the foreskin is on the sides and dorsal aspect of the penile shaft and deficient or absent ventrally. Some males with hypospadias, particularly those with proximal hypospadias, have **chordee,** in which there is ventral penile curvature during erection. The incidence of hypospadias appears to be increasing, possibly because of in utero exposure to estrogenic or antiandrogenic endocrine-disrupting chemicals (e.g., polychlorobiphenyls, phytoestrogens).

Clinical Manifestations

Hypospadias is classified according to the position of the urethral meatus after considering whether chordee is present (Fig. 581.1). The deformity is described as distal (further broken down into glanular [on the glans penis], coronal, or subcoronal), midpenile (distal penile, midshaft, or proximal penile), or proximal (penoscrotal, scrotal, or perineal). Approximately 65% of cases are distal, 25% are subcoronal or midpenile, and 10% are proximal. In the most severe cases, the scrotum is bifid, and sometimes there is moderate **penoscrotal transposition.** As many as 10% of affected males have a **megameatal variant of hypospadias** in which the foreskin is developed normally (megameatus intact prepuce variant), and there is either glanular or subcoronal hypospadias with a "fish mouth" meatus. These cases might not be diagnosed until after a circumcision is performed.

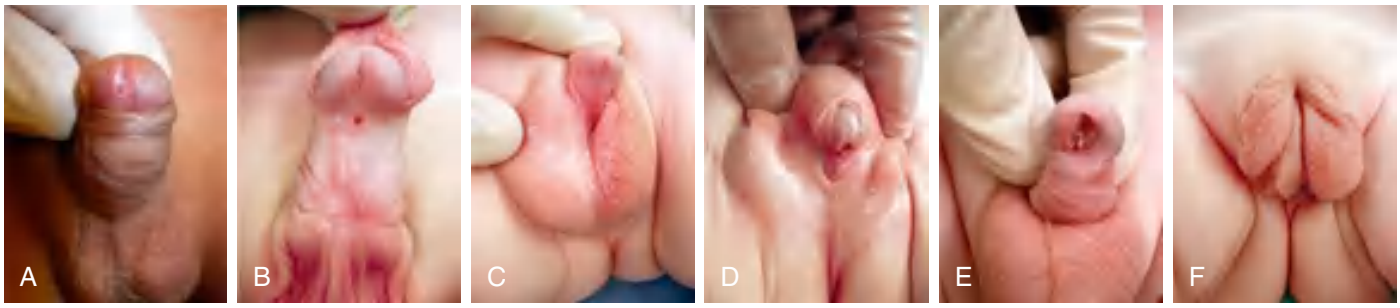

Fig. 581.1 Varying forms of hypospadias. A, Glanular hypospadias. B, Subcoronal hypospadias. Note the dorsal hood of foreskin. C, Penoscrotal hypospadias with chordee. D, Perineal hypospadias with chordee and partial penoscrotal transposition. E, Megameatal variant of hypospadias diagnosed following circumcision; note absence of hooded foreskin. F, Complete penoscrotal transposition with scrotal hypospadias.

Approximately 10% of males with hypospadias have an undescended testis; inguinal hernia(s) also are common. In the newborn, the differential diagnosis of midpenile or proximal hypospadias associated with an undescended testis should include forms of a **disorder of sex development,** particularly mixed gonadal dysgenesis, partial androgen insensitivity, true hermaphroditism, and congenital adrenal hyperplasia in a female (see Chapter 616). In the latter condition, neither gonad is palpable. *A karyotype should be obtained in patients with midpenile or proximal hypospadias and cryptorchidism* (see Chapter 628). In males with proximal hypospadias, a voiding cystourethrogram should be considered because 5–10% of these children have a dilated **prostatic utricle,** which is a remnant of the müllerian system (see Chapter 591). The incidence of upper urinary tract abnormalities is low unless there are abnormalities of other organ systems.

Complications of untreated hypospadias include deformity of the urinary stream, typically ventral deflection or severe splaying; sexual dysfunction secondary to penile curvature; infertility if the urethral meatus is proximal; meatal stenosis (congenital), which is uncommon; and cosmetic appearance. The goal of hypospadias surgery is to correct the functional and cosmetic deformities. Whereas hypospadias repair is recommended for all males with midpenile and proximal hypospadias, some males with distal hypospadias have no functional abnormality and do not need surgical correction.

Treatment

Management begins in the newborn period. *Circumcision should be avoided because the foreskin often is used in the repair in most cases.* The ideal age for repair in a healthy infant is 6-12 months because the risk of general anesthesia at this age is similar to older children; penile growth over the next several years is slow; the child does not remember the surgical procedure; and postoperative analgesic needs are less than in older children. With the exception of proximal hypospadias, virtually all cases are repaired in a single operation on an ambulatory basis. The most common repair involves tubularization of the urethral plate distal to the urethral meatus, with coverage by a vascularized flap from the foreskin, termed a tubularized incised plate repair. Proximal cases might require a two-stage repair.

The complication rate parallels severity: 5% for distal hypospadias, 10% for midpenile hypospadias, and 40% for proximal hypospadias. The most common complications include urethrocutaneous fistula and meatal stenosis. Other complications include a deformed urinary stream, persistent or recurrent penile curvature, and dehiscence of the hypospadias repair. Treatment of these complications generally is straightforward. In complex cases, a buccal mucosa graft from the mouth is used to create urethral mucosa. Repair of hypospadias is a technically demanding operation and should be performed by a surgeon with specialty training in pediatric urology and extensive experience.

CHORDEE WITHOUT HYPOSPADIAS

In some males, there is mild or moderate ventral penile curvature **(chordee)** and incomplete development of the foreskin **(dorsal hood),** but the urethral meatus is at the tip of the glans (Fig. 581.2). In most of these males, the urethra is normal, but there is insufficient ventral penile skin or prominent, inelastic ventral bands of dartos fascia that prevent a straight erection. In some cases, the urethra is hypoplastic, and a formal urethroplasty is necessary for repair. The only sign of this anomaly in the neonate may be the hooded foreskin, and delayed repair under general anesthesia after 6 months of age is recommended. **Lateral penile curvature** usually is caused by overgrowth or hypoplasia of a corporal (erectile) body and usually is congenital. Surgical repair is also recommended at age 6-12 months.

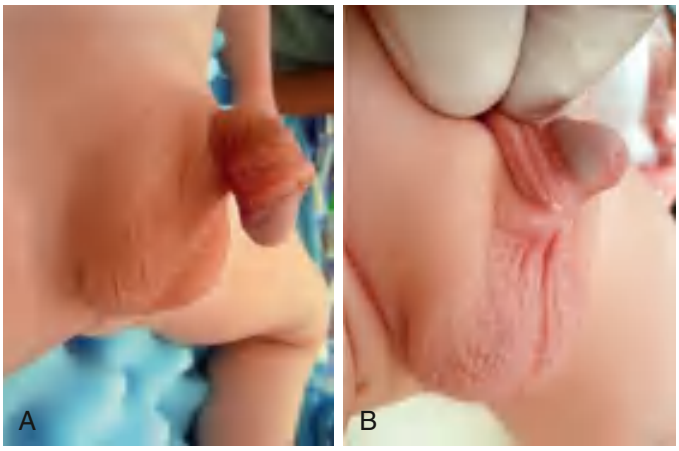

Fig. 581.2 A and B, Two examples of chordee without hypospadias. Note hooded foreskin and normal location of urethral meatus.

PHIMOSIS AND PARAPHIMOSIS

Phimosis refers to the inability to retract the prepuce. At birth, phimosis is physiologic. Over time, the adhesions between the prepuce and glans lyse and the distal phimotic ring loosens. In 80% of uncircumcised males, the prepuce becomes retractable by 3 years of age. Accumulation of epithelial debris under the infant's prepuce is physiologic and does not mandate circumcision. In older males, phimosis may be physiologic or may be pathologic from **lichen sclerosus (balanitis xerotica obliterans)** at the tip of the foreskin (Fig. 581.3A) and can also affect the meatus (see Fig. 581.3B). The prepuce might have been retracted forcefully on one or two occasions in the past, which can result in a cicatricial scar that prevents subsequent retraction of the foreskin. In males with persistent physiologic or pathologic phimosis, application of corticosteroid ointment to the tip of the foreskin twice daily for 1 month loosens the phimotic ring in two thirds of cases. *If there is ballooning of the foreskin during voiding or phimosis beyond 10 years of age and topical corticosteroid therapy is ineffective, circumcision is recommended.*

Paraphimosis occurs when the foreskin is retracted proximal to the coronal sulcus and the prepuce cannot be pulled back over the glans (Fig. 581.4). Painful venous stasis in the retracted foreskin results, with

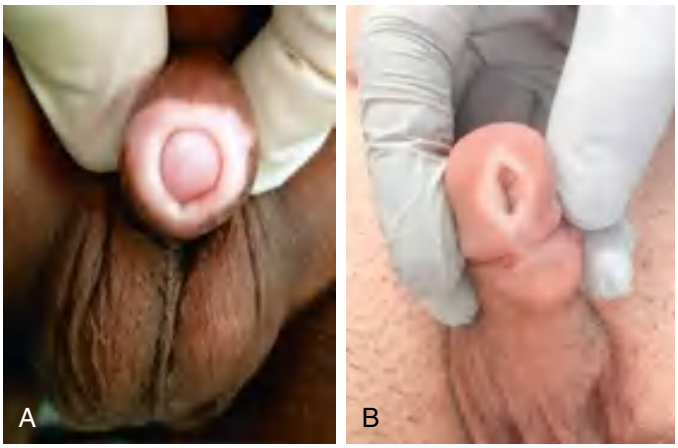

Fig. 581.3 A, Balanitis xerotica obliterans. Note whitish cicatricial plaque. B, Involvement of the urethral meatus necessitated a meatoplasty.

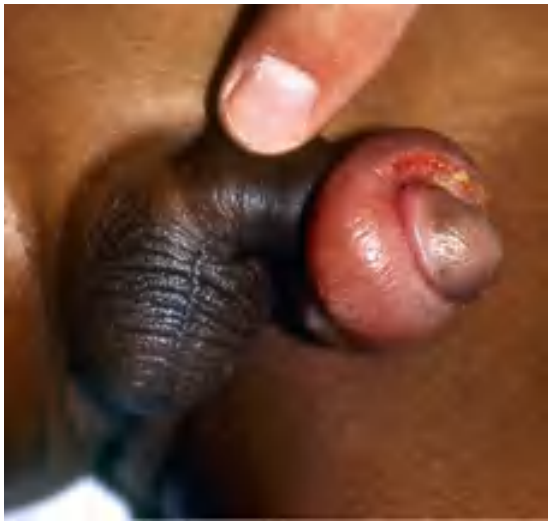

Fig. 581.4 Paraphimosis. The foreskin has been retracted proximal to the glans penis and is markedly swollen secondary to venous congestion.

edema leading to severe pain and inability to reduce the foreskin (pull it back over the glans). Treatment includes lubricating the foreskin and glans and then simultaneously compressing the glans and placing distal traction on the foreskin to try to push the phimotic ring past the coronal sulcus. Topical application of granulated sugar has been reported to aid in reduction of edema by creation of an osmotic gradient, facilitating reduction of paraphimosis. In addition, injection of hyaluronidase into the edematous skin has been reported to result in immediate reduction in swelling. In rare cases, emergency circumcision under general anesthesia is necessary.

CIRCUMCISION

In the United States, circumcision usually is performed for cultural reasons, but several health benefits have been identified that may outweigh the risks of the procedure. Specific benefits include prevention of urinary tract infections (UTIs) and penile cancer and reducing the risk and transmission of some sexually transmitted infections, including HIV.

UTIs are 10-15 times more common in uncircumcised *infant* males than in circumcised infants, with the urinary pathogens arising from bacteria that colonize the space between the prepuce and glans. The risk of febrile UTI (see Chapter 575) is highest between birth and 6 months, but there is an increased risk of UTI until at least 5 years of age, or age of completion of toilet training. Many recommend circumcision in infants who are predisposed to UTI, such as those with congenital hydronephrosis and vesicoureteral reflux. Circumcision reduces the risk of sexually transmitted infections in adults (see Chapter 163), in particular HIV (see Chapter 322). There have been only a handful of reports of adult males who were circumcised at birth and subsequently acquired penile carcinoma, but in Scandinavian countries, where few males are circumcised and hygiene is good, the incidence of penile cancer is low.

Circumcision should be performed by trained providers under sterile conditions. When performing a neonatal circumcision, local analgesia, such as a dorsal or penile ring block or application of EMLA (eutectic mixture of local anesthetics) cream (lidocaine 2.5% and prilocaine 2.5%) is recommended. Early and late complications after neonatal circumcision include bleeding, wound infection, meatal stenosis, secondary phimosis, removal of insufficient foreskin, and fibrous penile adhesions (skin bridge; Fig. 581.5); 0.2–3.0% of patients undergo a subsequent operative procedure. Males with a large hydrocele or hernia are at particular risk for secondary phimosis because the scrotal swelling tends to displace the penile shaft skin over the glans. Serious complications of newborn circumcision include sepsis, amputation of the distal part of the glans, removal of an excessive amount of foreskin, and urethrocutaneous fistula. Circumcision should not be performed in neonates with hypospadias, chordee without hypospadias, or a dorsal hood deformity (relative contraindication) or in those with a small penis (Fig. 581.6). In males with a "wandering raphe," in which the median raphe deviates to one side, there may be underlying penile torsion or hypospadias, and evaluation by a pediatric urologist is suggested before performing a circumcision.

PENILE TORSION

Penile torsion, a rotational defect of the penile shaft, usually occurs in a counterclockwise direction, usually to the left side (see Fig. 581.6D). In most cases, penile development is normal, and the condition is unrecognized until circumcision is performed or the foreskin is retractable. In many cases, the midline raphe of the penile shaft is deviated. Penile torsion also occurs in some males with hypospadias. The defect has primarily cosmetic significance, and correction is unnecessary if the rotation is <60 degrees from the midline. The severity of penile torsion may lessen during infancy.

INCONSPICUOUS PENIS

The term *inconspicuous penis* refers to a penis that appears to be small. A **webbed penis** is a condition in which the scrotal skin extends onto the ventral penile shaft. This deformity represents an abnormality of the attachment between the penis and scrotum. Although the deformity might appear mild, if a routine circumcision is performed, the penis can retract into the scrotum, resulting in secondary phimosis **(trapped penis).** The concealed **(hidden or buried)** penis is a normally developed penis that is camouflaged by the suprapubic fat pad (Fig. 581.7). This anomaly may be congenital, iatrogenic after circumcision, or a result of obesity. Surgical correction is indicated for cosmetic reasons or if there is a functional abnormality with a splayed stream.

A **trapped penis** is an acquired form of inconspicuous penis and refers to a phallus that becomes embedded in the suprapubic fat pad after circumcision (Fig. 581.8). This deformity can occur after neonatal circumcision in an infant who has significant scrotal swelling from a large hydrocele or inguinal hernia or after routine circumcision in an infant with a webbed penis. This complication can predispose to UTIs and can cause urinary retention. Initial treatment of a trapped penis should include topical corticosteroid cream, which often loosens the phimotic ring. In some cases, secondary repair is necessary at 6-9 months.

MICROPENIS

Micropenis is defined as a normally formed penis that is at least 2.5 standard deviations (SD) below the mean in size (Fig. 581.9). Typically, the ratio of the length of the penile shaft to its circumference is normal.

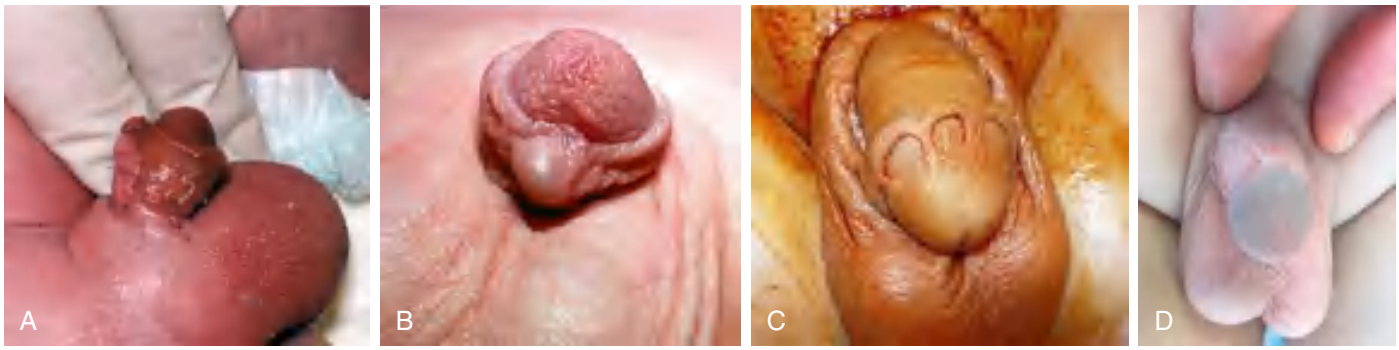

Fig. 581.5 Complications of circumcision. **A,** Denuded penile shaft. With local care, the penis healed and appeared normal. **B,** Midline epithelial inclusion cyst. **C** and **D,** Fibrous penile skin bridges.

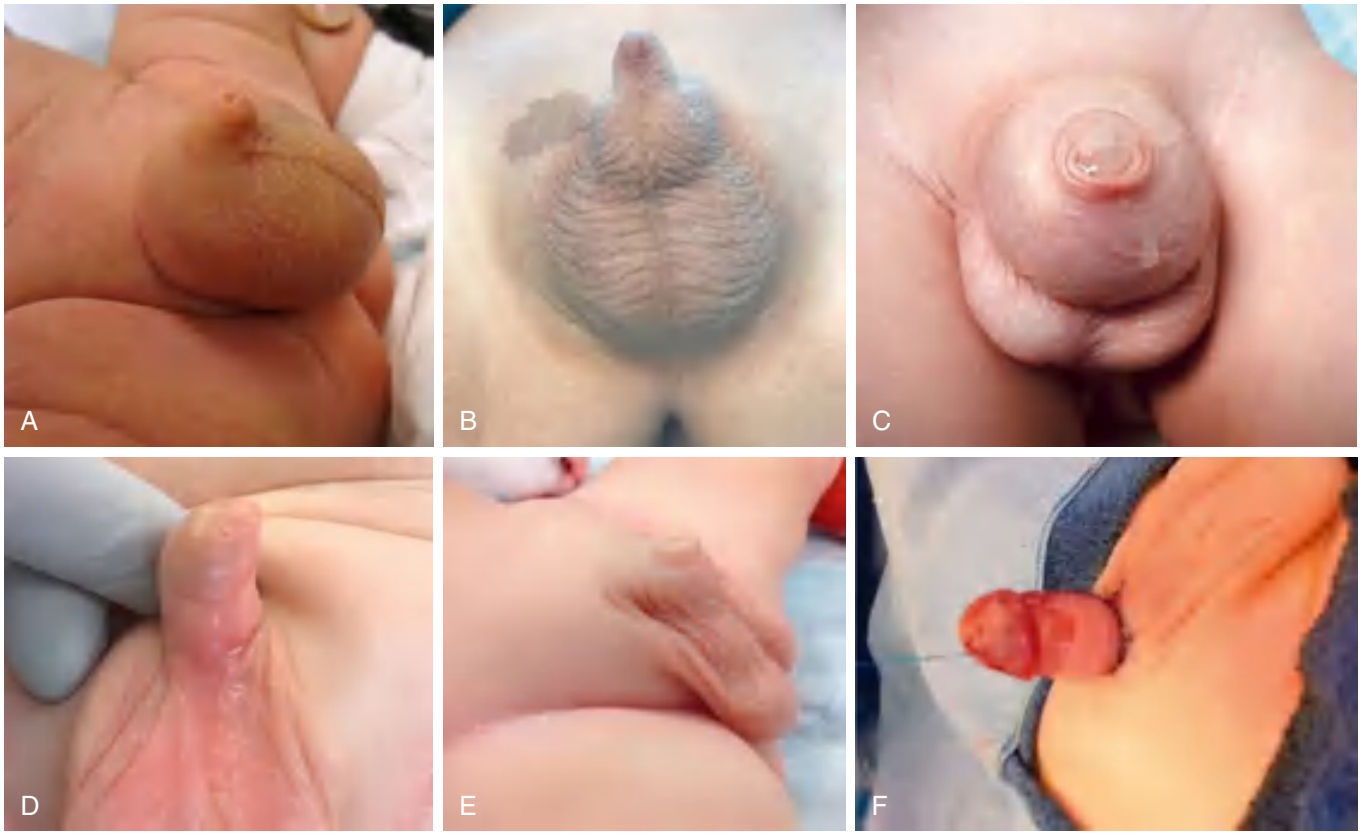

Fig. 581.6 Examples of congenital deformities in which neonatal circumcision is contraindicated. **A** and **B,** Hidden penis. **C,** Megaprepuce. **D,** Penile torsion to left side; note "wandering raphe." **E,** Webbed penis; note scrotal attachment to penile shaft. **F,** Same patient as in **E** following reconstruction at 6 mo.

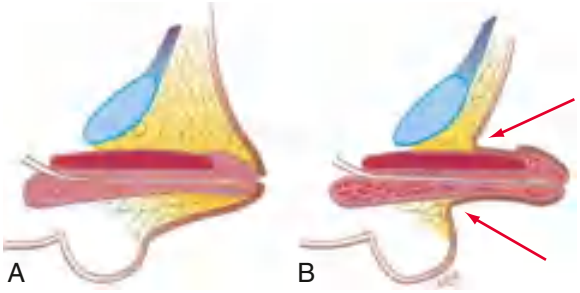

Fig. 581.7 Concealed penis **(A)**, which may be visualized by retracting skin lateral to penile shaft **(B)**. *(From Wein AJ, Kavoussi LR, Novick AC, et al., eds. Campbell-Walsh Urology, 9th ed. Philadelphia: WB Saunders; 2007: Fig. 126-4, p. 2339.)*

The pertinent measurement is the **stretched penile length**, which is measured by stretching the penis and measuring the distance from the penile base under the pubic symphysis to the tip of the glans. The mean length of the term newborn penis is 3.5 ± 0.7 cm and the diameter is 1.1 ± 0.2 cm. The diagnosis of micropenis in a male newborn is if the stretched length is <1.9 cm.

Micropenis usually results from a hormonal abnormality that occurs after the 14th week of gestation. Common causes include hypogonadotropic hypogonadism, hypergonadotropic hypogonadism (primary testicular failure), and idiopathic micropenis. If growth hormone deficiency is also present, neonatal hypoglycemia can occur. The most common cause of micropenis is failure of the hypothalamus to produce an adequate amount of gonadotropin-releasing hormone, as typically occurs in Kallmann syndrome (see Chapter 623), Prader-Willi syndrome (see Chapter 99), and Lawrence-Moon-Bardet-Biedl

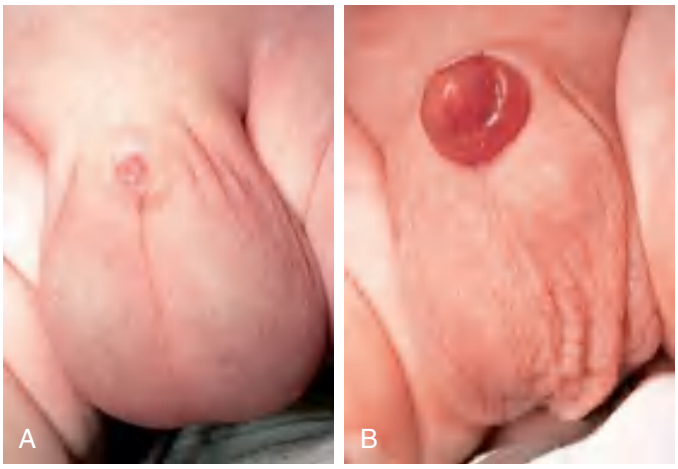

Fig. 581.8 A, Trapped (concealed) penis resulting from circumcision. B, Same patient after revision of circumcision. *(From Wein AJ, Kavoussi LR, Novick AC, et al., eds. Campbell-Walsh Urology, 9th ed. Philadelphia: WB Saunders; 2007: Fig. 126-2, p. 2340.)*

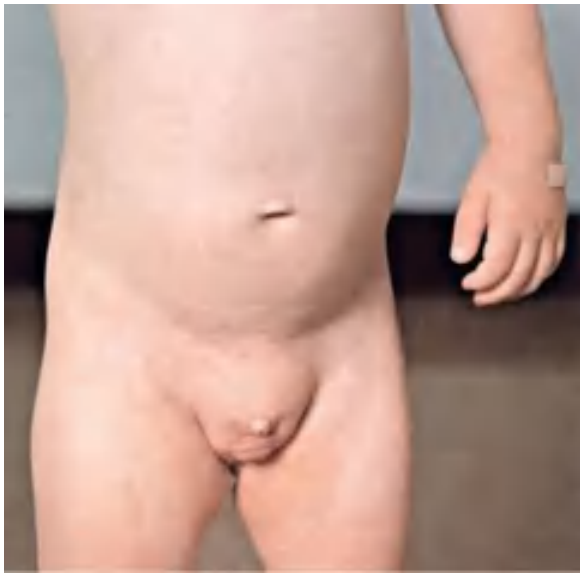

Fig. 581.9 Micropenis secondary to hypopituitarism in an 8-yr-old male. *(From Wein AJ, Kavoussi LR, Novick AC, et al., eds. Campbell-Walsh Urology, 9th ed. Philadelphia: WB Saunders; 2007: Fig. 126-5a, p. 2341.)*

syndrome. In some cases, there is growth hormone deficiency. Primary testicular failure can result from gonadal dysgenesis or rudimentary testes syndrome and also occurs in **Robinow syndrome** (characterized by hypoplastic genitals, shortening of the forearms, frontal bossing, hypertelorism, wide palpebral fissures, short broad nose, long philtrum, small chin, brachydactyly, and a normal karyotype).

A pediatric endocrinologist, geneticist, and pediatric urologist should examine all children with these syndromes, with participation by medical ethics. *Evaluation includes a karyotype, assessment of anterior pituitary function and testicular function, and MRI* to determine the anatomic integrity of the hypothalamus and the anterior pituitary gland as well as the midline structure of the brain. One of the difficult questions is whether androgen therapy is essential during childhood, because androgenic stimulation of penile growth in a prepubertal male can limit the growth potential of the penis in puberty. Studies of small groups of men with micropenis suggest that many, although not all, have satisfactory sexual function. Consequently, a decision for gender surgery in infancy is infrequently made.

PRIAPISM

Priapism is a persistent penile erection at least 4 hours in duration that continues beyond, or is unrelated to, sexual stimulation. Typically, only the corpora cavernosa is affected. There are three subtypes:

- Ischemic (venoocclusive, low-flow) priapism is characterized by little or no cavernous blood flow, and cavernous blood gases are hypoxic, hypercapnic, and acidotic. The corpora are rigid and tender to palpation. Immediate intervention is warranted.
- Nonischemic (arterial, high-flow) priapism is caused by unregulated cavernous arterial inflow. Typically, the penis is neither fully rigid nor painful. There is often a history of antecedent trauma resulting in a cavernous artery–corpora cavernosa fistula. Most cases resolve without intervention and expectant management is typical.
- Stuttering (intermittent) priapism is a recurrent form of ischemic priapism with painful erections with intervening periods of detumescence.

The most common cause of priapism in children is sickle cell disease, which is characterized by a predominance of sickle cell hemoglobin (see Chapter 511.1). As many as 29% of male patients with sickle cell disease develop priapism. The priapism is generally related to a low-flow state, secondary to sickling of red blood cells within the sinusoids of the corpora cavernosa during normal erection, resulting in venous stasis. This situation results in decreased local oxygen tension and pH, which potentiates further stasis and sickling. Priapism typically occurs during sleep, when mild hypoventilatory acidosis depresses oxygen tension and pH in the corpora. There is typically significant corporal engorgement with sparing of the glans penis. If the spongiosum is involved, voiding may be impaired. Evaluation may include a complete blood count. If the sickle cell status is unknown, hemoglobin electrophoresis should be performed. Corporal blood gas can help distinguish between a high-flow and low-flow state; ultrasound may also be used to differentiate these diagnoses. Other causes of low-flow priapism include sildenafil ingestion and leukemia.

In priapism secondary to sickle cell disease, medical therapy includes intravenous hydration, oxygen, alkalinization, and pain management with morphine. The American Urological Association guideline on priapism recommends concurrent intracavernous treatment beginning with corporal aspiration and irrigation with a sympathomimetic agent, such as phenylephrine. For patients with sickle cell disease, exchange transfusion may be considered but often takes several hours to arrange; therefore it is used when intracavernous treatment is not successful. If priapism has been present for >48 hours, ischemia and acidosis impair the intracavernous smooth muscle response to sympathomimetics. If irrigation and medical therapy are unsuccessful, a corporoglanular shunt should be considered. For stuttering priapism, administration of an oral α-adrenergic agent (pseudoephedrine) once or twice daily is first-line therapy. If this treatment is unsuccessful, an oral β-agonist (terbutaline) is recommended; a gonadotropin-releasing hormone analog plus flutamide is recommended as third-line therapy. Long-term follow-up of adults treated for sickle cell disease as children shows that satisfactory erectile function is inversely related to the patient's age at the onset of priapism and duration of priapism.

Nonischemic (high-flow) priapism most commonly follows perineal trauma, such as a straddle injury, that results in laceration of the cavernous artery. Typically, the aspirated blood is bright red, and the aspirate is similar to arterial blood. Color Doppler ultrasonography often demonstrates the fistula. The priapism spontaneously resolves in most cases. If it does not, angiographic embolization is indicated.

OTHER PENILE ANOMALIES

Aphallia (agenesis of the penis) affects approximately 1 in 10 million males. The karyotype is almost always 46, XY, and the usual appearance is that of a well-developed scrotum with descended testes and an absent penile shaft. Upper urinary tract abnormalities are common. In most cases, gender assignment surgery is recommended in the newborn period. **Diphallia** (duplication of the penis) ranges from a small accessory penis to complete duplication.

MEATAL STENOSIS

Meatal stenosis is a condition that almost always is acquired and occurs after neonatal circumcision. It most likely results from inflammation of

the denuded glans and is difficult to prevent. If the meatus is pinpoint, males void with a forceful, fine stream that goes a great distance. These males can experience dysuria, frequency, hematuria, or a combination of these conditions, typically around age 3-8 years. UTI is uncommon. Other males have dorsal deflection of the urinary stream. Although the meatus may be small, hydronephrosis or voiding difficulty is extremely rare unless there is associated balanitis xerotica obliterans (see Fig. 581.3; chronic dermatitis of unknown etiology, generally involving the glans and prepuce, occasionally extending into the urethra). Treatment is meatoplasty, in which the urethral meatus is opened surgically; this procedure can be performed either under anesthesia as an outpatient or in the office using local anesthesia (EMLA cream) with or without sedation. Routine cystoscopy is unnecessary.

OTHER MALE URETHRAL ANOMALIES

Parameatal urethral cyst manifests as an asymptomatic small cyst on one side of the urethral meatus. Treatment is excision under anesthesia. **Congenital urethral fistula** is a rare deformity in which a fistula is present from the penile urethra. It usually is an isolated abnormality. Treatment is fistula closure. **Megalourethra** is a large urethra that usually is associated with abnormal development of the corpus spongiosum. This condition is most commonly associated with prune-belly syndrome (see Chapter 577). **Urethral duplication** is a rare condition in which the two urethral channels lie in the same sagittal plane. There are many variations with complete and incomplete urethral duplication. These males often have a double stream. Most commonly, the dorsal urethra is small, and the ventral urethra is of normal caliber. Treatment involves excision of the small urethra. **Urethral hypoplasia** is a rare condition in which the entire male urethra is extremely small but patent. In some cases, a temporary cutaneous vesicostomy is necessary for satisfactory urinary drainage. Either gradual enlargement of the urethra or major urethroplasty is necessary. **Urethral atresia** refers to maldevelopment of the urethra and nearly always is fatal unless the urachus remains patent throughout gestation.

URETHRAL PROLAPSE (FEMALE)

Urethral prolapse occurs predominantly in females 1-9 years of age. The most common signs are bloody spotting on the underwear or diaper, although dysuria or perineal discomfort also can occur (Fig. 581.10). An inexperienced examiner can mistake the finding for sexual abuse. Initial therapy consists of application of estrogen cream 2-3 times daily for 3-4 weeks and sitz baths. Surgical repair is recommended for females that fail medical therapy and is curative. In some cases, this can be performed in the office under local anesthesia.

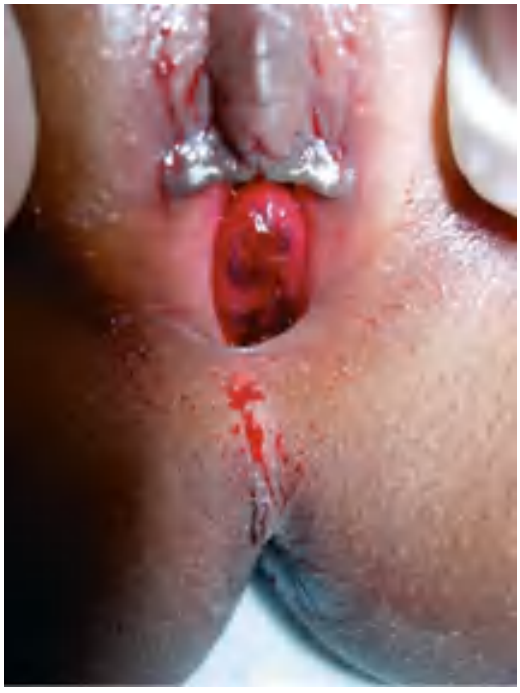

Fig. 581.10 Urethral prolapse in a 4-yr-old female who had bloody spotting on her underwear.

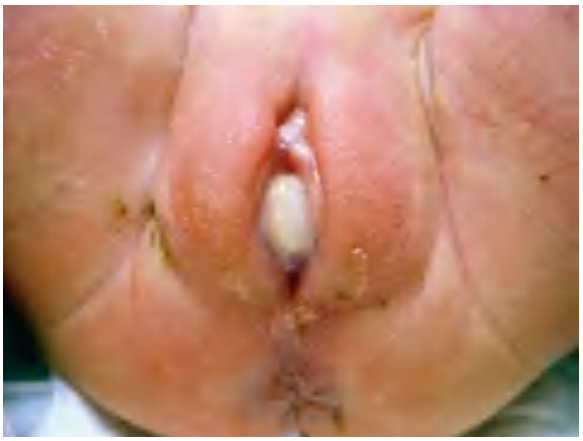

Fig. 581.11 Paraurethral cyst in a newborn female.

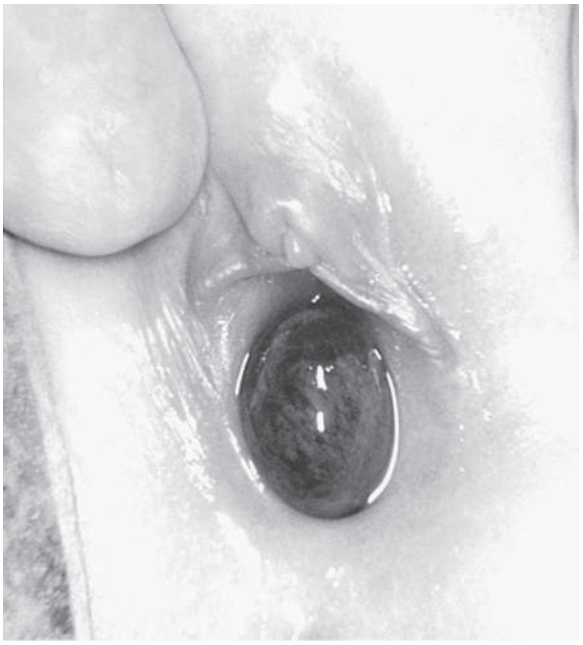

Fig. 581.12 Prolapsed ectopic ureterocele in a female infant. She had a nonfunctioning upper pole collecting system connected to the ureterocele.

OTHER FEMALE URETHRAL LESIONS

Paraurethral cyst results from retained secretions in the Skene glands secondary to ductal obstruction (Fig. 581.11). These lesions are present at birth, and most regress in size during the first 4-8 weeks, although occasionally incision and drainage is necessary. A **prolapsed ectopic ureterocele** appears as a cystic mass protruding from the urethra and is a presenting symptom in 10% of females with a ureterocele, which is a cystic swelling of the terminal ureter (Fig. 581.12). Ultrasonography should be performed to visualize the upper urinary tracts to confirm the diagnosis. Usually, either the ureterocele is incised or an upper urinary tract reconstructive procedure is necessary.

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Chapter 582

Disorders and Anomalies of the Scrotal Contents

Heather N. Di Carlo and Chad B. Crigger

UNDESCENDED TESTIS (CRYPTORCHIDISM)

The absence of a palpable testis in the scrotum indicates that the testis is undescended, absent, atrophic, or retractile.

Epidemiology

An undescended **(cryptorchid)** testis is the most common congenital genitourinary tract disorder in males. At birth, approximately 4.5% of males have an **undescended testis.** Because testicular descent occurs at 7-8 months of gestation, 30% of premature male infants have an undescended testis; the incidence is 3.4% at term. As many as 50% of congenital undescended testes descend spontaneously during the first 3 months of life, and by 6 months the incidence decreases to 1.5%. Spontaneous descent occurs secondary to a temporary testosterone surge (termed a *minipuberty*) during the first 2 months, which also results in significant penile growth. If the testis has not descended by 4 months, it will remain undescended. Cryptorchidism is bilateral in 10% of cases. There is some evidence that the incidence of cryptorchidism is increasing; this is attributed to increase in utero exposure to endocrine disrupting chemicals. Although cryptorchidism usually is considered to be congenital, some older males have a scrotal testis that "ascends" to a low inguinal position and therefore requires an orchiopexy. In addition, 1–2% of neonatal and young males undergoing hernia repair develop secondary cryptorchidism from scar tissue along the spermatic cord.

Pathogenesis

The process of testicular descent is regulated by an interaction among genetic, hormonal, and mechanical factors, including testosterone, dihydrotestosterone, müllerian-inhibiting factor, the gubernaculum, intraabdominal pressure, and the genitofemoral nerve (Table 582.1). The testis develops in the abdomen at 7-8 weeks of gestation. Insulin-like factor 3 controls the transabdominal phase. At 10-11 weeks, the Leydig cells produce testosterone, which stimulates differentiation of the Wolffian (mesonephric) duct into the epididymis, vas deferens, seminal vesicle, and ejaculatory duct. At 32-36 weeks, the testis, which is anchored at the internal inguinal ring by the gubernaculum, begins its process of descent and is controlled in part by a calcium gene-related peptide produced by the genitofemoral nerve. The gubernaculum descends the inguinal canal and guides the testis into the scrotum. Following testicular descent, the patent processus vaginalis (hernia sac) normally closes.

Clinical Manifestations

Undescended testes are classified as **abdominal** (which are nonpalpable), **peeping** (abdominal but can be pushed into the upper part of the inguinal canal), **inguinal, gliding** (can be pushed into the scrotum but retracts immediately to the pubic tubercle), and **ectopic** (superficial inguinal pouch or, rarely, perineal). Most undescended testes are palpable just distal to the inguinal canal over the pubic tubercle.

A **disorder of sex development** should be suspected in a newborn phenotypic male with bilateral nonpalpable testes, as the child could be a virilized female with congenital adrenal hyperplasia (see Chapter 616). *In a male with midpenile or proximal hypospadias and a palpable undescended testis, the risk of a disorder of sexual development is 15%; the risk is 50% if the testis is nonpalpable.*

The potential **consequences of cryptorchidism** include poor testicular growth, infertility, testicular malignancy, associated hernia, torsion of the cryptorchid testis, and the possible psychologic effects of an empty scrotum.

The undescended testis is normal at birth histologically with a plethora of germ cells, but pathologic changes occur by 6-12 months of age. Delayed germ cell maturation, germ cell depletion, hyalinization of the seminiferous tubules, and reduced Leydig cell number are typical; these changes are progressive over time if the testis remains undescended. At puberty, an undescended testis has no viable sperm components. Although less severe, changes may occur in the contralateral descended testis after 4-7 years. After treatment for a unilateral undescended testis, 85% of patients are fertile, which is slightly less than the 90% rate of fertility in an unaffected population of adult males. In contrast, following bilateral orchiopexy, only 50–65% of patients are fertile.

The risk of a **germ cell malignancy** (see Chapter 552) developing in an undescended testis is four times higher than in the general population and is approximately 1 in 80 with a unilateral undescended testis and 1 in 40-50 for bilateral undescended testes. Testicular tumors are less common if orchiopexy is performed before 10 years of age, but they still occur, and adolescents should be instructed in testicular self-examination. The peak age for developing a malignant testis tumor is 15-45 years of age. The most common tumor developing in an undescended testis in an adolescent or adult is a **seminoma** (65%); after orchiopexy, nonseminomatous tumors represent 65% of testis tumors. Orchiopexy seems to reduce the risk of testicular cancer; it is uncommon for testis tumors to occur if the orchiopexy was performed before the age of 2 years. The contralateral scrotal testis may also be at a slightly increased risk for malignancy.

An indirect inguinal hernia usually accompanies a congenital undescended testis but rarely is symptomatic. Torsion and infarction of the cryptorchid testis also are uncommon but can occur because of excessive mobility of undescended testes. Consequently, inguinal pain and/or swelling in a male with an undescended testis should raise the suspicion of an inguinal hernia or torsion of the undescended testis.

An *acquired* or **ascending undescended testis** occurs when a male has a descended testis at birth, but during childhood, usually between ages 4-10 years, the testis does not remain in the scrotum. Such males often have a history of a retractile testis. With testicular ascent on physical examination, the testis can often be manipulated into the upper scrotum, but there is obvious tension on the spermatic cord. This condition is speculated to result from incomplete involution of the processus vaginalis, restricting spermatic cord growth and resulting in the testis gradually moving out of its scrotal position during a male's somatic growth.

On physical examination of the scrotum, the child should be encouraged to relax. Careful consideration of a hypoplastic ipsilateral scrotum may clue the examiner in to a diagnosis of an undescended testicle. The examiner should examine the patient's scrotum and inguinal canal using their dominant hand. The nondominant hand is positioned over the pubic tubercle and is pushed inferiorly toward the scrotum. The examiner's dominant hand is used to try to palpate the testis. If the testis is nonpalpable, the *soap test* often is useful; soap is applied to the inguinal canal and the examiner's hand, significantly reducing friction and facilitating identification of an inguinal testis. In addition, pulling on the scrotum can pull a high inguinal testis into a palpable position. One soft sign that a testis is absent is contralateral testicular hypertrophy, but this finding is not 100% diagnostic.

Retractile testes may be misdiagnosed as undescended testes. Males older than 1 year of age often have a brisk cremasteric reflex, and if the child is anxious or ticklish during scrotal examination, the testis may be difficult to manipulate into the scrotum. Males should be examined with their legs in a relaxed frog-leg position, and if the testis can be manipulated into the scrotum comfortably, it is probably retractile. It should be monitored every 6-12 months with follow-up physical examinations, because it can become an acquired undescended testis. Overall, as many as one third of males with a retractile testis develop an acquired undescended testis requiring orchiopexy, and males younger than 7 years of age at diagnosis of a retractile testis are at greatest risk. Although definitive data are not available, it is generally thought that males with a retractile testis are not at increased risk for infertility or malignancy.

Approximately 10% of undescended testes are **nonpalpable testes.** Of these, 50% are viable testes in the abdomen or high in the inguinal canal, and 50% are atrophic or absent, almost always in the scrotum,

Table 582.1 Conditions Associated with Cryptorchidism

DISEASES OR SYNDROMES ASSOCIATED WITH DECREASED ANDROGEN LEVELS
Disorders of Sex Development (DSD)
Sex chromosome DSD 47,XXY (Klinefelter syndrome and variants) 45,X/46,XY (mixed gonadal dysgenesis) 46,XX/46,XY (chimerism)
46,XY DSD
Disorders of testicular development Complete or partial gonadal dysgenesis Variations in *ARX, ATRX, CBX2, DAX1 (NROB1), DHH, DHX37, DMRT1, EMX2, ESR2, FGFR2, GATA4, HHAT, MAP3K1, NR5A1, SF1, SOX9, SRY, TSPYL1, WNT4, WT1*(WAGR syndrome, Denys-Drash syndrome, Frasier syndrome), *ZFPM2*, and *ZNRF3* genes
Disorders in androgen synthesis or action Androgen biosynthetic defect • Abnormal LH (*LHB*) • Steroidogenic acute regulatory protein (StAR deficiency) (*STAR*) • 7-Dehydro-cholesterol desmolase deficiency (Smith-Lemli-Opitz syndrome) • Cholesterol desmolase deficiency (*CYP11A1*) • 3β -hydroxysteroid dehydrogenase type 2 deficiency (*HSD3B2*) • 17,20-lyase deficiency or combined 17 hydroxylase/17,20-lyase deficiency (*CYP17A1*) • P450-oxidoreductase deficiency (*POR*) • 17β -Hydroxysteroid-dehydrogenase type 3 (*HSD17B3*) • 5-α reductase type 2 enzyme deficiency (*SRD5A2*) • Cytochrome b5 deficiency (*CYB5A*) • Backdoor steroidogenetic enzyme deficiency (*AKR1C2, AKR1C4*) Defect in androgen action • Partial androgen insensitivity (*AR*) • Infantile onset X-linked spinal muscular atrophy LH receptor defects • Inactivating mutation of LH receptor gene (*LHCGR*) (Leydig cell hypoplasia, aplasia)
46,XX DSD Ovotesticular DSD Testicular DSD (e.g. *SRY*+, dup *SOX9*, *RSP01*) 46,XX male
Congenital Hypogonadotropic Hypogonadism in 46,XY
Isolated hypogonadotropic hypogonadism with anosmia (Kallmann syndrome) *KAL1, FGFR1/FGF8, PROK2/PROKR2, KAL1, NELF, HS6ST1, WDR11*, and *SEMA3A* gene variants *CHD7* gene variant (CHARGE syndrome)
Normosmic isolated hypogonadotropic hypogonadism Variants in *KISS1, GPR54, LEP, LEPR, TAC3/TACR3*, and *GNRH1/GNRHR* genes (also reported variants in *FGFR1/FGF8, PROKR2, CHD7*, and *WDR11* genes)
Multiple pituitary hormone deficiencies Variants in *PROP1* genes, *HESX1* gene (septo-optic dysplasia)
Congenital Hypergonadotropic Hypogonadism
Down syndrome Noonan syndrome
Syndromes Associated with Both Primary and Secondary Hypogonadism
Prader-Willi syndrome Bardet-Biedl syndrome
CONDITIONS ASSOCIATED WITH DECREASED INSL3 OR AMH LEVELS OR ACTIONS
INSL3 or *RXFP2* variants Persistent Müllerian duct syndrome: AMH and AMH receptor (*AMH, AMHR2*)
OTHER CONDITIONS RELATED WITH CRYPTORCHIDISM
Multiple syndromes not specifically involving pituitary-gonadal development or function

AMH, anti-Müllerian hormone; CHARGE, coloboma, heart defects, atresia choanal, growth restriction, genital abnormalities, ear abnormalities; INSL3, insulin like peptide 3;.LH, luteinizing hormone.

Modified from Rodprasert W, Virtanen HE, Mäkekä JA, Toppari J: Hypogonadism and cryptorchidism. *Front Endocrinol (Lausanne)*. 2020;10:906.

secondary to spermatic cord torsion in utero **(vanishing testis).** If the nonpalpable testis is abdominal, it will not descend after 3 months of age. *Although sonography often is performed to try to identify whether the testis is present, it rarely changes clinical management, because the abdominal testis and atrophic testis are not identified on sonography.* Inguinal/scrotal sonography might be beneficial in obese males with a nonpalpable testis; in this clinical setting, the undescended testis often is nonpalpable, and an inguinal/scrotal sonogram can be beneficial in surgical planning. Computed tomographic imaging is relatively accurate in demonstrating the presence of the testis, but the radiation exposure is significant. MRI is even more accurate, but the disadvantage is that general anesthesia or sedation is necessary in most young children.

None of these imaging studies are 100% accurate and in general do not add significantly to clinical decision-making by the pediatric urologist or pediatric surgeon. Consequently, routine use of imaging is discouraged. A diagnostic approach is noted in Figure 582.1.

Treatment

The congenital undescended testis that does not descend by 6 months (corrected for gestational age) should be treated surgically within the next 12 months. Most testes can be brought down to the scrotum with an orchiopexy, which involves an inguinal incision, mobilization of the testis and spermatic cord, and correction of an indirect inguinal hernia. The procedure is typically performed on an outpatient basis and has a success rate of 98%. In some males with a testis that is close to the scrotum, a prescrotal orchiopexy can be performed. In this procedure, the entire operation is performed through a high scrotal incision. Often the associated inguinal hernia also can be corrected through this incision. Advantages of this approach over the inguinal approach include shorter operative time and less postoperative discomfort.

In males with a nonpalpable testis, an exam under anesthesia should be done to reassess for palpability; if testes are still nonpalpable, diagnostic laparoscopy is performed in most centers. This procedure allows safe and rapid assessment of whether the testis is intraabdominal. In most cases, orchiopexy of the intraabdominal testis located adjacent to the internal inguinal ring is successful, but orchiectomy should be considered in more difficult cases or when the testis appears to be atrophic. A two-stage orchiopexy sometimes is needed in males with a high abdominal testis. Males with abdominal testes are managed with laparoscopic techniques at many institutions. Testicular prostheses are available for older children and adolescents when the absence of the gonad in the scrotum might have an undesirable psychologic effect. The FDA has approved a saline testicular implant. Solid silicone "carving block" implants also are used (Fig. 582.2). Placement of testicular prostheses early in childhood is recommended for males with anorchia (absence of both testes).

The American Urological Association guidelines for the evaluation and treatment of males with an undescended testis are summarized in Table 582.2.

SCROTAL SWELLING

Scrotal swelling may be acute or chronic and painful or painless (Table 582.3). Abrupt onset of painful scrotal swelling necessitates prompt evaluation because some conditions, such as testicular torsion and incarcerated inguinal hernia, require emergency surgical management. Tables 582.4 and 582.5 show the differential diagnosis.

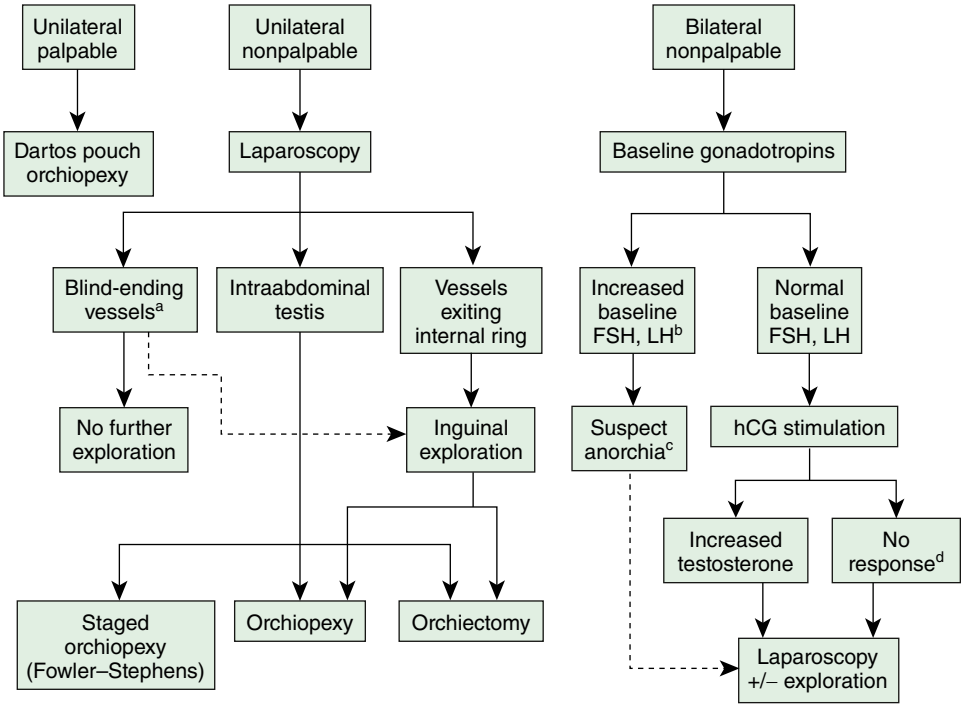

Fig. 582.1 Management algorithm for undescended testis. [a]If blind-ending vas deferens vessels are unequivocally identified, then there is no need for further exploration. [b]Baseline FSH and LH levels are elevated if values are 3 SD above the mean. *c,* Increased suspicion of anorchia with elevated baseline FSH and LH levels; however, exploration is still warranted. *d,* Testicular remnant tissue may be present despite a negative hCG stimulation test; therefore exploration for testicular remnant tissue should still be performed. *(From Bowlin PR, Lorenzo AJ. Undescended testes and testicular tumors. In: Holcomb III GW, Murphy JP, St. Peter SD, eds. Holcomb and Ashcraft's Pediatric Surgery, 7th ed. Philadelphia: Elsevier; 2020: Fig. 51-2, p. 808.)*

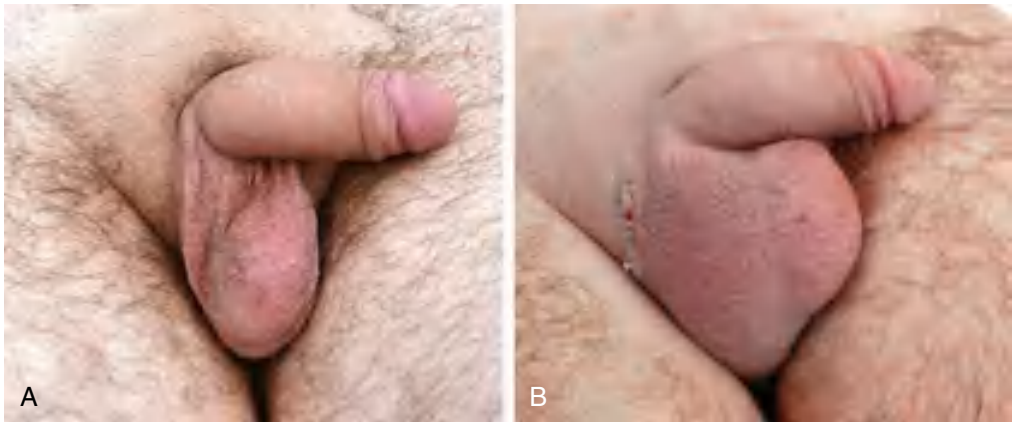

Fig. 582.2 A, Adolescent with solitary left testis. B, Appearance following implantation of right testicular prosthesis.

Table 582.2 American Urological Association Guidelines for Evaluation and Treatment of Males with an Undescended Testis

DIAGNOSIS

- Providers should obtain gestational history at initial evaluation of males with suspected cryptorchidism. *(Standard)*
- Primary care providers should palpate testes for quality and position at each recommended well-child visit. *(Standard)*
- Providers should refer infants with a history of cryptorchidism (detected at birth) who do not have spontaneous testicular descent by 6 months (corrected for gestational age) to an appropriate surgical specialist for timely evaluation. *(Standard)*
- Providers should refer males with the possibility of newly diagnosed (acquired) cryptorchidism after 6 months (corrected for gestational age) to an appropriate surgical specialist. *(Standard)*
- Providers must immediately consult an appropriate specialist for all phenotypic male newborns with bilateral, nonpalpable testes for evaluation of a possible disorder of sex development (DSD). *(Standard)*
- Providers should not perform ultrasound (US) or other imaging modalities in the evaluation of males with cryptorchidism before referral because these studies rarely assist in decision making. *(Standard)*
- Providers should assess the possibility of a disorder of sex development (DSD) when there is increasing severity of hypospadias with cryptorchidism. *(Recommendation)*
- In males with bilateral, nonpalpable testes who do not have congenital adrenal hyperplasia (CAH), providers should measure Mullerian Inhibiting Substance (MIS or Anti-Mullerian Hormone [AMH] level), and consider additional hormone testing, to evaluate for anorchia. *(Option)*
- In males with retractile testes, providers should monitor the position of the testes at least annually to monitor for secondary ascent. *(Standard)*

TREATMENT

- Providers should not use hormonal therapy to induce testicular descent because evidence shows low response rates and lack of evidence for long-term efficacy. *(Standard)*
- In the absence of spontaneous testicular descent by 6 months (corrected for gestational age), specialists should perform surgery within the next year. *(Standard)*
- In prepubertal males with palpable, cryptorchid testes, surgical specialists should perform scrotal or inguinal orchidopexy. *(Standard)*
- In prepubertal males with nonpalpable testes, surgical specialists should perform examination under anesthesia to reassess for palpability of testes. If nonpalpable, surgical exploration and, if indicated, abdominal orchidopexy should be performed. *(Standard)*
- At the time of exploration for a nonpalpable testis in boys, surgical specialists should identify the status of the testicular vessels to help determine the next course of action. *(Clinical Principle)*
- In males with a normal contralateral testis, surgical specialists may perform an orchiectomy (removal of the undescended testis) if a male has a normal contralateral testis and either very short testicular vessels and vas deferens, dysmorphic or very hypoplastic testis, or postpubertal age. *(Clinical Principle)*
- Providers should counsel males with a history of cryptorchidism and/or monorchidism and their parents regarding potential long-term risks and provide education on infertility and cancer risk. *(Clinical Principle)*

Adapted from Kolon TF, Herndon CDA, Baker LA, et al. Evaluation and treatment of cryptorchidism (2018): AUA Guideline. https://www.auanet.org/guidelines-and-quality/guidelines/cryptorchidism-guideline

Clinical Manifestations

A detailed history is helpful in determining the cause of the swelling and includes the rapidity of onset of pain. With testicular torsion, the pain often is sudden in onset and may be associated with exercise or minor genital trauma, duration of pain, and radiation of pain. Inguinal discomfort is common with testicular torsion, inguinal hernia, or epididymitis, and associated flank pain can occur with passage of a ureteral calculus; previous episodes of similar pain, which are common in males with intermittent testicular torsion or inguinal hernia; nausea and vomiting, which

Table 582.3 Differential Diagnosis of Pediatric Adolescent Acute Scrotal Pain

- Appendage torsion
  - Appendix testis
  - Other appendage (epididymis, paradidymis, vas aberrans)
- Spermatic cord torsion
  - Intravaginal, acute or intermittent
  - Extravaginal
- Epididymitis
  - Infectious
    - Urinary tract infection
    - Sexually transmitted infection
    - Viral including COVID-19
  - Sterile or traumatic
- Scrotal edema or erythema
  - Diaper dermatitis, insect bite, or other skin lesions
  - Idiopathic scrotal edema
  - IgA vasculitis (Henoch-Schönlein purpura)
- Orchitis
  - Associated with epididymitis with or without abscess
  - Vasculitis (e.g., IgA vasculitis)
  - Viral illness (mumps, COVID-19)
- Trauma
  - Hematocele or scrotal contusion or testis rupture
- Hernia or hydrocele
  - Inguinal hernia with or without incarceration
  - Communicating hydrocele
  - Encysted hydrocele with or without torsion
  - Associated with acute abdominal pathology (e.g., appendicitis, peritonitis)
- Varicocele
- Intrascrotal mass
  - Cystic dysplasia or tumor of testis
  - Epididymal cyst, spermatocele or tumor
  - Other paratesticular tumors
- Musculoskeletal pain from inguinal tendinitis or muscle strain
- Ilioinguinal neuropathy
- Genitofemoral nerve entrapment
- Referred pain (e.g., ureteral calculus or anomaly)

Modified from Palmer LS, Palmer JS. Management of abnormalities of the external genitalia in boys. In: Partin AW, Dmochowski RR, Kavoussi LR, Peters CW, eds. *Campbell-Walsh Urology,* 12th ed. Philadelphia: Elsevier; 2021: Box 44-2.

Table 582.4 Differential Diagnosis of Scrotal Masses in Male Children and Adolescents

PAINFUL	PAINLESS
Testicular torsion	Hydrocele
Torsion of appendix testis	Inguinal hernia*
Epididymitis	Varicocele*
Trauma: ruptured testis, hematocele	Spermatocele*
	Testicular tumor*
Inguinal hernia (incarcerated)	IgA vasculitis*
Mumps orchitis	Idiopathic scrotal edema
Testicular vasculitis	

*May be associated with discomfort.

Table 582.5 Differential Diagnosis of Scrotal Swelling in Newborn Males

- Hydrocele
- Inguinal hernia (reducible)
- Inguinal hernia (incarcerated)*
- Testicular torsion*
- Scrotal hematoma
- Testicular tumor
- Meconium peritonitis
- Epididymitis*

*May be associated with discomfort.

are associated with testicular torsion and inguinal hernia; and irritative urinary symptoms, such as dysuria, urgency, and frequency, which indicate a urinary tract infection that can cause epididymitis. Some males report a recent history of scrotal trauma. There are multiple reports of familial testicular torsion related to inheritance of bell clapper deformity (discussed later). Males with lower urinary tract pathology such as urethral stricture or neuropathic bladder may be prone to epididymitis.

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

Laboratory Findings and Diagnosis

Pertinent laboratory studies include urinalysis and culture. A positive urinalysis suggests bacterial epididymitis (uncommon before adolescence). Serum studies are not helpful in establishing a diagnosis unless a testicular malignancy is suspected. After initial evaluation in males with testicular pain, color Doppler ultrasonography often is helpful in establishing the diagnosis because it assesses whether testicular blood flow is normal, reduced, or increased (Fig. 582.3). If a hydrocele is present and the testis is nonpalpable, or if an abnormality of the testis is found, sonography also is indicated. *Imaging studies are not 100% accurate; they should not be used to decide whether a male with testicular pain should be referred for urologic evaluation.* As such, torsion is a clinical diagnosis.

Color Doppler ultrasonography allows assessment of testicular blood flow and testicular morphologic features. Accuracy is >95% if the ultrasonographer is experienced and the patient is older than 2 years of age. The "whirlpool" sign is pathognomonic. A false-negative study (demonstrates normal testicular blood flow) can occur in a male with testicular torsion if the degree of torsion is <360 degrees and the duration of torsion is short, because there may be continued testicular perfusion. In males <1 year of age, including neonates, blood flow may be difficult to demonstrate in 15% of normal testes.

TESTICULAR (SPERMATIC CORD) TORSION

Etiology

Testicular torsion requires prompt diagnosis and treatment to salvage the testis. Torsion is the most common cause of severe testicular pain in males 12 years of age and older and is uncommon before age 10. It is caused by inadequate fixation of the testis within the scrotum, resulting from a redundant tunica vaginalis and abnormal gubernacular attachment, allowing excessive mobility of the testis. The abnormal attachment is termed a **bell clapper deformity** and may be bilateral. Following spermatic cord torsion, venous congestion occurs, and subsequently arterial flow is interrupted. The likelihood of testis survival depends on the duration and severity of torsion. After 6 hours of absent blood flow to the testis, irreversible loss of spermatogenesis can occur. Torsion is familial in 10% of males.

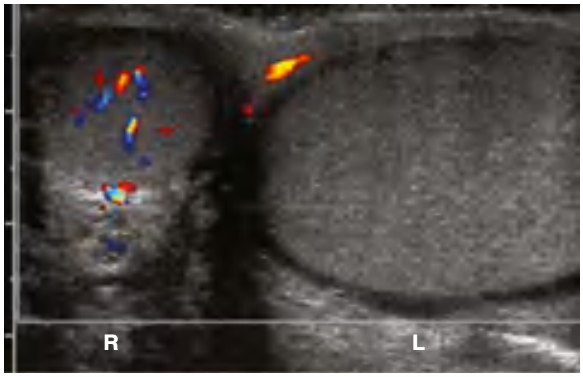

Fig. 582.3 Testicular torsion and axis change. A color Doppler ultrasound in the transverse plane shows color flow in the right testicle. The right testicle is oval to circular because it has been evaluated in the transverse plane. The left testicle is elongated as if it is in the longitudinal plane, indicating an abnormal lie within the scrotum worrisome for torsion. Lack of color Doppler flow in the left testicle confirms left testicular torsion. *(From Coley BD, ed. Caffey's Pediatric Diagnostic Imaging, 13th ed. Philadelphia: Elsevier; 2019: Fig. 125-13, p. 1195.)*

Diagnosis

Testicular torsion produces acute pain and swelling of the scrotum. On examination, the scrotum is swollen, and the testis is exquisitely tender and often difficult to examine. The cremasteric reflex is nearly always absent, though this may be absent at baseline in a proportion of males. The position (lie) of the testis is abnormal, and the testis is often located high in the scrotum. In addition, nausea and vomiting often occur. The condition can be differentiated from an incarcerated hernia because swelling in the inguinal area typically is absent with torsion. The Testicular Workup for Ischemia and Suspected Torsion (TWIST) score is a clinical tool that can be used determine the likelihood of testicular torsion. The score consists of testicular swelling (2 points), hard testis (2 points), high-riding testis (1 point), absent cremasteric reflex (1 point), and nausea/vomiting (1 point). Patients can then be stratified into low (0 points), intermediate (1-5), and high risk (6-7), which aids in determining further imaging and/or surgical consultation.

For patients who are high risk or meet the clinical diagnosis of testicular torsion, prompt surgical consultation should be obtained. If the pain duration is <4-6 hours, manual detorsion may be attempted. In 65% of cases the torsed testis rotates inward, so detorsion should be attempted in the opposite direction (e.g., the left testis is rotated clockwise). Successful manual detorsion results in dramatic pain relief. In the emergency department, patients with an intermediate risk TWIST score should undergo immediate scrotal ultrasound. In some centers, this is performed as a point of care procedure by the emergency department staff.

Some adolescents experience **intermittent testicular torsion**. These males report episodes of severe unilateral testicular pain that resolves spontaneously after 30-60 minutes. Treatment is elective bilateral scrotal orchiopexy. Close follow-up and clear return instructions are requisite in such cases until elective orchiopexy is performed.

Treatment

Treatment is prompt surgical exploration and detorsion. If the testis is explored within 6 hours of torsion, up to 90% will survive. Testicular salvage decreases rapidly with a delay of more than 6 hours. If the degree of torsion is 360 degrees or less, the testis might have sufficient arterial flow to allow the gonad to survive, even after 24-48 hours. Following detorsion, the testis is fixed in the scrotum with nonabsorbable sutures, termed **scrotal orchiopexy,** to prevent torsion in the future. The contralateral testis also should be fixed in the scrotum because the predisposing anatomic condition (bell clapper deformity) often is bilateral. If the testis appears nonviable, orchiectomy is performed (Fig. 582.4A). The detorsed testis may undergo compartment syndrome,

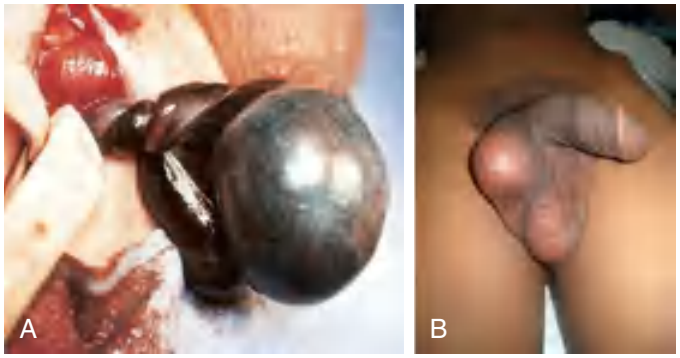

Fig. 582.4 A, Left testicular torsion in adolescent with acute scrotum; the testis is necrotic. B, "Late-phase torsion" in an adolescent with severe testicular pain 1 month prior. Note absence of inflammation and high position of testis in scrotum.

and following detorsion, despite blood flow to the testis, high intratesticular pressure may cause ischemia and necrosis. This condition has been treated intraoperatively by incising the tunica vaginalis (similar to a blunt testicular rupture) and placing a tunica vaginalis flap over the exposed tunica. Some adolescents do not undergo prompt evaluation and treatment and present with *late phase testicular torsion,* in which there is delayed diagnosis of torsion. Often the testis is high in the scrotum and nontender (see Fig. 582.4B). While males with torsion of longer duration prior to treatment may exhibit reduced spermatogenesis, current evidence shows pregnancy rates of couples in which the male has a history of acute testicular torsion to be similar to the general population.

Spermatic cord torsion can also occur in the fetus or neonate. This condition results from incomplete attachment of the tunica vaginalis to the scrotal wall and is "extravaginal." When torsion occurs just before delivery, the baby usually is born with a large, firm, nontender testis. Usually the ipsilateral hemiscrotum is ecchymotic (Fig. 582.5). In these cases, the testis rarely is viable because torsion was a remote event. However, the contralateral testis is at increased risk for torsion until 1-2 months beyond term. The pediatric urology community is divided regarding whether immediate exploration is necessary in a male newborn who has suspected testicular torsion at birth, but if observation is recommended, the family needs to be counseled regarding the risk of contralateral spermatic cord torsion. If the initial exam is normal and the newborn subsequently develops scrotal swelling and erythema, and imaging is consistent with spermatic cord torsion, emergency scrotal exploration is indicated.

TORSION OF THE APPENDIX TESTIS/EPIDIDYMIS

Torsion of the appendix testis is the most common cause of testicular pain in males age 4-10 years but is uncommon in adolescents. The appendix testis is a stalklike 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 occurs, resulting in testicular pain and scrotal erythema. The onset of pain is typically gradual. Palpation of the testis usually reveals a 3-5 mm tender indurated mass on the upper pole (Fig. 582.6A). In some cases, the appendage that has undergone torsion may be visible through the scrotal skin, termed the **"blue dot"** sign. In some males, distinguishing torsion of the appendix from testicular torsion is difficult. In such cases, color Doppler ultrasonography is useful because testicular blood flow is normal and shows hyperemia to the upper pole of the testis. In such cases, the radiologist often recognizes epididymal enlargement and makes the diagnosis of epididymitis, reflecting the inflammatory reaction (see Fig. 582.6B).

The natural history of torsion of the appendix testis is for the inflammation to resolve in 3-10 days. Nonoperative treatment is recommended, including bed rest for 24 hours and analgesia with nonsteroidal antiinflammatory medication for several days. If the diagnosis is uncertain, scrotal exploration is recommended.

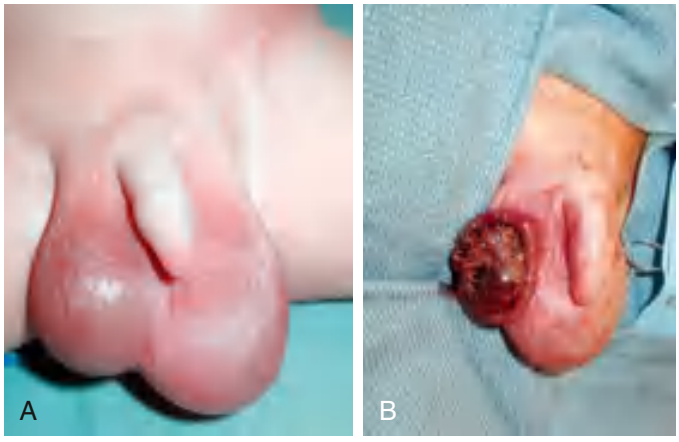

Fig. 582.5 A and B, Right testicular torsion in a newborn. The right hemiscrotum is darker, and the testis was indurated and enlarged.

EPIDIDYMITIS

Acute bacterial inflammation of the epididymis is an ascending retrograde infection from the urethra, through the vas deferens into the epididymis. This condition causes acute scrotal pain, erythema, 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. In younger males, the responsible organism is often *Escherichia coli* (see Chapter 246). After puberty, bacterial epididymitis becomes progressively more common and can cause acute painful scrotal swelling in young sexually active males. Urinalysis usually reveals pyuria. Epididymitis can be bacterial (usually gonococcus or *Chlamydia*; see Chapters 238 and 272) or viral (mumps, enterovirus, or adenovirus; see Chapters 295, 297, and 309), but often the organism remains undetermined. Familial Mediterranean fever is another cause. Treatment consists of bed rest and antibiotics as indicated. Differentiation from torsion is straightforward with scrotal ultrasonography.

IgA vasculitis, previously known as Henoch-Schönlein purpura, (see Chapter 210.1) is a systemic vasculitis that involves multiple organ systems and that can involve the kidney and spermatic cord. When the spermatic cord is involved, typically there is bilateral painful scrotal swelling with purpuric lesions involving the scrotum. Scrotal sonography should show normal testicular blood flow. Treatment is directed toward systemic treatment of the IgA vasculitis. Isolated testicular vasculitis is less common in IgA vasculitis and, in such cases, polyarteritis nodosa should be suspected.

VARICOCELE

A **varicocele** is a congenital condition in which there is abnormal dilation of the pampiniform plexus in the scrotum, often described as a "bag of worms" (Fig. 582.7). Dilation of the pampiniform venous plexus results from valvular incompetence of the internal spermatic vein. Approximately 15% of adult males have a varicocele; of these, approximately 10–15% are subfertile. Varicocele is the most common (and virtually the only) surgically correctable cause of infertility in males. A varicocele is found in 10–15% of adolescent males, but it rarely is diagnosed in males younger than 10 years old, because the varicocele becomes distended only after the increased blood flow associated with

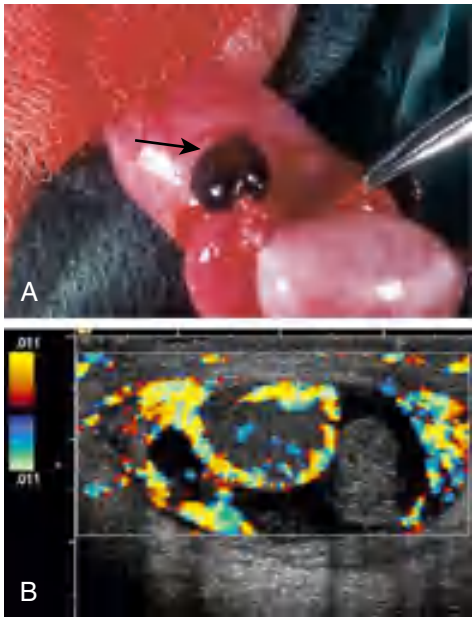

Fig. 582.6 A, Torsion of the appendix testis; the appendix testis is necrotic *(arrow)*. B, Color Doppler scrotal sonogram showing hyperemia to the testis and absent flow to the appendix testis *(right side)*. Symptoms resolved with medical therapy.

puberty occurs. Varicoceles occur predominantly on the left side, are bilateral in 2% of cases, and rarely involve the right side only. A varicocele in a male younger than 10 years or on the right side might indicate an abdominal or retroperitoneal mass; an abdominal ultrasound or CT scan should be performed in such cases.

A varicocele typically is a painless paratesticular mass. Occasionally patients describe a dull ache in the affected testis. Usually the varicocele is not apparent when the patient is supine because it is decompressed; in contrast, the varicocele becomes prominent when the patient is standing and enlarges with a Valsalva maneuver. Many pediatricians do not routinely screen adolescents for a varicocele. Varicoceles typically are graded from 1-3 with the male standing: **grade 1** is palpable only with Valsalva (clinically insignificant); **grade 2** is palpable without Valsalva but is not visible on inspection; and **grade 3** is visible with inspection. Males with a grade 3 varicocele are at greatest risk for testicular growth arrest, particularly if the varicocele is larger than the testis. Testicular size should be documented with calipers, an orchidometer, or scrotal sonography, because if the affected left testis is significantly smaller than the right testis, spermatogenesis probably has been adversely affected. A **semen analysis** should be considered in sexually mature adolescents who are Tanner stage V.

The goal of varicocelectomy is to maximize future fertility. Surgical treatment of varicoceles is indicated in males with a significant disparity in testicular size, with pain in the affected testis, if the contralateral testis is diseased or absent, or with oligospermia on semen analysis. Following treatment, typically the involved testis enlarges and catches up with the normal testis over the following 1-2 years. Varicocelectomy should also be considered in males with a large grade 3 varicocele, even if there is no disparity in testicular size. Surgical repair is accomplished with a variety of techniques by ligation of the veins of the pampiniform plexus laparoscopically or through an inguinal or subinguinal incision (with or without an operating microscope) or by ligating the internal spermatic vein in the retroperitoneum. The operation is performed on an ambulatory basis.

SPERMATOCELE

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

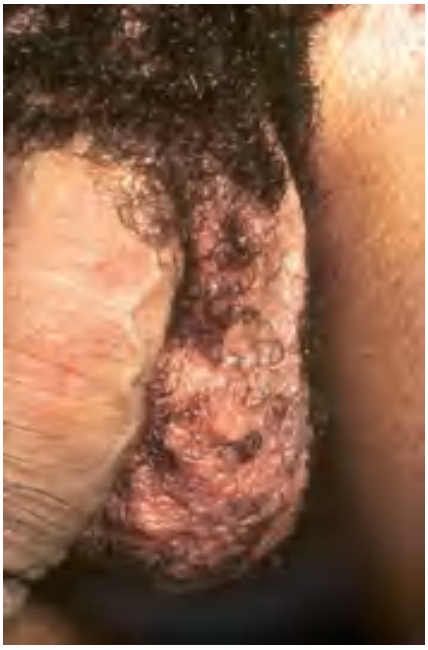

Fig. 582.7 Left varicocele in an adolescent male.

HYDROCELE

Etiology

A hydrocele is an accumulation of fluid in the tunica vaginalis (Fig. 582.8). Between 1% and 2% of 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 vaginalis, the hydrocele persists. It is typically small in the morning and may become larger during the day due to upright positioning. 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 males, a noncommunicating hydrocele can result from an inflammatory condition within the scrotum, such as testicular torsion, torsion of the appendix testis, epididymitis, or testicular tumor. The long-term risk of a communicating hydrocele is the development of an inguinal hernia. Some older males and adolescents also develop a hydrocele. In some cases, hydroceles develop acutely after an episode of scrotal trauma or epididymoorchitis, whereas others develop more insidiously.

Diagnosis

On examination, hydroceles are smooth and nontender. Transillumination of the scrotum confirms the fluid-filled nature of the mass. It is important to palpate the testis, because some young males develop a hydrocele in association with a testis tumor. If the testis is nonpalpable, a scrotal ultrasound should be performed to confirm that the testis is present and normal. If compression of the fluid-filled mass completely reduces the hydrocele, an inguinal hernia/hydrocele is the likely diagnosis.

Treatment

Most congenital hydroceles resolve by 12 months of age following reabsorption of the hydrocele fluid. If the hydrocele is large and tense, however, early surgical correction should be considered, because it is difficult to verify that the child does not have a hernia, and large hydroceles rarely disappear spontaneously. Hydroceles persisting beyond 12-18 months often are communicating and should be repaired. Surgical correction is similar to a herniorrhaphy (see Chapter 394). Through an inguinal incision, the spermatic cord is identified, the hydrocele fluid is drained, and a high ligation of the processus vaginalis is performed. If an older male has a large hydrocele, often diagnostic laparoscopy can be performed to determine whether there is a patent processus vaginalis, and if the internal ring is closed, then the hydrocele may be corrected with a scrotal incision.

Fig. 582.8 Newborn with large right hydrocele.

INGUINAL HERNIA

Inguinal hernia is discussed in Chapter 394.

TESTICULAR MICROLITHIASIS

Approximately 2–3% of pediatric scrotal ultrasound examinations demonstrate calcific depositions in the testis, termed testicular microlithiasis. Typically, it is found in males undergoing an examination for testicular pain, varicocele, or scrotal swelling. In adults, it is a common finding in males with infertility and with a germ cell tumor of the testis. In pediatric patients with microlithiasis, there are no guidelines for monitoring, but the condition should be monitored for changes in testicular size or induration, with follow-up ultrasound studies as indicated.

TESTICULAR TUMOR

Testicular and paratesticular tumors can occur at any age, even in the newborn. Approximately 35% of prepubertal testis tumors are malignant; most commonly they are yolk sac tumors, although rhabdomyosarcoma and leukemia also can occur in this age group. In adolescents, 98% of painless solid testicular masses are malignant (see Chapter 552). Most manifest as a painless, hard testicular mass that does not transilluminate. Scrotal ultrasonography should be performed to confirm the finding of a testicular mass, and it can help to delineate the type of testis tumor. Serum tumor markers, including *α-fetoprotein* and *β-human chorionic gonadotropin,* should be drawn. Definitive therapy includes surgical exploration through an inguinal incision. In most cases, a radical orchiectomy, consisting of removal of the entire testis and spermatic cord, is performed. In a prepubertal male, if the ultrasonographic study or surgical exploration suggests that the tumor is localized and benign, such as a teratoma or an epidermoid cyst, testis-sparing surgery with removal only of the mass may be appropriate.

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Chapter 583

Trauma to the Genitourinary Tract

Heather N. Di Carlo and Chad B. Crigger

Most injuries to the genitourinary tract in children result from blunt trauma during falls, athletic activities, or motor vehicle crashes (see Chapter 80). *Children are at greater risk of blunt renal injury than adults, because they have less body fat and because the kidneys are not located directly behind the ribs.* Children with a preexisting renal anomaly, such as hydronephrosis secondary to a ureteropelvic junction obstruction, horseshoe kidney, or renal ectopia, also are at increased risk for renal injury. Blunt abdominal or flank trauma often causes a renal injury. Falling can cause a deceleration injury that results in an injury to the renal pedicle, interrupting blood flow to the kidney. If the bladder is full, blunt lower abdominal trauma can cause a bladder rupture. Rupture of the membranous urethra occurs in 5% of pelvic fractures. Straddle injuries usually are associated with trauma to the bulbous urethra.

Symptoms and signs of urinary tract injury include gross or microscopic hematuria, bleeding from the urethral meatus, abdominal or flank pain, a flank mass, fractured lower ribs or lumbar transverse processes, and a perineal or scrotal hematoma.

In more than 50% of cases, there also are major injuries to the brain, spinal cord, skeleton, lungs, or abdominal organs.

DIAGNOSIS

Evaluation of the patient begins after an adequate airway has been established and the patient is hemodynamically stable (see Chapters 78 and 79). With significant abdominal injury, gross hematuria or >50 red blood cells per high-power field, or suspicion of renal injury (deceleration injury, flank pain, or bruise), renal imaging is indicated (Fig. 583.1). The bladder should be catheterized unless blood is dripping from the urethral meatus, which is an indication of potential urethral injury. Passing the catheter in the presence of a urethral injury can increase the extent of the damage and convert a partial membranous urethral tear into a total disruption. In these patients, a retrograde urethrogram should be performed by injecting radiopaque contrast medium into the urethral meatus under fluoroscopy. Oblique radiographs demonstrate the extent of the injury and whether urethral continuity is preserved or has been disrupted.

A three-phase spiral CT scan should be performed to evaluate the kidneys, ureters, and bladder. The delayed images are important to detect renal extravasation of blood or urine. Prompt function of both kidneys without extravasation usually excludes significant renal injury. Renal injuries are classified according to the grading scale presented in Table 583.1. Minor renal injuries are most common; these include contusion of the renal parenchyma and shallow cortical lacerations not involving the collecting system. Major renal injuries include deep lacerations involving the collecting system, shattered kidney, and renal pedicle injuries (Fig. 583.2). Complete absence of function of one kidney without contralateral compensatory hypertrophy (indicating congenital absence) should be regarded as an indication of major injury to the renal pedicle. Renal angiography, once used for further evaluation of renal injuries, particularly if a renal pedicle injury is suspected, now is rarely used because such patients are often hemodynamically unstable, and management is not significantly affected by the findings. In some cases, a preexisting renal anomaly is demonstrated on the study. A ruptured ureteropelvic junction obstruction may be apparent if the kidney is intact, but the distal ureter is not visualized.

If there is a pelvic fracture, a urethral transection injury should be suspected, particularly in males. The risk is directly related to the number of broken pubic rami and whether there is separation of the pubic symphysis or displacement of the posterior pubic arch. Radiographic evaluation with retrograde urethrography should be performed if there is blood at the urethral or vaginal meatus, inability to void, and a perineal or penile hematoma.

TREATMENT

Minor renal injuries such as contusions are managed by bed rest and monitoring of vital signs until abdominal or flank discomfort and gross hematuria have resolved. Children with a major renal injury usually are admitted to an intensive care unit for continuous monitoring of vital signs and urine output. Intravenous antibiotics are also administered. These injuries also are managed nonoperatively, because Gerota's fascia often causes tamponade of bleeding from the kidney, and dramatic healing of the injured parenchyma can occur even with significant urinary extravasation.

Approximately 10% of children with a major renal injury undergo surgical exploration because of associated abdominal injuries, hemodynamic instability, persistent extravasation, or persistent hematuria or to correct a congenital renal deformity. It can be difficult to identify normal and devitalized parenchyma, and the likelihood of having to remove the kidney is significant. If the child is undergoing exploration for other abdominal injuries, the injured kidney is examined. If there is persistent extravasation because of intermittent ureteral obstruction from a blood clot, passage of a temporary double-J stent endoscopically between the bladder and kidney might allow resolution. If the renal pedicle is injured, nephrectomy is necessary. The kidney can be salvaged by

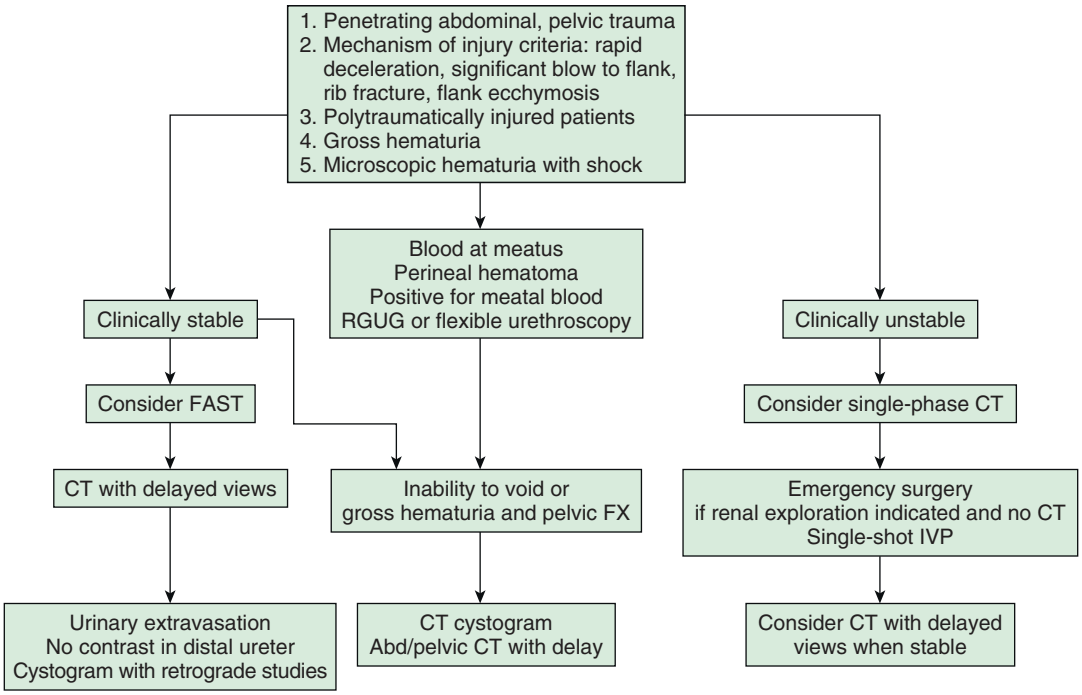

Fig. 583.1 Algorithm showing the recommended evaluation protocol for patients with a medical history or physical findings consistent with possible genitourinary injury. Abd, Abdominal; FAST, focused assessment with sonography for trauma; FX, fracture; IVP, intravenous pyelography; RGUG, retrograde urethrogram. *(From Husmann DA. Pediatric genitourinary trauma. Modified from Wein AJ, Kavoussi LR, Partin AW, Peters CA, eds. Campbell-Walsh Urology. 11th ed. Philadelphia: Elsevier; 2016: Fig. 154-6, p. 3546.)*

Table 583.1 Grading of Renal Injuries

GRADE	DESCRIPTION
1	Renal contusion or subcapsular hematoma
2	Nonexpanding perirenal hematoma, <1 cm parenchymal laceration, no urinary extravasation; all renal fragments viable; confined to renal retroperitoneum
3	Nonexpanding perirenal hematoma, >1 cm parenchymal laceration, no urinary extravasation; renal fragments may be viable or devitalized
4	Laceration extending into the collecting system with urinary extravasation; renal fragments may be vital or devitalized *or* Injury to the main renal vasculature with contained hemorrhage
5	Completely shattered kidney; by definition, multiple major lacerations >1 cm associated with multiple devitalized fragments *or* Injury to the main renal vasculature with uncontrolled hemorrhage, renal hilar avulsion

emergency renal revascularization only if the kidney is explored within 2-3 hours of the injury. Virtually all penetrating injuries of the kidneys should be explored.

In addition to loss of renal function, the main long-term complication of renal injury is renin-mediated hypertension. Children who sustain significant renal injuries should have periodic measurement of blood pressure if they have any residual renal abnormality.

Ureteral injuries usually are iatrogenic. Injuries of the ureter by blunt or penetrating trauma require immediate surgical attention.

When the bladder can be catheterized, a static cystogram is obtained, infusing a contrast solution through the catheter by gravity, ideally using fluoroscopy. Flat and oblique views are often obtained; a postvoid film also should be obtained because, in some cases, extravasation may be hidden by the full bladder. An alternative is a CT cystogram, which is highly accurate in demonstrating a bladder injury.

Bladder ruptures can be intraperitoneal or extraperitoneal. All intraperitoneal ruptures require surgical repair. Minor extraperitoneal near-ruptures might be treated by catheter drainage but generally require surgical treatment.

Treatment of a **membranous urethral injury** is controversial. Erectile dysfunction, urethral stricture, and urinary incontinence are the major late complications of rupture of the membranous urethra, and therapy is directed at minimizing the risk of these problems. A large pelvic hematoma with tamponade often is present, and an immediate attempt to repair the injury can be technically difficult and result in significant hemorrhage. Many such injuries are managed initially by temporary suprapubic cystostomy, with continuous bladder drainage for 3-6 months. Subsequently, open or endoscopic urethroplasty can be performed. Alternatively, some try to achieve urethral continuity under anesthesia and leave a urethral catheter for several months. These patients typically require subsequent open urethroplasty.

Penile injury is uncommon. Partial or complete glans amputation is a risk of newborn circumcision with a Mogen clamp. With immediate surgical repair, often the excised glans tissue can be replaced as a free graft. Some males who are in the process of toilet training sustain an injury to the glans penis if the lid of the toilet falls while they are urinating. These males often have a hematoma covering the distal half of the glans. Typically, they have no difficulty urinating and do not need extensive evaluation. Some male infants develop an inadvertent **hair tourniquet** or strangulation injury. Typically,

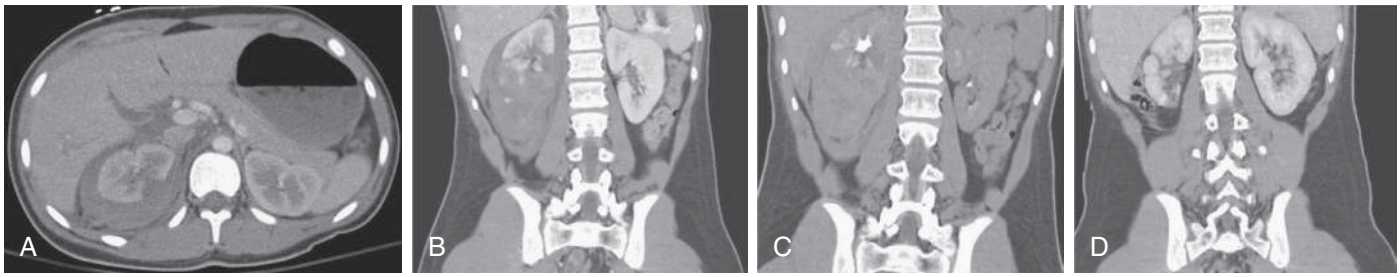

Fig. 583.2 CT images of grade 3 right renal trauma: acute, delayed, and at 3-month follow-up. **A,** Acute CT image of grade 3 renal trauma showing laceration of more than 1 cm of midrenal pole with perinephric hematoma. **B,** Acute CT image coronal reconstruction of grade 3 renal trauma, with possible devitalization of the entire lower pole of the kidney. **C,** Two-hour delayed CT image coronal reconstruction of grade 3 renal trauma, with no urinary extravasation noted and lower pole with questionable devitalization versus contusion. **D,** CT image coronal reconstruction 3 months after traumatic injury revealing parenchymal scarring at site of laceration with scarred but functional lower pole consistent with healed parenchyma following severe renal contusion. Scarring of lower pole was believed to have occurred with impoverished blood supply because of severe contusion. *(From Husmann DA. Pediatric genitourinary trauma. In: Wein AJ, Kavoussi LR, Partin AW, Peters CA, eds. Campbell-Walsh Urology. 11th ed. Philadelphia: Elsevier; 2016: Fig. 154-3, p. 3542.)*

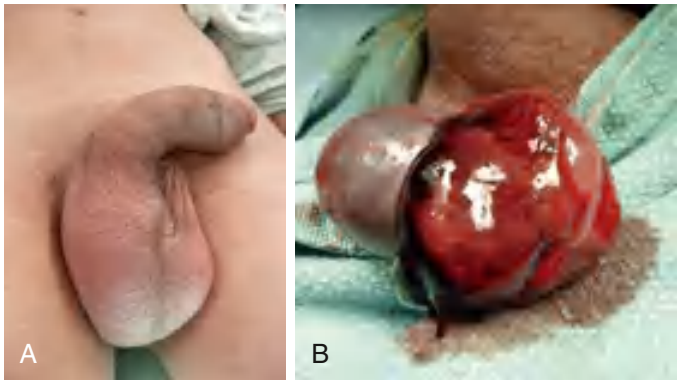

Fig. 583.3 **A,** Adolescent male with blunt right testicular injury. **B,** Tunica albuginea of testis is ruptured; the patient underwent debridement and closure of testicular capsule.

a very narrow constriction is noted with severe distal penile swelling and pain. Identification and incision of the hair allows prompt resolution of the edema. The urethra and penile vascularity should be assessed after release of the hair tourniquet. Adolescent males who indulge in extremely vigorous sexual intercourse may sustain rupture of one of the corporal bodies, resulting in penile fracture. These males have severe swelling of the penile shaft and require emergency exploration and repair. Males with penetrating injuries of the penis also require emergency debridement and repair.

Testicular injuries are relatively uncommon in children because of the small size of the testes and their mobility within the scrotum. Such injuries usually result from blunt trauma during athletic activity. Typically, these males have significant scrotal swelling, testicular pain, and tenderness (Fig. 583.3A). Ultrasonography demonstrates rupture of the tunica albuginea, which is the capsule of the testis, and surrounding hemorrhage. Prompt surgical treatment of testicular injuries increases the salvage rate (see Fig. 583.3B). An uncommon injury is the **zipper injury,** which can affect either the scrotum or foreskin. This problem generally occurs in males who do not wear underwear. The zipper can be cut with bone cutters or metal cutters. Sedation generally is unnecessary.

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Chapter 584

Urinary Lithiasis

Heather N. Di Carlo and Chad B. Crigger

Urinary lithiasis in children is related to genetic, climatic, dietary, and socioeconomic factors. The incidence increased steadily over the past several decades. Adolescents are 10 times more likely to have a symptomatic calculus compared with children age 0-3 years. The increase in stone disease in the United States is attributed to obesity and changes in dietary habits, such as increased sodium and fructose intake, and decreased calcium and water intake.

Urolithiasis is less common in the United States than in other parts of the world. In the United States, 1 in 685 pediatric hospital admissions is for stone disease. Approximately 7% of urinary calculi occur in children younger than 16 years of age. In the United States, many children with stone disease have a metabolic abnormality. The exceptions are patients with a neuropathic bladder (see Chapter 579), who are prone to infection-initiated renal stones, and those who have urinary tract reconstruction with small or large intestine, which predisposes to bladder calculi. The incidence of metabolic stones is similar in males and females; they are most common in the southeastern United States. Racial and ethnic differences have been noted, with the highest prevalence among Whites. In Southeast Asia, urinary calculi are endemic and are related to dietary factors.

STONE FORMATION

Nearly 90% of urinary stones contain calcium as a major constituent, and 60% are composed of calcium oxalate. Most *spontaneous* stones are composed of calcium oxalate, or calcium phosphate crystals; others are caused by uric acid, cystine, ammonium crystals, or phosphate crystals, or a combination of these substances (Table 584.1). The risk of stone formation increases in the presence of increasing concentrations of these crystals and is reduced with increasing concentrations of urinary inhibitors. Renal calculi develop from crystals that form on the calyx and aggregate to form a calculus. Bladder calculi may be stones that formed in the kidney and traveled down the ureter, or they can form primarily in the bladder.

Table 584.1 Classification of Urolithiasis

CALCIUM STONES (CALCIUM OXALATE AND CALCIUM PHOSPHATE)*
Hypercalciuria
Absorptive: increased Ca absorption from gut; types I and II
Renal leak: decreased tubular reabsorption of Ca
Resorptive
Primary hyperparathyroidism (rare in children)
Iatrogenic
Loop diuretics
Ketogenic diet
Corticosteroids
Adrenocorticotropic hormone administration
Methylxanthines (theophylline, aminophylline)
Distal renal tubular acidosis, type 1 (calcium phosphate)
Hypocitraturia—citrate most important inhibitor of Ca crystallization
Vitamin D excess
Immobilization
Sarcoidosis
Cushing disease
Hyperuricosuria
Heterozygous cystinuria
Hyperoxaluria (calcium oxalate)
Primary hyperoxaluria, types 1 and 2
Secondary hyperoxaluria
Enteric hyperoxaluria
CYSTINE STONES
Cystinuria
STRUVITE STONES (MAGNESIUM AMMONIUM PHOSPHATE)
Urinary tract infection (urea-splitting organism)
Foreign body
Urinary stasis
URIC ACID STONES
Hyperuricosuria
Lesch-Nyhan syndrome
Myeloproliferative disorders
After chemotherapy
Inflammatory bowel disease
OTHER
Indinavir stones
Melamine
Nephrocalcinosis

*Most common.

Low urine volume, low urine pH, calcium, sodium, oxalate, and urate are known to promote stone formation. Many inorganic (e.g., citrate, magnesium) and organic (e.g., glycosaminoglycans, osteopontin) substances are known to inhibit stone formation. Organic inhibitory compounds adsorb to the surface of the crystal, thereby inhibiting crystal growth and nucleation.

Stone formation depends on four factors: matrix, precipitation-crystallization, epitaxy, and the absence of inhibitors of stone formation in the urine. **Matrix** is a mixture of protein, nonamino sugars, glucosamine, water, and organic ash that makes up 2–9% of the dry weight of urinary stones and is arranged within the stones in organized concentric laminations. **Precipitation-crystallization** refers to supersaturation of the urine with specific ions composing the crystal. Crystals aggregate by chemical and electrical forces. Increasing the saturation of urine with respect to the ions increases the rate of nucleation, crystal growth, and aggregation and increases the likelihood of stone formation and growth. **Epitaxy** refers to the aggregation of crystals of different composition but similar lattice structure, thus forming stones of a heterogeneous nature. The lattice structures of calcium oxalate and monosodium urate have similar structures, and calcium oxalate crystals can aggregate on a nucleus of monosodium urate crystals. Urine also contains **inhibitors of stone formation,** including citrate, diphosphonate, and magnesium ion.

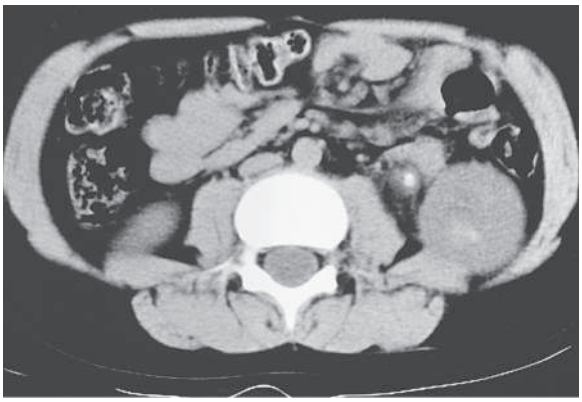

Fig. 584.1 Noncontrast CT scan of the midabdomen in a male infant with cystinuria shows a left-sided calculus at the ureteropelvic junction with proximal hydronephrosis.

CLINICAL MANIFESTATIONS

Children with urolithiasis usually have gross or microscopic hematuria. If the calculus causes ureteral or renal pelvic obstruction, then severe flank pain (renal colic) or abdominal pain occurs. The calculus typically causes obstruction at areas of narrowing of the urinary tract—the ureteropelvic junction, where the ureter crosses the iliac vessels, and the ureterovesical junction. The ureter progressively narrows distally, and its most narrow segment is the ureterovesical junction. The pain typically radiates anteriorly to the scrotum or labia. Often the pain is intermittent, corresponding to periods of obstruction of urine flow, which increases the pressure in the collecting system. If the calculus is in the distal ureter, the child can have irritative symptoms of dysuria, urgency, and frequency. If the stone passes into the bladder, the child usually becomes asymptomatic. If the stone is in the urethra, dysuria and difficulty voiding can result, particularly in males. Some children pass small amounts of gravel-like material. Stones can also be asymptomatic, although it is uncommon to pass a ureteral calculus without symptoms.

DIAGNOSIS

Approximately 90% of urinary calculi are calcified to some degree and are radiopaque on a plain abdominal film. However, many calculi are only a few millimeters in diameter and are difficult to see, particularly if they are in the ureter. Struvite (magnesium ammonium phosphate) stones are radiopaque. Cystine, xanthine, and uric acid calculi may be radiolucent but often are slightly opacified. Some children have **nephrocalcinosis,** which is calcification of the renal tissue itself. Nephrocalcinosis is seen most commonly in premature neonates receiving furosemide, which causes **hypercalciuria**, and in children with medullary sponge kidney.

In a child with suspected renal colic, there are multiple imaging options, including ultrasound, CT, and plain radiographs. The American Urological Association recommends ultrasound as the *initial* imaging modality in children as it avoids radiation. Ultrasound has high specificity (97%) but only moderate sensitivity (67%) in the diagnosis of urolithiasis; thus CT should be considered when clinical suspicion for stones is high, but ultrasound is negative. CT scan of the abdomen and pelvis is the most accurate study in diagnosis of stones with both sensitivity and specificity exceeding 96% (Fig. 584.1). This study takes only a few minutes to perform, is useful in delineating the number and location of calculi, and demonstrates whether the involved kidney is hydronephrotic. *Most pediatric imaging centers use low-dose CT to reduce radiation exposure.* A plain radiograph of the abdomen and pelvis is sometimes used to detect radiopaque stones but cannot identify obstruction and rarely visualizes renal calculi <3 mm.

In a child with a previously diagnosed calculus, renal ultrasonography can be used to follow the status of the calculus, such as whether it has grown or diminished in size or has moved. If a child has a renal pelvic calculus, a ureteropelvic junction obstruction should be suspected.

Table 584.2 Laboratory Tests Suggested for Evaluation of Urolithiasis

SERUM
Calcium
Phosphorus
Magnesium
Uric acid
Electrolytes and anion gap
Creatinine
Alkaline phosphatase
URINE
Urinalysis
Urine culture
Spot test for cystinuria
Stone analysis
If toilet-trained, 24 hour collection for:
Creatinine clearance
Calcium
Phosphate
Oxalate
Uric acid
Dibasic amino acids (if cystine spot test result is positive)
If not toilet-trained, random urine sample for:
Calcium
Creatinine
Oxalate
Citrate

In some cases, it can be difficult to determine whether hydronephrosis in such a child is secondary to an obstructing stone, ureteropelvic junction obstruction, or both.

Any material that resembles a calculus should be sent for analysis by a laboratory that specializes in identifying the components of urinary calculi.

METABOLIC EVALUATION

A metabolic evaluation for the most common predisposing factors should be undertaken in all children with urolithiasis, bearing in mind that structural, infectious and metabolic factors often coexist. This evaluation should not be undertaken in a child who is in the process of passing a stone, because the altered diet and hydration status, as well as the effect of obstruction on the kidney, can alter the results of the study. Table 584.2 lists the basic laboratory studies required, and Table 584.3 shows the normal values for 24-hour urine collections. In children with hypercalciuria, further studies of calcium excretion with dietary calcium restriction and calcium loading are necessary.

PATHOGENESIS OF SPECIFIC RENAL CALCULI

Calcium Oxalate and Calcium Phosphate Calculi

Most urinary calculi in children in the United States are composed of calcium oxalate and/or calcium phosphate. The most common metabolic abnormality in these patients is **normocalcemic hypercalciuria.** Between 30% and 60% of children with calcium stones have hypercalciuria without hypercalcemia. Other metabolic aberrations that predispose to stone disease include hyperoxaluria, hyperuricosuria, hypocitraturia, heterozygous cystinuria, hypomagnesuria, hyperparathyroidism, and **renal tubular acidosis** (RTA; see Chapter 569).

Hypercalciuria may be absorptive, renal, or resorptive. The primary disturbance in *absorptive hypercalciuria* is intestinal hyperabsorption of calcium. In some children, an increase in 1,25-dihydroxyvitamin D is associated with the increased calcium absorption, whereas in others, the process is independent of vitamin D. *Renal hypercalciuria* refers to impaired renal tubular reabsorption of calcium (see Chapter 562.4). Renal leak of calcium causes mild hypocalcemia, which triggers an increased production of parathyroid hormone, with increased intestinal absorption of calcium and increased mobilization of calcium stores. *Resorptive hypercalciuria* is uncommon and is found in patients with primary hyperparathyroidism. Excess parathyroid hormone secretion stimulates intestinal absorption of calcium and mobilization of calcium stores. Table 584.4 summarizes the metabolic evaluation of children with hypercalciuria.

Hyperoxaluria is another potentially important cause of calcium stones. Oxalate increases the solubility of calcium oxalate crystallization 7-10 times more than calcium. Consequently, hyperoxaluria significantly increases the likelihood of calcium oxalate precipitation. Oxalate is found in high concentrations in tea, coffee, spinach, and rhubarb. Primary hyperoxaluria is a rare autosomal recessive disorder that can be subclassified into glycolic aciduria and L-glyceric aciduria. Most patients with primary hyperoxaluria have glycolic aciduria; oxalic and glycolic acids are increased in the urine of affected persons. Both defects cause increased endogenous production of oxalate, with hyperoxaluria, urolithiasis, nephrocalcinosis, and injury to the kidneys. Death from renal failure occurs by age 20 in untreated patients. **Oxalosis,** defined as extrarenal deposition of calcium oxalate, occurs when renal insufficiency is present with elevated plasma oxalate. Calcium oxalate deposits appear first in blood vessels and bone marrow, and with time they appear throughout the body. Secondary hyperoxaluria is more common and can occur in patients with increased intake of oxalate and oxalate precursors such as vitamin C, in those with pyridoxine deficiency, and in children with intestinal malabsorption.

Enteric hyperoxaluria refers to disorders such as inflammatory bowel disease (see Chapter 382), pancreatic insufficiency (see Chapter 398), and biliary disease (see Chapter 404), in which there is gastrointestinal malabsorption of fatty acids, which bind intraluminal calcium and form salts that are excreted in the feces. Normally, calcium forms a complex with oxalate to reduce oxalate absorption, but if calcium is unavailable, there is increased absorption of unbound oxalate.

Hypocitraturia refers to a low excretion of citrate, which is an important inhibitor of calcium stone formation. Citrate acts as an inhibitor of calcium urolithiasis by forming complexes with calcium, increasing the solubility of calcium in the urine, and inhibiting the aggregation of calcium phosphate and calcium oxalate crystals. Disorders such as chronic diarrhea, intestinal malabsorption, and RTA can cause hypocitraturia. It may also be idiopathic.

Renal tubular acidosis (RTA) is a syndrome involving a disturbance of acid-base balance within the kidney that can be classified into three types, one of which predisposes to renal calculi that typically are calcium phosphate (see Chapter 569). In type 1 RTA, the distal nephron does not secrete hydrogen ion into the distal tubule. The urine pH is never <5.8, and hyperchloremic hypokalemic acidosis results. Patients acquire nephrolithiasis, nephrocalcinosis, muscle weakness, and osteomalacia. Type 1 RTA can be an autosomal dominant disorder, but more often it is acquired and associated with systemic diseases such as Sjögren syndrome, Wilson disease, primary biliary cirrhosis, and lymphocytic thyroiditis, or it results from amphotericin B, lithium, or toluene (an organic solvent associated with glue sniffing).

From 5–8% of patients with **cystic fibrosis** (see Chapter 454) have urolithiasis. Typically, the stones are calcium, and they often manifest in adolescence or young adulthood. Microscopic nephrocalcinosis also occurs in younger children with the disease. These patients do not have hypercalciuria, and the propensity for urolithiasis has been speculated to result from an inability to excrete a sodium chloride load or from intestinal malabsorption.

Other disorders can play a role in causing calcium stones. **Hyperuricosuria** may be related to the epitactic growth of calcium oxalate crystals around a nucleus of uric acid crystals or to the action of uric acid, which counteracts urinary mucopolysaccharides that then inhibit calcium oxalate crystallization. Heterozygous **cystinuria** is found in some patients with calcium stones. The mechanism is unknown but may be similar to that of uric acid. Sarcoidosis (see Chapter 209) causes an increased sensitivity to vitamin D_3 and thus an increased absorption of calcium from the gastrointestinal tract. In Lesch-Nyhan syndrome (see Chapter 110), there is excessive uric acid synthesis. These patients are more likely to form uric acid stones, but some of these stones may be calcified. **Immobility** can cause hypercalciuria by mobilization of calcium stores. High-dose

Table 584.3 Urine Chemistry: Normal Values

URINE CONSTITUENT	AGE	RANDOM	TIMED	COMMENTS
Calcium	0-6 mo	<0.8 mg/mg creat	<4 mg/kg/24 hours	Prandial variation
	7-12 mo	<0.6 mg/mg creat		Sodium-dependent
	≥2 yr	<0.21 mg/mg creat		
Oxalate*	<1 yr	0.15-0.26 mmol/mmol creat	≥2 yr: <0.5 mmol/1.73 m^2/24 hr	Random urine mmol/mmol highly age dependent
	1-<5 yr	0.11-0.12 mmol/mmol creat		Excretion rate/1.73 m^2 constant through childhood and adulthood
	5-12 yr	0.006-0.15 mmol/mmol creat		
	>12 yr	0.002-0.083 mmol/mmol creat		
Uric acid	Term infant	3.3 mg/dL GFR†	<815 mg/1.73 m^2/24 hr	Excretion rate/1.73 m^2 from >1 yr age; constant through childhood
	>3 yr	<0.53 mg/dL GFR		
Magnesium	>2 yr	<0.12 mg/mg creat	<88 mg/1.73 m^2/24 hr	Excretion rate/1.73 m^2 constant through childhood
Citrate		>400 mg/g creat		Limited data available for children
Cystine		<75 mg/g creat	<60 mg/1.73 m^2/24 hr	Cystine >250 mg/g creat suggests homozygous cystinuria

*Oxalate oxidase assay.
†(mg/dL uric acid) (serum creatinine concentration/urine creatinine concentration).
creat, Creatinine; GFR, glomerular filtration rate.
From Milliner DS. Urolithiasis. In: Avner ED, Harmon WE, Naiudet P, eds. Pediatric Nephrology. 6th ed. Berlin: Springer-Verlag; 2009: p. 1409, with permission.

Table 584.4 Metabolic Evaluation of Children with Hypercalciuria

TYPE	SERUM CALCIUM	RESTRICTED CALCIUM (URINE)	FASTING CALCIUM (URINE)	CALCIUM LOAD (URINE)	PARATHYROID HORMONE (SERUM)
Absorptive	N or I	N or I	N	I	D or N
Renal	N	I	I	I	I
Resorptive	I	I	I	I	I

I, Increased; N, normal; D, decreased

corticosteroids can cause hypercalciuria and calcium oxalate precipitation. Furosemide, which is often administered in the neonatal intensive care unit, also can cause severe hypercalciuria, urolithiasis, and nephrocalcinosis.

In some children, calcium calculi are idiopathic. A complete metabolic evaluation must be performed before this diagnosis is made.

Cystine Calculi

Cystinuria accounts for 1% of renal calculi in children. The condition is a rare autosomal recessive disorder of the epithelial cells of the renal tubule that prevents absorption of the four dibasic amino acids (cystine, ornithine, arginine, lysine) and results in excessive urinary excretion of these products. The only known complication of this familial disease is the formation of calculi, because of the low solubility of cystine. The patients usually have acidic urine, which leads to a higher rate of precipitation. In the homozygous patient, the daily excretion of cystine usually exceeds 500 mg, and stone formation occurs at an early age. Heterozygotes excrete 100-300 mg/day and typically do not have clinical urolithiasis. The sulfur content of cystine gives these stones their faint radiopaque appearance.

Struvite Calculi

Urinary tract infections (see Chapter 575) caused by urea-splitting organisms (most often *Proteus* spp., and occasionally *Klebsiella* spp., *Escherichia coli, Pseudomonas* spp., and others) result in urinary alkalinization and excessive production of ammonia, which can lead to the precipitation of magnesium ammonium phosphate (struvite) and calcium phosphate. In the kidney, these calculi often have a staghorn configuration, filling the calyces. The calculi act as foreign bodies, causing obstruction, perpetuating infection, and causing gradual kidney damage. Patients with struvite stones also can have metabolic abnormalities that predispose to stone formation. These stones often are seen in children with neuropathic bladder, particularly those who have undergone a urinary tract reconstructive procedure (see Chapter 579). Struvite stones also can form in the reconstructed bladder of children who have undergone augmentation cystoplasty or continent urinary diversion.

Uric Acid Calculi

Calculi containing uric acid represent <5% of all cases of lithiasis in children in the United States but are more common in less-developed areas of the world. Hyperuricosuria with or without hyperuricemia is the common underlying factor in most cases. The stones are radiolucent on x-ray. The diagnosis should be suspected in a patient with persistently acidic urine and urate crystalluria.

Hyperuricosuria can result from various inborn errors of purine metabolism that lead to overproduction of uric acid, the end product of purine metabolism in humans. Children with Lesch-Nyhan syndrome and patients with glucose-6-phosphatase deficiency (see Chapter 107) form urate calculi as well. In children with short-bowel syndrome (see Chapter 385.7), and particularly those with ileostomies, chronic dehydration and acidosis sometimes are complicated by uric acid lithiasis.

One of the most common causes of uric acid lithiasis is the rapid turnover of purine with some tumors and myeloproliferative diseases. The risk of uric acid lithiasis is especially great when treatment of these diseases causes rapid breakdown of nucleoproteins. Uric acid calculi or "sludge" can fill the entire upper collecting system and cause renal failure and even anuria. Urate is also present within calcium-containing stones. In these cases, more than one predisposing factor for stone formation can exist.

Indinavir Calculi

Indinavir sulfate is a protease inhibitor approved for treating HIV infection (see Chapter 322). Up to 4% of patients acquire symptomatic nephrolithiasis. Most of the calculi are radiolucent and are composed of indinavir-based monohydrate, although calcium oxalate and/or phosphate have been present in some. After each dose, 12% of the drug is excreted unchanged in the urine. The urine in these patients often contains crystals of characteristic rectangles and fan-shaped or starburst crystals. Indinavir is soluble at a pH of <5.5. Consequently, dissolution therapy by urinary acidification with ammonium chloride or ascorbic acid should be considered.

Nephrocalcinosis

Nephrocalcinosis refers to calcium deposition within the renal tissue. Often nephrocalcinosis is associated with urolithiasis. The most common causes are furosemide (administered to premature neonates), distal RTA, hyperparathyroidism, medullary sponge kidney, hypophosphatemic rickets, sarcoidosis, cortical necrosis, hyperoxaluria, prolonged immobilization, Cushing syndrome, hyperuricosuria, monogenetic causes of hypertension, and renal candidiasis.

TREATMENT

In a child or adolescent with a renal or ureteral calculus, the decision whether to remove the stone depends on its location, size, and composition (if known) and whether obstruction and/or infection is present. Pain is managed with nonsteroidal antiinflammatory drugs or, less often, opiates. Small ureteral calculi often pass spontaneously, although the child might experience severe renal colic. The narrowest segment of the ureter is the ureterovesical junction. Calculi <5 mm will pass 80–90% of the time. An α-adrenergic blocker, such as tamsulosin, 0.4 mg at bedtime, may facilitate stone passage by decreasing ureteral pressure below the stone and decreasing the frequency of the peristaltic contractions of the obstructed ureter. This intervention is termed **medical expulsive therapy**. In many cases, passage of a ureteral stent past the stone endoscopically relieves pain and dilates the ureter sufficiently to allow the calculus to pass. In cases such as children with a uric acid calculus or an infant with a furosemide-associated calculus, dissolution alkaline therapy may be effective. Fluid management with a forced diuresis is controversial and may not improve stone passage. Nonetheless, dehydration (from anorexia or emesis) must be corrected, and intravenous fluids may offset contrast-induced renal injury if CT contrast imaging is anticipated.

If the calculus does not pass or seems unlikely to pass or if there is associated urinary tract infection, removal is necessary (Table 584.5). Lithotripsy of bladder, ureteral, and small renal pelvic calculi using the holmium laser through a flexible or rigid ureteroscope is quite effective. Extracorporeal shock wave lithotripsy has been successfully applied to children with renal and ureteral stones, with a success rate of >75%. Another alternative is percutaneous nephrostolithotomy, in which access to the renal collecting system is obtained percutaneously and the calculi are broken down by ultrasonic lithotripsy. In cases in which these modalities are unsuccessful, an alternative is laparoscopic removal; this procedure can be performed using the da Vinci robot.

STONE PREVENTION

In children with urolithiasis, the underlying metabolic disorder should be addressed (Table 584.6). Because lithiasis results from elevated concentrations of specific substances in the urine, maintaining a continuous high urine output by maintaining a high fluid intake often is an effective method of preventing further stones. The high fluid intake should be continued at night, and usually it is necessary for the child to get up at least once at night to urinate and drink more water. A daily fluid intake of 2-2.5 L in adolescent stone formers is recommended, with greater intake during summer months.

Dietary sodium intake in children has increased significantly because of increased consumption of salty, processed foods. High sodium intake increases urinary excretion of calcium and may result in hypocitraturia. In addition, increased salt intake induces metabolic acidosis. To compensate for the acid load, the kidneys conserve anions, including urinary citrate, which contributes to hypocitraturia. Reduction in dietary intake of sodium and increased potassium intake is indicated.

Although counterintuitive, low-calcium diets are less effective in the treatment of calcium stones than diets containing normal amounts of calcium and limited amounts of sodium and animal protein. Low-sodium, low-protein diets reduce urinary calcium and oxalate excretion. Children with stone disease should avoid excess calcium intake. However, children require calcium for bone development, and

Table 584.5 Primary Surgical Treatment Options vs Stone Size and Location

STONES	SHOCK WAVE LITHOTRIPSY	URETEROSCOPY	PERCUTANEOUS NEPHROLITHOTOMY
RENAL			
<1 cm	Most common	Optional	Optional
1-2 cm	Most common	Optional	Optional
>2 cm	Optional	Rare	Most common
LOWER POLE			
<1 cm	Most common	Optional	Optional
>1 cm	Optional	Optional	Most common
URETERAL			
Proximal	Most common	Optional	Occasional
Distal	Optional	Most common	Rare

From Durkee CT, Balcom A. Surgical management of urolithiasis. Pediatr Clin North Am. 2006;53:465–477.

Table 584.6 Suggested Therapy for Urolithiasis Caused by Metabolic Abnormalities

METABOLIC ABNORMALITY	INITIAL TREATMENT	SECOND-LINE TREATMENT
Hypercalciuria	Reduction of dietary Na^+	Potassium citrate
	Dietary calcium at RDA	Thiazides
	Thiazides*	Neutral phosphate
Hyperoxaluria	Reduce dietary oxalate	Neutral phosphate†
	Potassium citrate	Magnesium
		Pyridoxine†
Hypocitric aciduria	Potassium citrate	Bicarbonate
Hyperuricosuria	Alkalinization	Allopurinol
Cystinuria	Alkalinization	Tiopronin (Thiola)
	Reduction of dietary Na^+	D-Penicillamine
		Captopril

*If hypercalciuria is severe or there is osteopenia.
†Initial therapy in primary hyperoxaluria.
RDA, Recommended dietary allowance.
From Milliner DS. Urolithiasis. In: Avner ED, Harmon WE, Naiudet P, eds. Pediatric Nephrology. 6th ed. Berlin: Springer-Verlag; 2009: p. 1412, with permission.

recommendations for daily calcium intake vary by age. *Consequently, calcium restriction in children should be avoided.* Thiazide diuretics also reduce renal calcium excretion. The addition of potassium citrate, an inhibitor of calcium stones, with a dosage of 1-2 mEq/kg/24 hours is beneficial. An excellent source of citrate is lemonade, because 4 oz of lemon juice contains 84 mEq of citric acid. A daily mixture of 4 oz of reconstituted lemon juice in 2 L of water and sweetened to taste should significantly increase the urinary citrate level. In difficult cases, neutral orthophosphate should be given, although it is poorly tolerated.

In patients with uric acid stones, allopurinol is effective. Allopurinol is an inhibitor of xanthine oxidase and is effective in reducing the production of both uric acid and 2,8-dihydroxyadenine and can help control the recurrence of both types of stones. In addition, urinary alkalinization with sodium bicarbonate or sodium citrate is beneficial. The urine pH should be ≥6.5 and can be monitored at home by the family.

Maintaining a high urine pH can also prevent the recurrence of cystine calculi. Cystine is much more soluble when the urinary pH is >7.5, and alkalinization of urine with sodium bicarbonate or sodium citrate is effective. Another important medication is D-penicillamine, which is a chelating agent that binds to cysteine or homocysteine, increasing the solubility of the product. Although poorly tolerated by many patients, it has been reported to be effective in dissolving cystine stones and in preventing recurrences when hydration and urinary alkalinization fail. *N*-Acetylcysteine appears to have low toxicity and may be effective in controlling cystinuria, but long-term experience with it is lacking.

Treatment of type 1 RTA involves correcting the metabolic acidosis and replacing lost potassium and sodium. Sodium or potassium citrate therapy, or both, is necessary. When the metabolic acidosis is corrected, the urinary citrate excretion returns to normal.

Treatment of primary hyperoxaluria involves liver transplantation because the defective enzymes are hepatic. Ideally, this procedure is performed before renal failure occurs. In the most severe cases, kidney transplantation is also necessary. A U.S. Food and Drug Administration (FDA)-approved agent (lumasiran) greatly decreases oxalate production in children with primary hyperoxaluria type 1. It is hoped that it will prevent end-stage renal disease in this disorder.

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