Infections of the urinary tract

Mark W. Ball
The James Buchanan Brady Urological Institute and Department of Urology, The Johns Hopkins School of Medicine, Baltimore, MD, USA

KEY POINTS

- Urinary tract infections (UTIs) are commonly diagnosed maladies and account for a significant number of healthcare visits and dollars.
- Infections of the bladder include uncomplicated cystitis, complicated cystitis, pyocystis, and emphysematous cystitis.
- Infections of the kidney include pyelonephritis, emphysematous pyelonephritis, xanthogranulomatous pyelonephritis, infected hydronephrosis, renal abscess and perinephric abscess.
- Infections of the genitalia and reproductive organs include orchitis, epididymitis, prostatitis, and Fournier gangrene.

CASE STUDY

A previously healthy 27-year-old woman presents to the Emergency Department with fever to 39°C, tachycardia to 150 bpm, respirations of 25 breaths per minute, and a leukocytosis to 13,000 WBC. Urinalysis is significant for large leukocyte esterase, positive nitrite, and bacteria are too numerous to count. CT of the abdomen and pelvis reveals a 6-mm left mid-ureteral stone with ipsilateral hydronephrosis and perinephric fat stranding.

The patient is taken emergently to the operating room for left-sided ureteral stent placement. Upon cannulating the ureter, purulent urine drains from the ureteral orifice. Postoperatively, the patient has a profound systemic inflammatory response syndrome (SIRS), requiring several days of mechanical ventilation, vasoactive infusions, and broad-spectrum antibiotics. She eventually makes a full recovery.

Nomenclature

Urinary tract infection (UTI) refers to bacterial invasion of the urothelium causing an inflammatory response. When the site of infection is known, it is more informative to name the site of infection; in other words, cystitis should be used for bladder infection and pyelonephritis for kidney infection, rather than using the generic UTI. Bacteriuria, on the other hand, refers to the presence of bacteria in the urine, which may be either asymptomatic or associated with infection. Pyuria refers to the presence of white blood cells (WBCs) in the urine, which can occur in the setting of either infection or other inflammatory states (nephrolithiasis, malignancy, or foreign body).

Epidemiology

UTI is the most common bacterial infection, responsible for at least 7 million office visits and 100,000 hospitalizations per year. Most infections are diagnosed...
Interpreting the urinalysis

While urine culture is the gold standard for diagnosing UTIs, it is a test that takes 1–2 days to provide results and potentially longer for antibacterial sensitivity analysis. UA is more expeditious and can support the diagnosis made by history and physical. A UA often consists of two parts: a dipped UA and a microscopic UA. The dipped component tests for pH and the presence of leukocyte esterase (LE), nitrates, and blood. The microscopic component identifies red and white blood cells, red and white blood cells casts, granular casts, bacteria, and yeast.

- **Pyuria:** >5 WBC/hpf
- **Leukocyte esterase (LE):** an enzyme released by white blood cells. Positive LE correlates with pyuria
- **Nitrite:** Urine contains nitrates from protein catabolism. Gram-negative bacteria are able to reduce nitrate to nitrite creating a positive result. One notable exception is pseudomonas which although gram-negative, is associated with negative nitrite on UA.

A UA suggestive of infection typically has positive LE, pyuria, microscopic hematuria, and bacteria. Nitrite is present with gram-negative infection. The presence of epithelial cells can indicate contamination with vaginal flora and should prompt repeat mid-stream collected urine after adequate cleaning [1].

Bladder infections

Cystitis

Cystitis, or infection of the bladder, may be classified as uncomplicated or complicated. Factors that make cystitis complicated are infections in a male, the elderly, children, diabetics, the immunosuppressed, in the presence of anatomic abnormality, during pregnancy, after recent instrumentation, in the presence of a urinary catheter, and after recent antimicrobials or hospitalization. The typical presentation of cystitis includes symptoms of dysuria, frequency, urgency, + suprapubic pain, and +hematuria. Notably, constitutional symptoms including fever and chills are usually absent. This history is crucial in making diagnosis since as many as 50–90% of patients presenting with these symptoms will have cystitis. The diagnosis is supported by urinalysis findings of pyuria, bacteriuria, and the presence of nitrite and LE [1].

Treatment of uncomplicated UTI is dependent on availability, allergy, and local resistance patterns. The
Pyocystis

Pyocystis is a condition in which purulent material is retained in the bladder. Typically, the bladder is defunctionalized as a result of urinary diversion or hemodialysis. Presenting symptoms include purulent discharge, fever, or suprapubic pain. Treatment begins with placing a catheter to drain the purulent material and antibiotics. Oral antibiotics may be used in nonseptic patients, while intravenous (IV) antibiotics should be chosen in ill patients. Additionally, intravesical instillation of an antibiotic or antiseptic may be considered as well as periodic self-catheterization and saline irrigation. Refractory cases warrant more aggressive management—including cystectomy, bladder sclerosis, or surgically created fistula (vaginal or perineal vesicostomy) [1].

Emphysematous cystitis

Emphysematous cystitis is a rare type of cystitis in which gas is found within the wall of the urinary bladder. It is caused by infection with gas-forming bacteria and most often presents in diabetics and elderly patients. Symptoms are essentially the same as in typical cystitis, and treatment consists of culture-specific antibiotics. This condition must be distinguished from air within the lumen of bladder, which is much more common, and often caused by urinary tract instrumentation, indwelling Foley catheter, or by colovesical or enterovesical fistula [1].

Asymptomatic bacteriuria

Asymptomatic bacteriuria is defined as bacteria in the urine in the absence of clinical signs of infection. It is more common in women than men, but increases in prevalence in both sexes with age. Patients with indwelling catheters, bladder reconstruction using bowel, and patients with neurogenic bladders almost always have bacteriuria. Asymptomatic bacteriuria should not be screened for or treated with a few important exceptions. Pregnant women and patients undergoing urologic procedures should be screened and treated [5].

Recurrent UTI

Unresolved UTI refers to an infection that has not responded to antimicrobial therapy. This commonly occurs because of resistant bacteria or can occur in the case of other unrealized complicating factors (see section Cystitis).

Recurrent UTI is an infection that occurs after resolution of a previous infection. These infections may represent either reinfection or bacterial persistence. Reinfec tion designates a new event in which the same or different organism enters the urinary tract, or bacterial persistence. Persistence, on the other hand, is when the same bacteria reappear from a nidus such as infected stone or hardware. Reinfection is responsible for 80% of recurrent UTIs [1].

Kidney

Acute pyelonephritis

Diagnosis and workup

Acute pyelonephritis is a renal parenchymal infection that is usually caused by ascending infection from the bladder. *Escherichia coli* is the most common organism. The classic presentation is acute onset of fever, chills, and flank pain; however, presentation is variable and there is no *sine qua non* to make the diagnosis. Abdominal pain, nausea or vomiting often accompanies the condition. Physical examination often reveals costovertebral angle tenderness. Laboratory tests often reveal an elevated serum WBC count, while UA findings are similar to those found in acute cystitis. Figure 1.1 shows classic radiographic
(e.g., levofloxacin or ciprofloxacin), or ampicillin plus gentamicin. Early radiologic investigation is warranted in these patients as well [1, 2].

Chronic pyelonephritis

Chronic pyelonephritis is an often asymptomatic condition caused by multiple bouts of acute pyelonephritis. It can result in renal insufficiency. The diagnosis is made with imaging, which demonstrates atrophic, scarred, and pitted kidneys. Management is to treat active infection and prevent future infections. The condition is rare in patients without underlying urinary tract disease but may occur in vesicoureteral reflux and other abnormalities [1].

Emphysematous pyelonephritis

Emphysematous pyelonephritis is an acute, necrotizing infection of the renal parenchyma resulting from infection with gas-producing organisms. It is more common in diabetic patients and in the presence of obstruction. Diagnosis is made by cross-sectional imaging, demonstrating air in the renal parenchyma. Treatment consists of IV antibiotics, relief of any obstruction, supportive care, and often nephrectomy. Despite aggressive treatment, the mortality rate is over 50% [1].

Renal abscess

Renal abscess (or renal carbuncle) is a collection of purulent material within and confined to the parenchyma. Gram-negative organisms from ascending infection are the most common causative organisms. Hematogenous spread can also occur and gram-positive organisms are often isolated in this mechanism. Risk factors include diabetes mellitus and recurrent UTIs. Presentation begins identical to pyelonephritis, but it does not respond to typical antimicrobial therapy. Failure to respond after 72 hours of therapy warrants imaging to rule out an abscess [1].

Treatment

Treatment is dependent upon the severity of illness and comorbidities. Patients who are nonseptic and can tolerate oral antibiotics may be treated empirically with a fluoroquinolone as an outpatient after urine culture is obtained. Most patients will improve within 72 hours of antimicrobial initiation. Failure to improve warrants more aggressive therapy with hospitalization and broad spectrum antibiotics initiated if culture data are not available. Additionally, radiologic investigation is indicated to rule out obstruction or development of an abscess. Abscesses may require drainage, and obstruction should be relieved with a ureteral stent or percutaneous nephrostomy tube.

In septic patients, blood and urine cultures should be obtained and intravenous antibiotics should be initiated. Common regimens include third-generation cephalosporins (e.g., ceftriaxone), fluoroquinolones
Perinephric abscess

Perinephric abscess is a collection of purulence outside the kidney parenchyma but inside Gerota’s fascia. Gram-negative organisms are usually causative, with *E. coli* being the most common. Clinical presentation, diagnosis, and treatment are similar to parenchymal infection. Up to 50% of blood cultures will be positive.

Treatment of perinephric abscess almost always requires drainage. Percutaneous drainage should be considered first line for smaller lesions. Larger abscess or those associated with a nonfunctioning kidney may require nephrectomy [1].

Infected hydronephrosis

Infected hydronephrosis is an infection in an obstructed, hydronephrotic kidney. It is a urologic emergency. Patients are typically very ill, often in urosepsis, with flank pain. It can lead to pyonephrosis or suppurrative damage to renal parenchyma. Treatment consists of broad spectrum antibiotics and emergent drainage with either retrograde ureteral stent or percutaneous nephrostomy tube. In decompensating patients, percutaneous nephrostomy is preferred given that it may be performed under less sedation, and to avoid high pressure from irrigation on the collecting system. Drainage should be followed by 10–14 day course of culture-specific antibiotics [1, 7].

Xanthogranulomatous pyelonephritis

Xanthogranulomatous pyelonephritis (XGP) is a chronic, destructive renal infection. It is often associated with unilateral obstructing calculi. The end result is an enlarged, nonfunctioning kidney. The differential diagnosis includes renal cell carcinoma; consequently, this entity must be ruled out. The pathognomonic feature at the cellular level is the presence of lipid-laden macrophages. Treatment often requires nephrectomy [1].

Prostate

Prostatitis

The most common urologic diagnosis in men younger than 50 years is prostatitis and is most prevalent in men between aged 20 and 49 years.

Enterobacteriaceae and *Enterococci* are the two most common pathogens. The NIH classifies prostatitis into four categories.

**Category I: Acute bacterial prostatitis**

Patients with acute bacterial prostatitis present with lower urinary tract symptoms, including dysuria, frequency and urgency, and often obstruction. It typically is associated with a profound systemic inflammatory response, including fever, chills, and malaise. Systemic symptoms include fever, chills, or perineal pain. Digital rectal examination demonstrates a swollen, exquisitely tender prostate.

Treatment should be tailored to cultures. Fluoroquinolones may be empirically started with duration of 4–6 weeks. Bladder obstruction has classically been treated with a suprapubic cystostomy tube, since indwelling Foley catheters are through to cause further obstruction of urethral ducts. However, straight catheterization to relieve the initial obstruction is an appropriate first step [8].

**Category II: Chronic bacterial prostatitis**

The hallmark of chronic bacterial prostatitis is a history of recurrent UTIs. The traditional classification of chronic prostatitis relied on the Meares–Stamey four-glass test. This technique consists of collecting four samples of urine to distinguish urethral, bladder, and prostate infection. The voided bladder 1 (VB1) specimen is the first 10 mL of urine, representing the ureteral specimen. Voided bladder 2 (VB2) is a midstream specimen, representing the bladder specimen. Next, the prostate is massage, and the expressed prostatic secretions (EPSs) are collected. Finally, voided bladder 3 (VB3) is the first 10 mL of urine after massage. Each specimen is analyzed for leukocytes and microbes, as well as sent for culture. Alternatively, a two-cup test has been proposed that consists of collecting urine before and after massage. Chronic bacterial prostatitis will have both WBCs and positive cultures in both the EPS and VB3 specimens [8].

**Category III: Chronic pelvic pain syndrome**

Patients with chronic pelvic pain syndrome (CPPS) present with pain lasting greater than 3 months. The pain is most often in the perineum. Men often complain of pain associated with ejaculation. This category is subdivided into inflammatory (IIla) and noninflammatory (IIIB) CPPS. This is distinguished by
the four-glass test that demonstrates WBCs in the EPS and VB3 in category IIIA, and no WBC in IIIB. Cultures are negative for both. More information about chronic pelvic pain can be found in Chapter 15 [8].

Category IV: Asymptomatic inflammatory prostatitis
This classification is reserved for asymptomatic patients who are found to have inflammation incidentally during prostate biopsy or fertility workup. Treatment is not warranted unless treating an elevated prostate-specific antigen (PSA) with a trial of antimicrobials [8].

Prostate abscess
Prostate abscesses typically evolve from cases of acute bacterial prostatitis. An abscess should be suspected when a patient with acute prostatitis fails to respond to antimicrobial therapy. The diagnosis is confirmed with transrectal ultrasound or computed tomography (CT). Treatment involves drainage of the abscess by one of several methods. Classically, transurethral incision has been used for most prostatic abscess, though transperineal incision and drainage may be required for abscesses that extend beyond the prostacy capsule. Percutaneous drainage may also be employed to drain a prostatic abscess and may offer a less morbid approach [8].

Testis and epididymis
Orchitis often presents with associated epididymitis, or epididymo-orchitis. The presence of orchitis alone suggests viral infection, such as mumps orchitis. More commonly, the combined epididymo-orchitis usually occurs via retrograde spread of bacteria through the ejaculatory ducts and vas deferens into the epididymis. The original source is often the bladder, urethra, or prostate. In prepubescent patients, a chemical etiology is more common than an infectious etiology and is related to the reflux of urine up the genital tract in dysfunctional voiders. In adults younger than 35 years, the most common cause of epididymitis is sexually transmitted infection, most common Neisseria gonorrhoeae and Chlamydia trachomatis. In men older than 35 years, the source is often coliform bacteria that have colonized the bladder or prostate, with E. coli being the most common.

Clinical presentation reveals tender epididymis and testis. The spermatic cord is often tender as well. Radiographic presentation with ultrasound demonstrates increased vascularity in the epididymis, testis, or both. Ultrasound should be obtained when the diagnosis is unclear to rule out torsion, which has decreased or no flow, as well as malignancy. Untreated epididymitis sometimes progresses to a paratesticular abscess or pyocele. Figure 1.2 demonstrates the appearance of pyocele on ultrasound. This requires open incision and drainage [8].

Treatment
Treatment of isolated orchitis is mainly supportive—scrotal support, bed rest, antipyretics. Antimicrobials may be used when a bacterial origin is presumed with fluoroquinolones being the agent of choice. There is no antiviral regimen for mumps orchitis. Treatment of epididymitis is dependent on age. The Center for Disease Control and Preventions guidelines recommend ceftriax-
one and doxycycline for men younger than 35 years and levofloxacin or ofloxacin for men older than 35 years. The antibiotic course is typically 10 days but may be longer if concomitant prostatitis is suspected [8].

**Special infections**

**Genitourinary tuberculosis**

While tuberculosis (TB) is most commonly a pulmonary process, 10% of cases occur in extrapulmonary sites. Of these, 30–40% of extrapulmonary TB occurs in the GU tract. Seeding of the GU tract occurs via hematogenous spread from the alveoli to hilar lymph nodes to the blood stream. The primary landing site is the kidney due to its high vascularity. Downstream infection of the bladder and urethra can occur. The epididymis may also be seeded due to hematogenous spread [9].

**Fournier gangrene**

Fournier Gangrene is necrotizing fasciitis of the perineum. It is a rapidly progressive, potentially life-threatening infection that is usually polymicrobial, consisting of gram-positive, gram-negative, and anaerobic bacteria. Because of the high morbidity and mortality (16–40%) associated with the infection, it must be ruled out in every case of soft tissue infection of the genitalia. Diabetes mellitus, peripheral vascular disease, alcoholism, and malnutrition are risk factors. Examination may demonstrate cellulitis, blisters, or frankly necrotic areas. Pain out of proportions to visible infection may indicate more extensive underlying infection. Treatment includes broad-spectrum parenteral antibiotics and extensive surgical debridement [1, 9].

**Antimicrobial therapy**

The goal of antimicrobial therapy is to eliminate microbial growth in the urinary tract. Table 1.1 lists the most common antibiotics used to treat infections of the urinary tract, along with the mechanism of action, spectrum, and common adverse reactions of each drug. Institutional antibiograms and regional resistance patterns should guide antimicrobial therapy [1].

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**Table 1.1 Common antimicrobials**

<table>
<thead>
<tr>
<th>Antimicrobials</th>
<th>Mechanism of Action</th>
<th>Spectrum</th>
<th>Adverse reactions/Cautions</th>
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</thead>
<tbody>
<tr>
<td>Beta-lactams</td>
<td>Inhibition of bacterial cell wall synthesis</td>
<td><em>Streptococcus, Staphylococcus saprophyticus, Enterococcus, Escherichia coli, Proteus</em></td>
<td>• PCN allergy cross-reactivity</td>
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<td></td>
<td></td>
<td></td>
<td>• High prevalence of <em>E. coli</em> resistance in some regions</td>
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<td></td>
<td></td>
<td></td>
<td>• Disruption of normal vaginal flora</td>
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<td>• Frequent gastrointestinal intolerance and diarrhea</td>
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<td>• Acute interstitial nephritis</td>
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<td>• 10% cross-reactivity with PCN allergy</td>
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<td>• Synergistic toxicity with aminoglycosides</td>
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</table>
| Cephalosporins| Inhibition of bacterial cell wall synthesis | Spectrum by generation: 1st: *Streptococcus*, methicillin-sensitive *Staphylococcus aureus*, some gram-negative rods 2nd: Strep, some gram-negative rods, some anaerobes. 3rd: Strep, most gram-negative rods, moderate *Pseudomonas* 4th: Most gram-negative rods, and good pseudomonal coverage | | (continued)
### KEY WEB LINKS

- **Johns Hopkins Antibiotic Guide**

- **Infectious Disease Society of America Practice Guidelines**

- **American Urological Association Clinical Guidelines**
  [http://www.auanet.org/content/clinical-practice-guidelines](http://www.auanet.org/content/clinical-practice-guidelines)

### WHAT TO AVOID

- Avoid initiating antimicrobial therapy before obtaining cultures, except in cases where treatment delay could lead to patient harm.
- Avoid prescribing antimicrobials without considering renal or hepatic dose adjustments, drug interactions, and/or potential drug toxicities.
- Avoid the overuse and misuse of antimicrobials which can lead to bacterial resistance.

### Table 1.1 (Continued)

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<thead>
<tr>
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<th>Mechanism of Action</th>
<th>Spectrum</th>
<th>Adverse reactions/Cautions</th>
</tr>
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</table>
| **Trimethoprim/sulfamethoxazole** (TMP/SMX) | Inhibition of bacterial folic acid metabolism required for DNA synthesis. | *Streptococcus*, *Staphylococcus*, gram-negative rods (not *Pseudomonas*), and atypical *Mycobacteria* | • Interacts with Coumadin to prolong INR  
• May be associated with hematological abnormalities (especially in G6PD and AIDS), nephrotoxicity, hepatotoxicity, and Stevens–Johnson syndrome  
• Avoid in pregnancy |
| Nitrofurantoin | Inhibits multiple bacterial enzymes. Sterilizes urine without affecting GI or vaginal flora | • *E. Coli* and *S. saprophyticus*  
• Achieves high urinary levels but poor tissue penetration—contraindicated in pyelonephritis. | • Neurotoxicity  
• Pulmonary fibrosis, interstitial pneumonitis  
• Hematologic abnormalities and frequent GI intolerance  
• Requires longer treatment course (7 days instead of 3)  
• Avoid in G6PD, renal failure |
| **Aminoglycosides** | Inhibition of protein synthesis | Gram-negative rods including *Pseudomonas* | • Otoxicity (usually irreversible)  
• Nephrotoxicity (usually reversible, nonoliguric ARF after 5–10 days)  
• Avoid in pregnancy  
• Neuromuscular blockade (rare)  
• Once-daily dosing has less nephrotoxicity but similar ototoxicity |
| **Fluoroquinolones** | Inhibition of DNA gyrase | Gram-positives, most gram-negative rods including *Pseudomonas*, *N. gonorrhoeae* | • Avoid during pregnancy and in children  
• May cause false-positive urine opiate test  
• Peripheral neuropathy (rare)  
• Tendinitis/tendon rupture |
| **Vancomycin** | Inhibition of bacterial cell wall | Gram-positives, including MRSA | • Nephrotoxicity & ototoxicity  
• “Red-man syndrome”: caused by histamine release caused by rapid infusion. Causes erythematous rash of the face, neck, or torso with pruritus. Severe cases cause hypotension |
| **Clindamycin** | Inhibition of protein synthesis | Gram-positives (including MRSA) and anaerobes | • Association with *Clostridium difficile* colitis |
Multiple choice questions

1 Which of the following antimicrobials is not appropriate in the treatment of pyelonephritis?
   a Ciprofloxacin
   b Nitrofurantoin
   c Ceftriaxone
   d Trimethoprim/Sulfamethoxazole

2 Which of the following is the mechanism of action of levofloxacin?
   a Inhibition of cell wall synthesis
   b Inhibition of DNA gyrase
   c Inhibition of protein synthesis
   d Inhibition of folic acid synthesis

References


Answers to multiple choice questions

1 Nitrofurantoin is not appropriate for the treatment of pyelonephritis. The drug does not reach adequate tissue levels to irradiate parenchymal infection.
2 Fluoroquinolones inhibit the enzyme DNA gyrase, blocking the unzipping of double stranded DNA required for DNA replication.