Diagnosis and Management of Urinary Tract Infection and Pyelonephritis

David R. Lane, MD[a,*], Sukhjit S. Takhar, MD[b,c]

KEYWORDS

• Urinary • Pyelonephritis • Cystitis

Urinary tract infections (UTIs) are one of the most common bacterial infections encountered in outpatient settings[1,2] In 2005, 1.8 million patients in emergency departments (EDs) were diagnosed with UTI, and nearly 5% of all patients in EDs had a genitourinary (GU) complaint.[3] More than 50% of women experience 1 UTI in their lifetime, and approximately 10% of women have a UTI annually.[4] Familiarity with the most recent literature and clinical practice guidelines, and local patterns of resistance, is crucial for practicing emergency physicians (EPs). Targeted and appropriate therapy can significantly reduce the morbidity and mortality associated with this spectrum of illness, and may also reduce the development of antimicrobial resistance in uropathogens. This article reports the epidemiology and risk factors of UTIs, and clarifies the diagnostic tools and therapeutic measures that best streamline practices and effectively treat patients with UTIs. This article concentrates on the adult woman with upper and lower tract infections, unless otherwise indicated. Treatment options are discussed in light of bacterial resistance in the twenty-first century.

DEFINITIONS

UTIs are divided into 2 major categories: lower tract infections and upper tract infections. Broadly defined, they can be considered an inflammatory response of the

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[a] Department of Emergency Medicine, Georgetown University Hospital & Washington Hospital Center, Georgetown University School of Medicine, 3800 Reservoir Road Northwest, Washington, DC 20007, USA
[b] Department of Emergency Medicine, Brigham and Women's Hospital, Neville House, 75 Francis Street, Boston, MA 02115, USA
[c] Harvard Medical School, Boston, MA, USA
* Corresponding author.
E-mail address: david.lane@gunet.georgetown.edu

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urinary tract to microorganisms. UTIs range from asymptomatic cases to life-threatening septic shock. They can be community acquired or catheter associated.

Asymptomatic bacteriuria (ABU) is the presence of significant bacteria with or without pyuria on urinalysis without signs or symptoms that are referable to a UTI. The usual cutoff is a single organism isolated in a quantity of at least 100,000 colony forming units (CFU) per milliliter.[5] Screening and treatment is not generally recommended, with the exception of women who are pregnant or men who are going to undergo a transurethral prostate resection.[6,7]

Cystitis, or lower UTI, is an acute bacterial infection of the urinary bladder and urethra, whereas pyelonephritis is an infection of the upper urinary tract structures, including the ureters or kidneys. Differentiation of the 2 is based on history and examination.

Uncomplicated UTI occurs in young, healthy, nonpregnant women with structurally and functionally normal urinary tracts.[8] Complicated UTI is UTI occurring in anyone else: all men, and women who have a structural or functional GU abnormality or an underlying predisposing medical condition that increases the risk of infection and recurrence or that reduces the effectiveness of antimicrobial therapy (**Box 1**). Both cystitis and pyelonephritis can be defined as either uncomplicated or complicated according to these parameters.

EPIDEMIOLOGY AND RISK FACTORS

UTIs are common, particularly in women, with 11% of women reporting a UTI in any given year, and more than 50% of women having at least 1 infection during their lifetime.[4] Other groups at increased risk for UTI, as well as complications of UTI, include infants, pregnant women, the elderly, and individuals with diabetes, human immunodeficiency virus (HIV)/AIDS, spinal cord injuries, indwelling catheters, or urologic abnormalities.[1]

There is much misunderstanding among patients surrounding risk factors for, and prevention of, UTIs. Proven risk factors for UTI in young women are prior episodes of cystitis, recent sexual activity, and use of spermicidal agents during intercourse.[9] The odds of a UTI increase by a factor of 60 during the initial 48 hours after sexual intercourse.[10,11] Commonly recommended treatments to reduce incidence of UTI, such as increased hydration and prompt postcoital voiding or douching, are not supported by evidence.[12] Cranberries, cranberry tablets, and cranberry juice may have a benefit in preventing recurrent UTIs; the evidence is best in sexually active adult

Box 1
Patient characteristics qualifying UTI as complicated

- Pregnancy
- Diabetes
- Male gender
- Immunosuppression
  - Immunosuppressive agents, acquired immune deficiency syndrome (AIDS), others
- Functional genitourinary abnormality
  - Indwelling urinary catheter, neurogenic bladder, others
- Structural genitourinary abnormality
  - Renal stones, fistula from intestinal tract to bladder, polycystic kidney disease, renal transplant, other

women. However, it requires daily cranberry juice intake at a dose of 200 to 750 mL, taken in divided doses daily, and the benefit is only modest.[13,14]

Additional risk factors have been shown to have significance in specific subgroups of the population. In postmenopausal women, cystoceles, urinary incontinence, or prior GU surgery are significant risk factors for recurrent cystitis.[15] In elderly women, the risk of UTI increases with age and debility, specifically increasing in those with impaired voiding or poor hygiene, and is also higher in patients with diabetes.[16–19] In men, risk factors for the development of UTI include insertive anal intercourse, lack of circumcision, urinary tract instrumentation, renal stone disease, and prostatic hypertrophy.[20]

MICROBIOLOGY

The bacterial pathogens responsible for UTI have remained consistent for many years. Gram-negative bacilli are the culprit organisms in most cases. However, the response of some pathogens to common antimicrobials has gradually evolved in the past 2 decades. *Escherichia coli* continues to be the primary offender, causing 75% to 90% of episodes of acute uncomplicated cystitis, and most episodes of complicated UTI and pyelonephritis.[4] Gram-positive organisms are less common; however, *Staphylococcus saprophyticus* accounts for 5% to 15% of UTI, mainly in younger women, and is generally confined to cystitis.[21] If *Staphylococcus aureus* is isolated from the urine, a bacteremic source that has seeded the kidney must be considered. Other aerobic gram-negative rods such as *Klebsiella* species and *Proteus mirabilis*, and the gram-positive enterococci are isolated in most of the remaining cases.[4]

CLINICAL PRESENTATION

The typical clinical presentation for cystitis is a well-appearing woman with urinary frequency, dysuria, and urgency. Suprapubic pain and low back pain may also be present. The symptoms of cystitis are sufficiently classic and repetitive that self-diagnosis can be accurate in this disease: if a woman who previously has had cystitis has symptoms suggesting a recurrence, there is an 84% to 92% chance that an infection is present.[22,23]

The probability of cystitis in a woman with dysuria, urinary frequency, or gross hematuria is 50%.[24] The absence of symptoms suggesting vaginitis or cervicitis, such as vaginal irritation, bleeding, or discharge, raises the probability of UTI to more than 90%, whereas the presence of such symptoms reduces the likelihood to about 30%.[24] Further evaluation of women with symptoms of vaginitis or cervicitis should include a pelvic examination with evaluation for potential gonorrhea, chlamydia, bacterial vaginosis, trichomoniasis, and candidiasis.

For older women, increased or new incontinence is a common symptom of cystitis.[25] Elderly patients may present with any number of nonspecific symptoms, including altered mental status or delirium, general malaise, or, in extreme cases, systemic inflammatory response syndrome, sepsis, or septic shock.

As mentioned earlier, differentiation of cystitis from pyelonephritis is based on history and physical examination. Pyelonephritis presents in a spectrum from well appearing to critically ill with severe sepsis. Classic symptoms include flank or abdominal pain, fever and chills, and nausea or vomiting. Up to 25% of patients with pyelonephritis may have bilateral infection and thus present with pain that is not unilateral.[6] Typically patients report preceding symptoms consistent with cystitis, but this is not essential. As in many diseases, diabetics and the elderly have a predilection for presenting atypically. The lack of fever and presence of altered mental status is common in the elderly.[26]

DIAGNOSTIC TOOLS

Urine Collection

Clean-catch midstream collection of urine is a common technique for obtaining urine samples. However, there is evidence showing that the clean-catch technique does not decrease contamination rates and that routine urination into a sterile container may be considered an adequate specimen collection technique.[27–29] For obtaining samples with minimal contamination, straight catheter collection is only bettered by suprapubic aspiration; however, both techniques introduce unnecessary patient discomfort and resource use, as well as the risk of introducing bacteria into the bladder.[5]

Urinalysis

Urine dipstick has largely replaced urine microscopy as the initial diagnostic tool of choice in UTI in the ambulatory setting, because it is less expensive, more convenient, and its accuracy is comparable with urine microscopy.[5,30] On urine dipstick, the 2 tests of interest are leukocyte esterase, a measure of pyuria, and nitrite, a measure of bacteriuria. Dipsticks are the most predictive when the presence of either nitrite or leukocyte esterase is considered positive, yielding a sensitivity of 75% (67%–100%) and specificity of 82% (67%–98%).[31] If both leukocyte esterase and nitrite must be positive, the specificity improves to 98% to 100%, but the sensitivity declines to 35% to 84%.[5] These diagnostic tests in isolation have limitations. Nitrite positivity alone seems to be more specific than leukocyte esterase alone in the diagnosis of UTI (95%–98% vs 59%–96%), but the usefulness of nitrite positivity in isolation is limited because the uropathogens *S saprophyticus*, *Pseudomonas*, or enterococci do not reduce nitrate.[32,33] Leukocyte esterase sensitivity is decreased by high levels of protein or glucose in the urine, and may be falsely positive when there is contamination by bacteria in vaginal fluid, as occurs in vaginitis or cervicitis.[5]

Urine microscopy previously relied on the manual counting of leukocytes for measuring pyuria or Gram stain evaluation for measuring bacteriuria. Automated instruments now perform most microscopic analyses in modern hospital laboratories.[5] For pyuria, typically a count of greater than 10 leukocytes/mm^3 correlates with high bacterial concentrations of ($\geq 10^5$ CFU/mL). The Gram stain is only reliable with high concentrations of bacteria ($\geq 10^5$ CFU/mL). Thus, it is not always positive for patients with uncomplicated UTI, who may be symptomatic with much lower bacterial concentrations (10^2–10^3 CFU/mL). Because of its labor intensity, Gram stain of the urine is often impractical in most laboratory settings, and thus is unavailable in many hospitals.

The difficulty for the EP remains in diagnosing UTI in patients with questionable urinary symptoms based on the presence, for instance, of urinary leukocyte esterase alone. It is prudent to remember that the specificity of this finding in isolation is good, but imperfect. It is important to consider a broad differential, including other potential causes of abdominal or pelvic inflammation or infection. Likewise, consideration of alternate diagnoses in questionable cases is important before administration of antimicrobials. Antibiotic treatment may mask signs and symptoms or otherwise delay definitive diagnosis of alternative conditions.

Urine Culture

Urine culture is not necessary to make the diagnosis in patients with uncomplicated UTI; a positive dipstick or findings on microscopy, combined with suggestive clinical symptoms, is adequate. The urine culture has much more usefulness in patients with complicated UTI, recurrent UTI, or pyelonephritis, because it helps guide treatment in failed antibiotic therapy. It is also advisable to obtain a urine culture in patients with

a high pretest likelihood of UTI but a negative urine dipstick or microscopy result. However, the diagnosis of a UTI should be questioned if pyuria is not present.

There is some debate about the definition of a positive culture. Several factors must be considered in dealing with this question. For example, suprapubic aspirates can be considered positive if there is any degree of bacteriuria. The traditional definition used by most laboratories is 100,000 CFU/mL, which provides a test with high specificity and low sensitivity. However, it has been shown that many women with UTI symptoms have bacterial counts of less than 100,000 CFU/mL with uropathogens.[34] If there are greater than or equal to 10^2 CFU/mL in a clean-catch acquired urine culture with a single bacterial isolate, this should be considered a positive test.[35] If there is more than 1 bacterial isolate in the clean-catch acquired urine culture, then a cutoff of greater than or equal to 10^5 CFU/mL is more appropriate.[5] Therefore, a urine culture with fewer than 10^2 CFU/mL should be considered an indeterminate or negative test. Ultimately, the degree of bacteriuria, sampling method, and patient symptoms must be taken into account when interpreting the results of a urine culture.

Imaging

Imaging is largely unnecessary in the evaluation and treatment decisions in uncomplicated UTI, and imaging is not recommended for routine use in the evaluation of pyelonephritis.[36] The usefulness of ED imaging is primarily for patients with pyelonephritis who are septic or who are not responsive to initial antimicrobial therapy. Those with an initial presentation of septic shock from presumed pyelonephritis should have urgent imaging to evaluate for an infected, obstructed ureteral stone. In general, patients who do not have an appropriate clinical response to therapy within 48 to 72 hours should be evaluated for a perinephric abscess.

Computed tomography (CT) imaging of the abdomen and pelvis with intravenous contrast yields the most information in the evaluation of UTI, identifying renal stones, perinephric abscesses, renal enlargement, obstruction, gas, hemorrhage, and masses.[37] Ultrasound may be considered for detecting masses and obstruction in cases where CT is not feasible, and increasing ED availability as well as research into its usefulness in the acute care setting may increase its everyday use.

TREATMENT

Uncomplicated Cystitis

Treatment of uncomplicated cystitis has been the subject of much study in recent years as rates of microorganism resistance to standard antimicrobials have evolved. In addition, greater importance has been placed on the adverse effects of broad-spectrum antimicrobial therapy. Prudent empiric therapy is often based on analysis of local antibiograms. However, a key limitation in this approach is that antibiograms may falsely overestimate resistance for uropathogens because many patients with simple cystitis and typical symptoms of a UTI do not have a culture performed.

Recently, the Infectious Diseases Society of America (IDSA) released updated clinical practice guidelines.[7] The prior IDSA guidelines, released in 1999, recommended treatment with oral trimethoprim-sulfamethoxazole (TMP-SMX) twice daily by mouth for 3 days as initial therapy for uncomplicated cystitis, except in communities with rates of resistance exceeding 10% to 20%, in which case empiric therapy with a fluoroquinolone was recommended.[38] For unclear reasons, physicians' prescribing practices did not regularly match these recommendations, and fluoroquinolones were more regularly used.[4,39,40]

The 2010 IDSA guidelines suggest stronger consideration for the use of oral nitrofurantoin monohydrate/macrocrystals (Macrobid) 100 mg by mouth twice daily for

5 days as a first-line treatment in patients with suspected UTI (**Table 1**).[7] The primary reasons for this recommendation are increasing resistance among uropathogens to TMP-SMX and clinical failure when the isolate is resistant. TMP-SMX is still considered an appropriate choice for therapy if the local resistance rates of uropathogens do not exceed 20%, or if the infecting strain is known to be susceptible; however, availability of these data to practicing physicians is often limited.

Nitrofurantoin previously has been regarded as an antimicrobial for UTI in pregnancy and, because of its longer treatment course, had been avoided by many EPs for uncomplicated UTI. The standard recommendation was a 7-day course to achieve equivalence to the cure rates of the 3-day TMP-SMX. However, recent studies have shown a 5-day course of oral nitrofurantoin to be clinically equivalent to a 3-day course of oral TMP-SMX, allowing shortened treatment with fewer adverse drug events.[41] With increasing antimicrobial resistance to TMP-SMX, the prominence of nitrofurantoin in the treatment of uncomplicated UTI should increase. The overall clinical cure rate with nitrofurantoin is 88% to 93%.[42,43] Nitrofurantoin is less active against aerobic gram-negative rods, and inactive against *Proteus* and *Pseudomonas* species, and thus should be reserved for uncomplicated UTI.

TMP-SMX is still a reasonable choice in regions in which resistance levels are lower than 20%. It is administered as a 3-day, twice-daily oral course. In areas where resistance is in the 10% to 15% range, the cure rates are equivalent to those with nitrofurantoin and ciprofloxacin.[42–44] Studies of duration of treatment have found that efficacy rates for TMP-SMX peak with a 3-day course, whereas complication rates continue to increase with additional days of therapy. Single-dose oral therapy with TMP-SMX was 87% effective with a complication rate of 11%, whereas a 3-day course was 94% effective with an 18% complication rate, and a 7-day course was 95% effective with a 30% complication rate.[45] The 3-day course maximizes efficacy, and minimizes complications.

Alternatives to nitrofurantoin and TMP-SMX include fluoroquinolones, fosfomycin trometamol, pivmecillinam, and β-lactam agents such as amoxicillin-clavulanate, cefdinir, cefaclor, and cefpodoxime-proxetil.

Table 1
Antimicrobial therapy for uncomplicated cystitis

	Antimicrobial	Comment
First line	Nitrofurantoin 100 mg by mouth twice a day for 5 d	Low rate of resistance. Need a 5-d course
	TMP-SMX 1 tablet DS by mouth twice a day for 3 d	Only if local resistance is less than 20%
Alternative	Ciprofloxacin 250 mg by mouth twice a day for 3 d (or ofloxacin or levofloxacin for 3 d)	Concern for resistance has made quinolones second-line agents
	Fosfomycin trometamol 3 g by mouth single dose	Not available in the United States
	β-Lactam agents (cefpodoxime, cephalexin, amoxicillin/clavulanate)	Multiple trials have shown β-lactam antibiotics inferior to TMP-SMX and quinolones. Third-generation oral cephalosporins may be an exception
Not accepted	Amoxicillin, ampicillin	Resistance rates extremely high worldwide

Abbreviations: DS, double strength; TMP-SMX, trimethoprim-sulfamethoxazole.

The most frequently used and most well-studied alternative to TMP-SMX and nitrofurantoin is the fluoroquinolone ciprofloxacin. The 3-day oral course of ciprofloxacin 250 mg twice a day, with its low cost, widespread success, and equivalent cure rates to TMP-SMX, has been widely regarded by many physicians as the alternative of choice and even a first-line agent. A 500-mg extended-release, once-daily oral ciprofloxacin dosing regimen has been shown to be equivalent, thus increasing the ease of use of this drug.[46,47] Other fluoroquinolones including ofloxacin, norfloxacin, and levofloxacin are considered equally effective to ciprofloxacin. However, the concern of increasing uropathogen resistance to fluoroquinolones, as well as increasing resistance among other organisms that will lead to more difficult-to-treat infections at other sites, has led to strong calls for restricting the use of fluoroquinolones to only those cases in which other antimicrobials are not effective.[7,39] Ciprofloxacin, despite its clear efficacy, convenience, low cost, and equivalence to TMP-SMX and nitrofurantoin, should be considered an alternative agent because of increasing fluoroquinolone antimicrobial resistance among a wide spectrum of organisms.

Additional alternatives for uncomplicated UTI, such as fosfomycin trometamol and pivmecillinam, are not widely available in the United States. Fosfomycin trometamol in a single oral dose of 3 g has been compared with the 5-day course of TMP-SMX and the 7-day course of nitrofurantoin, with equivalent or nearly equivalent clinical cure rates.[43,48] It has also been shown to have efficacy against vancomycin-resistant enterococci (VRE), methicillin-resistant *S aureus* (MRSA), and extended-spectrum β-lactamase (ESBL) –producing gram-negative rods, and thus may increase in usefulness as antimicrobial resistance continues to increase.[49] It is recommended as a first-line agent for uncomplicated UTI by the European Association of Urology, with the obvious advantage of single-dose therapy, although it is not widely available in the United States despite its approval for use by the US Food and Drug Administration (FDA). Pivmecillinam is an extended gram-negative spectrum penicillin used specifically for the treatment of UTI. It has lower bacterial and clinical cure rates than the first-line agents, and is not FDA approved or available in the United States.

β-Lactam antimicrobials are generally considered inferior in cure rates to the fluoroquinolones, nitrofurantoin and TMP/SMX, and also have similar challenges with antimicrobial resistance to the fluoroquinolones.[50] However, one recent study compared the oral third-generation cephalosporin cefpodoxime with TMP/SMX and found equivalent cure rates, but the study had limited power because of a small sample size.[51] Further studies are needed to strengthen support for β-lactam antimicrobials in this setting, particularly given the danger of increasing antimicrobial resistance to broad-spectrum cephalosporins by organisms such as ESBL-producing gram-negative bacteria. Empiric therapy with ampicillin and amoxicillin specifically should be avoided because of frequent bacterial resistance and low cure rates. Ampicillin resistance rates for *E coli* are greater than 30% in most parts of the United States and the world.[8]

Phenazopyridine (Pyridium) acts as a urinary anesthetic and its use for 1 or 2 days may relieve symptoms, but controlled trial data are limited. Side effects are rare; however, it may cause hemolysis in patients with known glucose-6-phosphate dehydrogenase deficiency.[4] In addition, phenazopyridine has been associated with the development of methemoglobinemia with prolonged use.

Complicated UTI

There are limited data to rely on for treatment recommendations for complicated UTI. Common measures include sending a urine culture before treatment, starting with broad-spectrum antibiotic coverage and refining the antimicrobial selection after

sensitivity results have returned, and treating for 7 to 14 days. The standard approach has been to treat all UTIs in men as complicated; 7 days of antimicrobial therapy with a fluoroquinolone or TMP-SMX should achieve clinical cure in most. Men with presumed prostatitis need a longer course.[52,53] Further information on UTI in men can be found in previously published reviews.[54–57]

Acute Pyelonephritis

Fluoroquinolones remain the standard recommended antimicrobial for acute uncomplicated pyelonephritis, despite concerns of the expected increase of fluoroquinolone resistance (**Table 2**).[7,58–60] For patients not requiring hospitalization, multiple options are available. Oral ciprofloxacin 500 mg twice daily for 7 days, extended-release ciprofloxacin 1000 mg daily for 7 days, and levofloxacin 750 mg for 5 days are all supported in regions where the fluoroquinolone resistance rates are lower than 10%.[7] If fluoroquinolone resistance rates are unknown or higher than 10%, an intravenous (IV) dose of a longer acting β-lactam antibiotic, such as 1 g of ceftriaxone or a dose of 5 to 7 mg/kg gentamicin, is recommended.[7] As well as potential difficulty in determining the inciting allergen, there is an increased risk of an allergic reaction when using 2 distinct antibiotic classes simultaneously in the same patient. Therefore, a clear understanding of the resistance patterns in a particular area is invaluable in making the decision to initiate this additional therapy. Urine culture and sensitivity should be attained, and follow-up should be performed within 72 hours to ensure appropriate antimicrobial treatment.

TMP-SMX twice daily for 14 days or an oral β-lactam twice daily for 10 to 14 days continue to be second-tier options. If susceptibility is not known, a single IV dose of 1 g of ceftriaxone or a single dose of IV aminoglycoside is recommended. Resistance rates for uropathogens causing uncomplicated pyelonephritis were found to be 27% (range 13%–45%) for TMP-SMX, and only 1% to 3% for ciprofloxacin and levofloxacin in a sample of 11 academic EDs.[58] Note that nitrofurantoin is not an

Table 2
Antimicrobial therapy for uncomplicated pyelonephritis

	Antimicrobial	Comment
First line	Ciprofloxacin 500 mg by mouth twice a day for 7 d Ciprofloxacin ER 1000 mg by mouth twice a day for 7 d Levofloxacin 750 mg by mouth twice a day for 5 d	Consider giving an IV dose of the same or similar fluoroquinolone before staring oral dosing If there is a high level of quinolone resistance in the community, consider giving a dose of ceftriaxone 1 g IV, followed by oral fluoroquinolone
Alternative	TMP-SMX by mouth twice a day for 14 d Cefpodoxime 400 mg by mouth twice a day for 10–14 d Amoxicillin/clavulanate 875 mg by mouth twice a day for 10–14 d	High rates of resistance. Give an IV dose of ceftriaxone or another long acting agent Oral third-generation cephalosporins are more effective than first generation, but more expensive
Not acceptable	Nitrofurantoin	Does not achieve acceptable levels in tissue or serum. Only used for uncomplicated cystitis

Abbreviation: IV, intravenous.

acceptable antibiotic for pyelonephritis. It does not achieve appreciable serum levels and therefore should not be used for pyelonephritis, because these patients are often bacteremic.[61,62]

Broader-spectrum antimicrobial therapy covering pseudomonal species should be considered in patients who present with septic shock or in patients with a prior history of resistant organisms. Piperacillin/tazobactam, imipenem, meropenem, ampicillin plus tobramycin, and vancomycin plus gentamicin or tobramycin are options for such patients.

Therapy can be outpatient if patients do not have factors associated with complicated infection or signs of systemic toxicity, can tolerate oral medications, and can be closely followed (**Box 2**).[63] Follow-up on urine culture results is important, particularly in areas that have increasing resistance to fluoroquinolones. Hospitalization is necessary for patients who are unable to tolerate oral medications or who have sepsis, and often recommended for patients who are pregnant or have complicated pyelonephritis. For patients who are hospitalized, parenteral antibiotic recommendations have not changed, and include a fluoroquinolone, an aminoglycoside, an extended-spectrum cephalosporin or penicillin with or without an aminoglycoside, or a carbapenem. For patients who have a history of recurrent UTIs, it is important to review previous culture results. Carbapenems remain the drug of choice for patients with an ESBL-producing organism. After sensitivity results are determined, therapy can be tailored appropriately. Blood cultures are not routinely warranted for uncomplicated pyelonephritis; urine culture is nearly always sufficient. However, blood cultures may be useful when the initial diagnosis of pyelonephritis is uncertain or if an alternative cause for pyuria and fever is identified, such as in endocarditis.[64,65]

Pyelonephritis Complications

Patients typically improve rapidly with appropriate therapy. For patients who do not improve within 48 to 72 hours, further evaluation with CT or ultrasound diagnostic imaging should be strongly considered. Pyonephrosis, renal abscess, and emphysematous pyelonephritis are uncommon, but potentially severe, complications of pyelonephritis, and prompt recognition and therapy can significantly affect morbidity and mortality.

Pyonephrosis is the combination of infection and obstruction (pus under pressure) with a collection of purulent material trapped in the renal collecting system by a stone, a mass, or other obstruction. In addition to antimicrobial therapy and supportive treatment of sepsis, emergent urologic or interventional radiology consultation for percutaneous nephrostomy tube or ureteral stent placement is indicated. Most patients

Box 2
Criteria for discharge of patients with acute pyelonephritis

- Stable vital signs
- Normal renal function
- No urinary obstruction
- Adequate pain control
- Adequate hydration
- Ability to tolerate oral medication

improve rapidly after surgical treatment, and the obstruction can be definitively treated 1 to 2 weeks after resolution of the infection.

Renal abscess includes perirenal or intrarenal abscess, acute focal or multifocal bacterial nephritis, and xanthogranulomatous pyelonephritis (XGP). XGP is an inflammatory disorder of the renal parenchyma with a central area of necrosis and hemorrhage. It is typically unilateral, is caused by long-term urinary tract obstruction, and can spread to surrounding structures. For intrarenal abscess larger than 3 cm or perirenal abscess, percutaneous drainage after medical stabilization and antibiotic therapy is widely recommended in the urology literature.[66] However, many patients with smaller abscesses require drainage as well. The importance of source/nidus control in dealing with a septic or otherwise unstable patient from a urinary source cannot be overstated.

Emphysematous pyelonephritis is a necrotizing infection with gas formation in the renal parenchyma, with a mortality ranging from 20% to 40% even when treated.[67,68] Patients with diabetes represent approximately 95% of reported cases. An infected obstructing renal calculus is the major predisposing risk factor. Patients typically are clinically very ill, requiring aggressive cardiopulmonary stabilization and early broad-spectrum antibiotic therapy, followed by urologic consultation for either percutaneous drainage or immediate nephrectomy.

Pregnancy

Pregnancy changes the therapeutic approach to UTI and pyelonephritis in 2 crucial ways. First, antibiotic therapy is adjusted. Asymptomatic bacteriuria (ABU), defined by isolation of greater than or equal to 10^5 CFU/mL of a single microorganism, should be empirically treated in pregnancy, because progression to pyelonephritis from both ABU and UTI is more likely.[6] Three days of oral nitrofurantoin 100 mg twice daily or a 3-day course of oral cephalexin 500 mg 4 times daily are among the recommended regimens. Pregnant patients with UTI are commonly treated with oral nitrofurantoin 100 mg twice daily for 7 days; other options include oral amoxicillin/clavulanate or oral cephalosporins. Fluoroquinolones and tetracyclines are contraindicated because of their teratogenic effects on the fetus. Aminoglycosides should also be avoided. Trimethoprim should be used with caution during the first trimester, and sulfonamides should be avoided in the third trimester because of the concern of precipitating kernicterus.

Second, management of acute pyelonephritis is more conservative, because pyelonephritis can induce preterm labor, and also approximately 20% of pregnant women with pyelonephritis develop evidence of sepsis.[69] Admission should be considered in most pregnant patients with pyelonephritis, although outpatient therapy has become accepted in well-hydrated and stable patients when rapid follow-up can be ensured. Ceftriaxone 1 g IV every 24 hours is a standard antimicrobial choice. Aztreonam is an option in a pregnant patient with a severe penicillin or cephalosporin allergy. More extensive information regarding UTI in pregnancy is available in recent reviews.[70,71]

SUMMARY

UTIs are the most common bacterial infections treated in the outpatient setting. These infections can range in severity from minimally symptomatic cystitis to severe septic shock, and affect a wide array of patients. Diagnosis of uncomplicated cystitis can be inferred from history and physical, and confirmed by urinalysis. Only in some circumstances is obtaining a urine culture necessary: complicated UTI, recurrent infections, and in those who have failed empiric treatment. CT or ultrasound imaging

is limited to patients with severe or nonresponsive pyelonephritis. Appropriate antimicrobial therapy should rapidly improve symptoms in all UTIs. Antimicrobial selection should be guided by local antibiograms, with caution exercised to minimize growing community antibiotic resistance. EPs should consider a 5-day course of nitrofurantoin in uncomplicated cystitis, and a 7-day fluoroquinolone course in uncomplicated pyelonephritis as first-line regimens. Treatment can then be further tailored according to severity of illness, analysis of individualized risk factors, and antimicrobial resistance patterns.

REFERENCES

1. Foxman B. Epidemiology of urinary tract infections: incidence, morbidity, and economic costs. Am J Med 2002;113(Suppl):5S–13S.
2. Foxman B. Epidemiology of urinary tract infections: incidence, morbidity, and economic costs. Dis Mon 2003;49:53–70.
3. Nawar EW, Niska RW, Xu J. National Hospital Ambulatory Medical Care Survey: 2005 emergency department summary. Adv Data 2007;386:1–32.
4. Fihn SD. Acute uncomplicated urinary tract infection in women. N Engl J Med 2003;349:259–66.
5. Wilson ML, Gaido L. Laboratory diagnosis of urinary tract infections in adult patients. Clin Infect Dis 2004;38:1150–8.
6. Sheffield JS, Cunningham FG. Urinary tract infection in women. Obstet Gynecol 2005;106:1085–92.
7. Gupta K, Hooton TM, Naber KG, et al. International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: a 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. Clin Infect Dis 2011;52(5): e103–20.
8. David RD, DeBlieux PMC, Press R. Rational antibiotic treatment of outpatient genitourinary infections in a changing environment. Am J Med 2005;118(7A): 7S–13S.
9. Scholes D, Hooton TM, Roberts PL, et al. Risk factors for recurrent urinary tract infection in young women. J Infect Dis 2000;182:1177–82.
10. Nicolle LE, Harding GK, Preiksaitis J, et al. The association of urinary tract infection with sexual intercourse. J Infect Dis 1982;46:574–83.
11. Strom BL, Colins M, West SL, et al. Sexual activity, contraceptive use, and other risk factors for symptomatic and asymptomatic bacteriuria: a case-control study. Ann Intern Med 1987;107:816–23.
12. Krieger JN. Urinary tract infections: what's new? J Urol 2002;168(6):2351–8.
13. Raz R, Chazan B, Dan M. Cranberry juice and urinary tract infection. Clin Infect Dis 2004;38:1413–9.
14. Avorn J, Monane M, Gurwitz JH, et al. Reduction of bacteriuria and pyuria after ingestion of cranberry juice. JAMA 1994;274:751–4.
15. Raz R, Gennesin Y, Wasser J, et al. Recurrent urinary tract infection in postmenopausal women. Clin Infect Dis 2000;30:152–6.
16. Sourander LB. Urinary tract infection in the aged – an epidemiological study. Ann Med Intern Fen Suppl 1966;45:7–55.
17. Brocklehurst JC, Dillane JB, Griffith L, et al. The prevalence and symptomatology of urinary infection in an aged population. Gerontol Clin 1968;10:242–53.
18. Powers JS, Billings FT, Behrendt D, et al. Antecedent factors in urinary tract infections among nursing home patients. Southampt Med J 1988;81:734–5.

19. Boyko EJ, Fihn SD, Scholes D, et al. Diabetes and the risk of acute urinary tract infection among postmenopausal women. Diabetes Care 2002;5:1778–83.
20. Wong ES, Stamm WE. Sexual acquisition of urinary tract infection in a man. JAMA 1983;250(22):3087–8.
21. Ronald A. The etiology of urinary tract infection: traditional and emerging pathogens. Am J Med 2002;113(Suppl 1A):14S–9S.
22. Wong ES, McKevitt M, Running K, et al. Management of recurrent urinary tract infections with patient-administered single dose therapy. Ann Intern Med 1985; 102:302–7.
23. Gupta K, Hooton TM, Roberts PL, et al. Patient-initiated treatment of uncomplicated recurrent urinary tract infections in young women. Ann Intern Med 2001; 135:9–16.
24. Bent S, Nallamothu BK, Simel D, et al. Does this woman have an acute uncomplicated urinary tract infection? JAMA 2002;287:2701–10.
25. Nicolle LE. Uncomplicated urinary tract infection in adults including uncomplicated pyelonephritis. Urol Clin North Am 2008;35:1–12.
26. Ramakrishnan K, Scheid DC. Diagnosis and management of acute pyelonephritis in adults. Am Fam Physician 2005;71(5):933–42.
27. Lifshitz E, Kramer L. Outpatient urine culture: does collection technique matter? Arch Int Med 2000;160:2537–40.
28. Leisure MK, Dudley SM, Donowitz LG. Does a clean-catch urine sample reduce bacterial contamination? N Engl J Med 1993;328:289–90.
29. Immergut MA, Gilbert EC, Frensilli FJ, et al. The myth of the clean catch urine specimen. Urology 1981;17(4):339–40.
30. Mayo S, Acevedo D, Quinonenes-Torrelo C, et al. Clinical laboratory automated urinalysis: comparison among automated microscopy, flow cytometry, two test strips analyzers, and manual microscopic examination of the urine sediments. J Clin Lab Anal 2008;22(4):262–70.
31. Hurlbut TA, Littenberg B. The diagnostic accuracy of rapid dipstick tests to predict urinary tract infection. Am J Clin Pathol 1991;96:582–8.
32. Rehmani R. Accuracy of urine dipstick to predict urinary tract infections in an emergency department. J Ayub Med Coll Abbottabad 2004;16(1):4–7.
33. Pappas PG. Laboratory in the diagnosis and management of urinary tract infections. Med Clin North Am 1991;75:313–25.
34. Stamm W, Counts GW, Running KR, et al. Diagnosis of coliform infection in acutely dysuric women. N Engl J Med 1982;307:463–8.
35. Platt R. Quantitative definition of bacteriuria. Am J Med 1983;75(1B):44–52.
36. Sandler CM, Choyke PL, Bluth E, et al. Expert panel on urologic imaging. Acute pyelonephritis. Reston (VA): American College of Radiology (ACR); 2005. p. 1–5.
37. Papanicolaou N, Pfister RC. Acute renal infections. Radiol Clin North Am 1996;34: 965–95.
38. Warren JW, Abrutyn E, Hebel JR, et al. Guidelines for antimicrobial treatment of uncomplicated acute bacterial cystitis and acute pyelonephritis in women. Clin Infect Dis 1999;29:74.
39. Hooton TM, Besser R, Foxman B, et al. Acute uncomplicated cystitis in an era of increasing antibiotic resistance: a proposed approach to empirical therapy. Clin Infect Dis 2004;39:75–80.
40. Taur Y, Smith M. Adherence to the Infectious Diseases Society of America guidelines in the treatment of uncomplicated urinary tract infection. Clin Infect Dis 2007;44:769–74.

41. Gupta K, Hooton TM, Roberts PL, et al. Short-course nitrofurantoin for the treatment of acute uncomplicated cystitis in women. Arch Intern Med 2007;167(20): 2207–12.
42. Iravani A, Klimberg I, Briefer C, et al. A trial comparing low-dose, short-course ciprofloxacin and standard 7 day therapy with co-trimoxazole or nitrofurantoin in the treatment of uncomplicated urinary tract infection. J Antimicrob Chemother 1999; 43(Suppl A):67–75.
43. Stein GE. Comparison of single-dose fosfomycin and a 7 day course of nitrofurantoin in female patients with uncomplicated urinary tract infection. Clin Ther 1999;21(11):1864–72.
44. Arredondo-Garcia JL, Figueroa-Damian R, Rosas A, et al. Comparison of short-term treatment regimen of ciprofloxacin versus long-term treatment regimens of trimethoprim/sulfamethoxazole or norfloxacin for uncomplicated lower urinary tract infections: a randomized, multicentre, open-label, prospective study. J Antimicrob Chemother 2004;54(4):840–3.
45. Warren JW, et al. Guidelines for antimicrobial treatment of uncomplicated acute bacterial cystitis and acute pyelonephritis in women. Infectious Diseases Society of America. Clin Infect Dis 1999;29:745–58.
46. Fourcroy JL, et al. Efficacy and safety of a novel once-daily extended-release ciprofloxacin tablet formulation for treatment of uncomplicated urinary tract infection in women. Antimicrob Agents Chemother 2005;49(10):4137–43.
47. Henry DC, et al. Comparison of once-daily extended-release ciprofloxacin and conventional twice-daily ciprofloxacin for the treatment of uncomplicated urinary tract infection in women. Clin Ther 2002;24(12):2088–104.
48. Minassian MA, et al. A comparison between single-dose fosfomycin trometamol and a 5-day course of trimethoprim in the treatment of uncomplicated lower urinary tract infection in women. Int J Antimicrob Agents 1998;10(1):39–47.
49. Popovic M, et al. Fosfomycin: an old, new friend? Eur J Clin Microbiol Infect Dis 2010;29(2):127–42.
50. Hooton TM, Scholes D, Gupta K, et al. Amoxicillin-clavulanate vs ciprofloxacin for the treatment of uncomplicated cystitis in women: a randomized trial. JAMA 2005; 293(8):949–55.
51. Kavatha D, Giamerellou H, Alexiou Z, et al. Cefpodoxime-proxetil versus trimethoprim-sulfamethoxazole for short-term therapy of uncomplicated acute cystitis in women. Antimicrob Agents Chemother 2003;47(3):897–900.
52. Lipsky BA. Prostatitis and urinary tract infection in men: what's new; what's true? Am J Med 1999;106:327–34.
53. Hooton TM. The current management strategies for community-acquired urinary tract infection. Infect Dis Clin North Am 2003;17:303–32.
54. Krieger JN, Ross S, Simonsen J. Urinary tract infections in healthy university men. J Urol 1993;149(5):1045–8.
55. Lipsky B. Urinary tract infection in men. Epidemiology, pathophysiology, diagnosis and treatment. Ann Intern Med 1989;110(2):138–50.
56. Sharp VJ, Takacs EB. Prostatitis: diagnosis and treatment. Am Fam Physician 2010;82(4):397–406.
57. Lipsky BA, Byren I, Hoey CT. Treatment of bacterial prostatitis. Clin Infect Dis 2010;50(12):1641–52.
58. Talan DA, Krishnadasan A, Abrahamian FM, et al. Prevalence and risk factor analysis of trimethoprim-sulfamethoxazole and fluoroquinolone-resistant *Escherichia coli* infection among emergency department patients with pyelonephritis. Clin Infect Dis 2008;47:1150–8.

59. Lautenbach E. Finding the path of least antimicrobial resistance in pyelonephritis. Clin Infect Dis 2008;47:1159–61.
60. Czaja CA, Scholes D, Hooton TM, et al. Population-based epidemiologic analysis of acute pyelonephritis. Clin Infect Dis 2007;45(3):273–80.
61. Halliday A, Jawetz E. Sodium nitrofurantoin administered intravenously. A limited study to define its clinical indication. N Engl J Med 1962;266:427–32.
62. Jawetz E, Hopper J, Smith D. Nitrofurantoin in chronic urinary tract infection. AMA Arch Intern Med 1957;100(4):549–57.
63. Stamm WE, McKevitt M, Counts GW. Acute renal infection in women: treatment with trimethoprim-sulfamethoxazole or ampicillin for two or six weeks: a randomized trial. Ann Intern Med 1987;106:341–5.
64. Schrock J, Reznikova S, Weller S. The effect of an observation unit on the rate of ED admission and discharge for pyelonephritis. Am J Emerg Med 2010;28: 682–8.
65. Velasco M, Martinez JA, Moreno-Martinez A, et al. Blood cultures for women with uncomplicated acute pyelonephritis: are they necessary? Clin Infect Dis 2003;37: 1127–30.
66. Dembry LM. Renal and perirenal abscesses. Curr Treat Options Infect Dis 2002; 4:21–30.
67. Huang JJ, Tseng CC. Emphysematous pyelonephritis: clinicoradiological classification, management, prognosis, and pathogenesis. Arch Intern Med 2000; 160(6):797–805.
68. Wan YL, Lo SK, Bullard MJ, et al. Predictors of outcome in emphysematous pyelonephritis. J Urol 1998;159(2):369–73.
69. Hill JB, Sheffield JS, McIntire DD, et al. Acute pyelonephritis in pregnancy. Obstet Gyn 2005;105:18–23.
70. Macejko AM, Schaeffer AJ. Asymptomatic bacteriuria and symptomatic urinary tract infections during pregnancy. Urol Clin North Am 2007;34(1):35–42.
71. Gilstrap LC 3rd, Ramin SM. Urinary tract infections during pregnancy. Obstet Gynecol Clin North Am 2001;28(3):581–90.