Chapter

6 Genitourinary Tract Infections

Urinary tract infections (UTIs) can have multiple risk factors, including anatomic etiologies, the presence of a foreign body, urinary tract stone disease, and immunologic factors. Table 6-1 describes these risk factors and the common etiologies.

In addition to risk factors, the body has established defense mechanisms aimed at preventing infections. Some of the common urinary tract defense mechanisms are listed in Box 6-1.

UPPER TRACT INFECTIONS

Upper tract infections involve the kidney or the surrounding tissues or both.

Acute Pyelonephritis

Acute pyelonephritis is an acute bacterial infection of the renal parenchyma and collecting system. Most commonly, pathogens

TABLE 6-1 Risk Factors and Common Etiologies for Urinary Tract Infections

Risk Factor	Examples
Anatomic anomaly causing obstruction, stasis, or reflux	Prostatic hyperplasia Neurogenic bladder Strictures Vesicoureteral reflux Other congenital urinary tract anomalies
Foreign body	Urinary catheter, stent, nephrostomy tube Instrumentation (cystoscope)
Infected urinary stones	Struvite calculi Secondarily infected calculi
Immunologic or biologic disorders allowing bacterial persistence	Chronic bacterial prostatitis Immunosuppression Pregnancy Renal papillary necrosis End-stage renal disease on hemodialysis

BOX 6-1 Urinary Tract Defense Mechanisms

Maintenance of urine flow
Bladder emptying
Low pH
Extremes in osmolality
High urea concentration
High organic acid concentration
Prostatitic secretions
Antiadherence factors (uromucoid, Tamm-Horsfall protein)
Immunoglobulins
Phagocytosis

ascend from the bladder via the ureter to the renal pelvis and parenchyma. The second route of infection, hematogenous spread, is associated with other extrarenal infections such as staphylococcal septicemia and tuberculosis. Acute pyelonephritis is characterized by suppurative infection accompanied by fever, flank pain, bacteriuria, and pyuria. Progressive renal scarring is a consequence of repeated attacks of acute pyelonephritis.

Pathogenesis

The origin of most bacteria causing pyelonephritis is in fecal flora. *Escherichia coli* and other Enterobacteriaceae account for over 90% of infections. Other less common pathogens include *Proteus, Pseudomonas, Klebsiella*, and *Enterococcus*. Certain virulence factors have been identified that enhance bacterial ability to colonize, ascend the urinary tract, and produce disease. Of these factors, the most important is bacterial adherence by pili to the vaginal mucosa and uroepithelium. It has also been found that patients with chronic pyelonephritis have a higher P-fimbriae receptor accessibility on uroepithelial cells.

Diagnosis

The classic presentation of acute pyelonephritis is fever, flank pain, and lower urinary tract symptoms with bacteriuria. Flank pain is often unilateral but rarely can be bilateral. Upper abdominal pain is unusual, and radiation of pain to the groin is suggestive of a ureteral stone. Fever may be accompanied by rigors and chills. Other nonspecific symptoms may include nausea, vomiting, anorexia, and malaise.

On physical examination, the patient generally appears ill. Flank or costovertebral angle (CVA) tenderness is most commonly unilateral over the involved kidney, although bilateral discomfort

may be present. A systolic blood pressure less than 90 mm Hg suggests shock secondary to sepsis or perinephric abscess.

The urinalysis typically reveals pyuria, bacteriuria, and gross or microscopic hematuria. The complete blood count (CBC) reveals leukocytosis with a predominance of neutrophils. The serum creatinine level may be elevated due to the transient renal dysfunction. Urine cultures are diagnostic, and the sensitivity results help to determine the appropriate antibiotic therapy. Obtaining blood cultures is important because bacteremia is present in 33% of patients.

Computed tomographic (CT) scan with contrast helps to define the renal parenchyma and surrounding tissues. Contrast-enhanced CT scan may show wedge-shaped areas of decreased contrast enhancement secondary to decreased perfusion of renal parenchyma due to constriction of arterioles caused by acute bacterial infection.

Treatment

Acute pyelonephritis is a serious illness that requires prompt treatment. Empiric therapy should cover gram-negative pathogens and can be adjusted according to culture and sensitivity results. One-drug therapy with a third-generation cephalosporin or fluoroquinolone is usually effective. Aminoglycosides plus ampicillin may be required for compromised hosts with nosocomial infections, primarily *Pseudomonas*. Acute pyelonephritis requires 2 weeks of combined IV and oral antibiotics. If symptoms do not begin to improve within 3 to 5 days, further investigation is needed to rule out obstruction or renal abscess, which may require percutaneous drainage or surgical intervention.

Pyonephrosis

Urinary obstruction in the presence of pyelonephritis may lead to a collection of bacteria, purulent drainage and debris in the collecting system, and subsequent pyonephrosis. In this last situation, patients may deteriorate rapidly and become septic.

Risk factors for developing pyonephrosis include immunosuppression, diabetes, and urinary tract obstruction resulting from stones, tumors, or ureteropelvic junction obstruction. Fungal balls, commonly associated with immunocompromised patients, may obstruct the renal pelvis or the ureter, also resulting in pyonephrosis.

Diagnosis

Patients usually present with high fever, chills, and flank pain. Ultrasound is usually sufficient to establish the diagnosis. Findings

include a dilated collecting system with dependent echoes suggestive of the accumulation of purulent sediment. CT scan is also helpful in diagnosing and delineating the extent of pyonephrosis. Diagnostic criteria for pyonephrosis on CT scan include increased wall thickness of the renal pelvis greater than or equal to 2 mm, the presence of renal pelvic contents and debris, and parenchymal and perirenal findings, such as perirenal fat stranding.

Treatment

In addition to broad-spectrum parenteral antibiotics, drainage via ureteral catheter or via percutaneous nephrostomy tube may be necessary to relieve the obstruction.

Emphysematous Pyelonephritis

Emphysematous pyelonephritis (EPN) is a life-threatening, fulminant, necrotizing upper urinary tract infection associated with gas within the kidney or perinephric space or both. This condition typically occurs in patients who are immunocompromised. Diabetics account for 87% to 97% of patients with EPN. The most frequently associated pathogen is *E. coli*, which is believed to utilize necrotic tissue to ferment glucose and produce carbon dioxide gas.

Diagnosis

EPN can be diagnosed when acute pyelonephritis fails to resolve within 3 days of appropriate antibiotic therapy. Gas in the region of the kidney on a plain film of the abdomen is a hallmark finding. Ultrasound findings include strong focal echoes suggesting the presence of intraparenchymal gas. CT scan is the ideal study to identify localized gas and to determine the extent of infection.

Treatment

Treatment involves aggressive antibiotic therapy and prompt control of blood glucose levels. Surgical treatment includes drainage procedures to relieve obstruction and prompt nephrectomy in life-threatening situations. The mortality rate is as high as 54%. Patients who portend a worse prognosis with EPN include those with an elevated serum creatinine level, thrombocytopenia, and the presence of a perirenal fluid collection associated with gas in the collecting system.

Renal and Perirenal Abscess

Renal abscess is a collection of purulent material confined to the renal parenchyma. A **perirenal abscess** results from the extension of an acute cortical abscess into the perinephric space confined by Gerota's fascia. When a perinephric abscess ruptures through Gerota's fascia into the pararenal space, the abscess is known as a **paranephric abscess**. Historically, most perirenal abscesses evolve from a hematogenous spread from a skin lesion. Patients at high risk for the development of a perirenal abscess include patients on hemodialysis, diabetics, and intravenous drug abusers.

Diagnosis

The most common presenting symptoms include fever, flank pain, abdominal pain, chills, and dysuria. Most symptoms will have been ongoing for approximately 2 weeks prior to diagnosis. A flank mass may be palpable in some patients. Urinalysis often reveals white blood cells, but it can be normal in 25% of patients. Urine cultures are positive in 33%, whereas blood cultures are positive in 50%. Renal abscesses can be diagnosed on CT scan or ultrasound. CT scan may demonstrate an enlarged kidney, thickening of Gerota's fascia, perinephric stranding, and obliteration of the soft tissue planes. Ultrasound may reveal an anechoic mass within or displacing the kidney.

Treatment

Empiric broad-spectrum antibiotics (ampicillin or vancomycin in combination with an aminoglycoside or third-generation cephalosporin) are recommended. If the patient does not respond to therapy within 48 hours of initiating treatment, percutaneous drainage under CT or ultrasound guidance should be undertaken. Fluid from percutaneous drainage procedures should be sent for microbiologic evaluation with determination of culture and sensitivity. If the abscess still persists, open surgical drainage or nephrectomy may be indicated.

Chronic Pyelonephritis

Chronic pyelonephritis is induced by recurrent or persistent renal infection. It occurs almost exclusively in patients with urologic anomalies, including urinary tract obstruction, struvite calculi, renal dysplasia, or, most commonly, vesicoureteral reflux (VUR). Infection without reflux is less likely to produce injury, whereas

repeated bacterial infections with underlying VUR can cause renal insufficiency. Chronic pyelonephritis is associated with progressive renal scarring, which can lead to end-stage renal disease (ESRD).

■ Diagnosis

Symptoms of chronic pyelonephritis are nonspecific, although patients may report fever, lethargy, nausea and vomiting, and flank pain. Failure to thrive may be an initial complaint in some children. Urinalysis may show pyuria, bacteriuria, and proteinuria if significant renal insufficiency is present. In addition, creatinine and blood urea nitrogen levels may be elevated.

An intravenous pyelogram can reveal small, atrophic kidneys, caliceal dilatation with blunting, and cortical scarring. Ultrasound can also demonstrate these findings. Renal scan may reveal renal scarring. A voiding cystourethrogram (VCUG) should be done if VUR is suspected.

■ Treatment

Medical therapy consists of long-term antibiotic therapy to prevent further renal damage. Surgical therapy of VUR is necessary if bacteruria persists despite prophylactic antibiotic therapy. Nephrectomy is usually necessary in patients with renal atrophy, large stone burden in a nonfunctioning kidney, and renin-mediated hypertension.

Xanthomatous Pyelonephritis

Xanthomatous pyelonephritis (XGP) is a chronic inflammatory disorder of the kidney characterized by a mass originating in the renal parenchyma. The clinical characteristics of XGP include calculi (35% of patients) or obstruction in the urinary tract and subsequent renal damage, anemia, increased sedimentation rate, and hepatic dysfunction (50% of patients). The condition is commonly associated with *Proteus* or *E. coli* infection, but the precise etiology is not known.

The gross appearance of XGP is a mass of yellow tissue with regional necrosis and hemorrhage, superficially resembling that of a renal cell carcinoma, which makes it clinically and radiographically difficult to differentiate XGP from renal cell carcinoma. Therefore, nephrectomy is the standard treatment for XGP for diagnostic and therapeutic reasons.

LOWER TRACT INFECTIONS

Cystitis

Cystitis is classified into two categories: simple and recurrent. Approximately 20% of women will have recurrent infections after their first UTI, although subsequent UTIs can be due to a different pathogen than found initially. Factors that promote infection include glucosuria, pregnancy (which changes urine pH and promotes urinary stasis), obstruction, incomplete bladder emptying, atrophic vaginal mucosa, and frequent sexual intercourse. Obstruction is considered the most important predisposing factor. Causes of recurrent cystitis include inadequate treatment, inadequate duration of treatment, and poor patient compliance.

Pregnant women are not only more susceptible to developing UTIs, due to the anatomic and physiologic changes of pregnancy, but also are more susceptible to the ensuing development of pyelonephritis. Untreated pyelonephritis during pregnancy is associated with a high rate of premature delivery and infant mortality. For this reason, bacteriuria in pregnant women is treated regardless of the presence or absence of symptoms.

■ Pathogenesis

Fecal flora is the principal source of bacterial organisms that cause cystitis. Women are predisposed to cystitis because of a short urethra, which allows bacteria to ascend via a fecal-perineal-urethral route. Cystitis can then ensue. The most common pathogens are *E. coli* (80%) and *Staphylococcus saprophyticus* (15%). Less common pathogens include *Proteus mirabilis* and *Klebsiella pneumoniae*.

■ Diagnosis

Symptoms of frequency, urgency, and dysuria are the hallmarks of acute cystitis. Patients may also complain of low back and suprapubic pain. In simple cystitis, fever and other constitutional symptoms are absent. Urinalysis shows pyuria, bacteriuria, and occasionally hematuria. Urinary dipstick tests are positive for bacterial nitrites and leukocyte esterase. Urine culture is necessary to determine the causative organism(s) and antimicrobial sensitivities.

■ Treatment

First-line treatment for uncomplicated cystitis is a short (3–5 day) course of trimethoprim-sulfamethoxazole (TMP-SMX). However, it is estimated that resistance to TMP-SMX by *E. coli* is 20%.

For this reason, nitrofurantoins and fluoroquinolones have been utilized in treatment of UTIs because they have excellent coverage against uropathogens and decreased resistance.

Prostatitis

Prostatitis is an infection or inflammation of the prostate gland that presents as several syndromes with varying clinical features. Prostatitis is one of the most common urologic diagnoses in men under 50, accounting for over 1 million visits per year, with the chronic and nonbacterial prostatitis variants being the most frequently diagnosed.

The four most common syndromes of prostatitis are acute bacterial prostatitis, chronic bacterial prostatitis, chronic nonbacterial prostatitis/chronic pelvic pain syndrome (CP-CPPS), and granulomatous prostatitis. Individuals with acute and chronic bacterial prostatitis have documented bacterial infections of the prostate. Patients with CP-CPPS have signs of prostatic inflammation but no signs of bacterial infection. Examination of prostatic secretions under the microscope may reveal inflammatory cells. Granulomatous prostatitis is an uncommon form of prostatitis that can result from bacterial, viral, or fungal infection or the use of bacille Calmetle-Guérin (BCG) therapy.

Acute Bacterial Prostatitis

Acute bacterial prostatitis is thought to result from an ascending urethral infection or from reflux of infected urine into the prostatic ducts, or both. *Escherichia coli* is the most common cause of acute bacterial prostatitis. Other etiologic organisms include *Enterobacter*, *Proteus*, *Klebsiella*, and *Pseudomonas*. Patients present with acute onset of lower back pain and perineal pain, fever, chills, urinary urgency and frequency, dysuria, and hematuria. Digital rectal examination (DRE) reveals a warm, tender, enlarged, boggy prostate. Prostatic massage and vigorous prostate examination should be avoided, because these can promote bacteremia. Patients with persistent urinary retention secondary to acute prostatitis should be managed with a suprapubic catheter because transurethral catheterization or instrumentation is not recommended.

Physical examination reveals the classic findings mentioned previously. A complete blood count may show leukocytosis. Voided urine often reveals pyuria, microscopic hematuria, and bacteria. Urine culture usually isolates the causative organism.

Either fluoroquinolone or trimethoprim-sulfamethoxazole for 30 days is adequate for treatment and may be important in the prevention of chronic bacterial prostatitis.

Chronic Bacterial Prostatitis

The causative organisms of chronic bacterial prostatitis are the same as those of acute prostatitis. In addition to the intraprostatic reflux described previously, free zinc (known as a prostatic antibacterial factor) is found in low levels in men with chronic bacterial prostatitis. Zinc has been shown to have some bactericidal activity against some gram-negative organisms.

Patients present with milder symptoms compared with those of acute prostatitis, including perineal and low abdominal pain, dysuria, poor stream, pain on ejaculation, and hematospermia. A DRE is usually normal. However, it is not uncommon to have tenderness or firmness of the prostate on DRE.

Fractionated urine specimens remain the hallmark of the diagnosis of chronic bacterial prostatitis. Serial collection of the urine (first voided bladder specimen [VB_1], midstream bladder specimen [VB_2], expressed prostatic secretions [EPS], and residual bladder specimen [VB_3]) is used to define and identify the involved organisms. A positive VB_1 culture indicates urethritis or prostatitis or both. A positive VB_2 culture indicates cystitis. Positive EPS or VB_3 indicate prostate infection. Urine cultures before and after massage of the prostate may also help in the diagnosis. Chronic bacterial prostatitis can be diagnosed if the culture of the prostatic secretions and postmassage urine cultures grow the same bacteria as the first-voided specimen and if the colony count of the two cultures is at least 10 times greater than the first-void specimen.

Choices of antimicrobial agents are similar to that of acute prostatitis, although they are prescribed for at least 6 weeks' duration. Therapy for 12 weeks is recommended.

Chronic Nonbacterial Prostatitis/Chronic Pelvic Pain Syndrome

Nonbacterial prostatitis is an inflammatory condition of unknown etiology with symptoms similar to those of chronic bacterial prostatitis. Some studies have shown that *Chlamydia trachomatis* may play a role. Nonbacterial prostatitis is estimated to be 8 times more frequent than its bacterial counterpart.

Clinical features are similar to those of chronic bacterial prostatitis. Perineal, penile, and testicular pain predominate, and voiding symptoms include dysuria, frequency, urgency, and weak stream. Patients may have symptoms of bladder outlet obstruction and decreased urinary flow rate. Spasms of the bladder neck and external sphincter due to increased adrenergic stimulation may cause intraprostatic reflux of urine. DRE may reveal an increased sphincter tone and tender paraprostatic tissue, although the prostate itself is nontender. Urodynamic studies may demonstrate incomplete relaxation of the bladder neck and prostatic urethra with diminished flow rates.

DRE usually reveals a normal prostate, though patients may have tenderness of pelvic floor musculature on palpation. Examination of the EPS shows leukocytes and lipid-laden macrophages.

Treatment of nonbacterial prostatitis is controversial. Some patients do improve with several weeks of oral antibiotics. In addition to fluoroquinolones, doxycycline may be added empirically to treat fastidious organisms such as *Chlamydia* that are not detected in initial cultures. Pentosan polysulfate (Elmiron) has shown promise in improving symptoms in 40% of patients. Alpha blockers (doxazosin, terazosin, or tamsulosin) are efficacious in patients with obstructive voiding symptoms. Antidepressants such as amitriptyline are useful in patients with significant pelvic and perineal pain.

Interstitial Cystitis

Epidemiology

Interstitial cystitis (IC) is a chronic disorder characterized by urinary frequency, nocturia, and suprapubic pain on bladder filling. Hematuria has been reported in 20% to 30% of cases. The disease occurs primarily in women aged 30 to 70 years. There is a 10:1 female to male preponderance.

Diagnosis

The diagnosis of IC is one of exclusion based on clinical and cystoscopic criteria. Patient have a chronic history of irritative bladder symptoms and pain. Urinary frequency occurs with small voided volumes. Physical examination fails to reveal any pertinent findings. Urinalysis and urine culture are often negative. Cystoscopy when performed reveals diffuse pinpoint submucosal hemorrhage after repeated bladder distension. If bladder biopsy is performed, inflammatory cells are often present, but no evidence of carcinoma in situ or transitional cell carcinoma is seen. Urodynamic studies often reveal sensory urgency with incomplete relaxation of the external urinary sphincter in voiding. Because IC is a diagnosis of exclusion, patients need to be worked up with a urinalysis, urine culture, voiding record, intravenous pyelogram, and cystoscopy.

Treatment

Treatment of IC often involves several different therapeutic options. Cystoscopy with hydrodistention under anesthesia has been effective in approximately 30% of patients. Intravesical installation of dimethyl sulfoxide (DMSO) is a useful treatment and

gives temporary relief in approximately 50% of patients. Amitriptyline, a tricyclic antidepressant, is useful in the management of neuropathic pain. Its use in IC patients has been well described. Pentosan polysulfate (Elmiron) is a synthetic sulfated polysaccharide that is used to repair the glycosaminoglycan layer, which is thought to be deficient in IC. This agent improves pain and voiding symptoms in approximately 50% to 65% of patients. Anticholinergic agents are useful in the management of associated detrusor overactivity. Sacral nerve stimulation is reserved for patients who have failed medical therapy.

Epididymitis and Orchitis

Epididymitis is an inflammation of the epididymis. Most cases are due to ascending infection from the lower urinary tract. Increased pressure in the prostatic urethra during voiding allows infected urine to enter the ejaculatory ducts and traverse via the vas deferens to reach the epididymis. In men younger than 40 years, sexually transmitted pathogens such as *Neisseria gonorrhoeae* and C*hlamydia trachomatis* are common causes of epididymitis. In older men, *E. coli* is the most common organism.

Orchitis is an acute infection of the testis. Because the testis possesses a relatively high infection resistance, orchitis is rare without an initial epididymitis. The two major distinguishing etiologies of orchitis are blood-borne bacterial infection and viral infection. Pyogenic bacterial orchitis is usually secondary to bacterial involvement of the epididymis. The most common bacterial pathogens are *E. coli*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa*. Viral orchitis is most commonly caused by mumps. This is rarely seen in prepubertal boys, but occurs in 20% to 30% of postpubertal boys with mumps.

Diagnosis

The clinical presentation of epididymitis and orchitis involves scrotal swelling and pain that is usually severe and develops rapidly. Symptoms and signs of cystitis, prostatitis, or urethritis may also be present. Physical examination reveals scrotal erythema and swelling. It is important to rule out testicular torsion, a urologic emergency, in a patient presenting with acute scrotal pain. Prehn's sign, alleviation of pain with scrotal elevation, is present in acute epididymitis but generally not in testicular torsion. It may be important to rule out testicular torsion by performing a duplex Doppler ultrasound study of the testicle. In cases of epididymitis, normal blood flow to the testicle is identified, and the involved epididymis is enlarged with hyperemia (increased blood flow).

In testicular torsion, no appreciable blood flow is identified in the involved testicle.

■ Treatment

Epididymo-orchitis related to *N. gonorrhoeae* or C. *trachomatis* should be treated with single-dose ceftriaxone or with a 10-day course of tetracycline or erythromycin. If an enteric pathogen is suspected, a 2-week course of broad-spectrum oral antibiotics such as trimethoprim-sulfamethoxazole is recommended. Additional supportive management includes bed rest, scrotal elevation, and pain medications.

Fournier's Gangrene

Fournier's gangrene is a rare, progressive, necrotizing fascitis of the genitalia or the perineum. It is a true urologic emergency and demands early recognition and prompt medical and surgical treatment.

■ Risk Factors

Increased risk for developing Fournier's gangrene is associated with conditions of immunodeficiency such as diabetes, malnutrition, alcoholism, intravenous drug abuse, hemodialysis, and use of steroid medications. Local trauma, including procedures and operations such as circumcision, penile prosthesis insertion, and vasectomy, may also increase risk.

■ Pathogenesis

The source of infection is either the genitourinary or gastrointestinal tract. Fournier's gangrene is a polymicrobial infection, with causative organisms including *E. coli*, *Bacteroides*, *Clostridium*, streptococci, and staphylococci. Ultimately, an obliterative endarteritis develops, and the ensuing cutaneous and subcutaneous vascular necrosis leads to localized ischemia and further bacterial proliferation. Rates of fascial destruction as high as 2 to 3 cm/h have been described. As gangrene develops, pain actually may subside as nerve tissue becomes necrotic.

■ Diagnosis

Patients present with irritation, itching, and erythema of the perineal region. The genital, perianal, or rectal discomfort is usually out of proportion to the physical examination findings. The skin overlying the affected region may be erythematous, edematous, cyanotic, bronzed, indurated, blistered, or even gangrenous.

A feculent odor may be present secondary to infection with anaerobic bacteria. Crepitus may be present, but its absence does not exclude the presence of *Clostridium* species or other gas-producing organisms.

Treatment

Initiation of prompt broad-spectrum intravenous antibiotic therapy is important because wound and tissue cultures often grow multiple aerobic and anaerobic organisms. Triple-antibiotic therapy that includes an aminoglycoside, penicillin derivative, and anaerobic coverage is recommended. Typically, ampicillin, gentamicin, and metronidazole are given intravenously. Prompt surgical wound débridement minimizes progression of necrosis. Multiple débridements in the operating room may be required to remove all necrotic tissue effectively. In some cases, diverting colostomy and suprapubic cystotomy are required to divert the fecal and urinary streams, respectively.