

## Evaluation, Identification, and Treatment of Urinary Tract Infections

**Urgent message:** Urinary tract infections are a common cause of abdominal pain and a common presenting complaint in urgent care. Proper diagnosis, treatment, and patient education on preventive measures are key to optimal outcomes.

William Gluckman, DO, MBA, FACEP, Karen Keaney Gluckman, MSN, APN, C, CWCN, CCCN

### Introduction

The global term *urinary tract infection* (UTI) incorporates cystitis and infection involving the bladder (a lower tract source), as well as pyelonephritis, an infection involving the kidneys (an upper tract source).

Acute cystitis occurs when bacteria attach to and/or invade the bladder wall.

Pyelonephritis is a more serious disorder that can lead to bacteremia, sepsis, or renal abscess formation.

Interstitial cystitis (also known as painful bladder syndrome) is a disorder that causes chronic abdominal pain and urinary symptoms, particularly frequency and dysuria, but by definition does not involve an infection.

Acute cystitis is very common, affecting 8 million to 10 million people per year and prompting 9.6 million doctor visits at a cost of over \$4.5 billion. Forty



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percent to 50% of women will have at least one UTI in their lifetimes, and approximately 20% of those who get a UTI will have a recurrent episode.

Urinary tract infections can affect male and female infants, children, and adults. Each of these groups has differences in causes, treatments, and work-ups. This article will focus on adult female infections.

### Pathophysiology

Urine is a good culture medium for bacteria, as it is typically sterile but can become infected either by retrograde transmission of

pathogens up the urethra or hematogenously.

Women are at great risk for UTI primarily because of the significantly shorter urethra and closer proximity to the rectum. The female genitalia may become colonized with pathogenic bacteria that can more

**FIGURE 1.**  
**Fimbriae seen on *E coli*.**



Source: Hybrid Medical Animation / Photo Researchers, Inc.

easily enter the urethra. In addition, woman lack the bacteriostatic protection that prostatic secretions offer the male.

Typically, the urinary tract is kept sterile via urination, which causes a washing out of any bacteria that may have entered the urethra.

Periurethral colonization is limited by the acidic pH of the vagina, which is maintained by non-pathogenic bacteria such as *Lactobacillus* species. When the pH is altered, bacteria are more likely to grow, colonize the area, and thus increase the likelihood of urethral entry.

Risk Factors for getting a UTI include:

- sexual intercourse
- diaphragm use
- spermicidal use
- pregnancy
- urethral catheterization
- previous UTI
- maternal history
- female sex
- postmenopausal

### Common Pathogens

*Escherichia coli* is the number-one uropathogen, accounting for approximately 85% to 90% of UTIs. This gram-negative rod has the ability to adhere to the

bladder wall by its finger-like projections known as fimbriae, or P Pili (**Figure 1**). When instituting empiric therapy, this organism must be given consideration.

*Enterococcus* is a troublesome gram-negative pathogen found primarily in the gut but it may infect the urine. Many resistant strains exist and treatment may be challenging. Infection with this organism typically occurs from poor hygiene or recent instrumentation.

*Pseudomonas aeruginosa* is another gram-negative pathogen more commonly found in nursing homes and frequently hospitalized patients. *P aeruginosa* is an opportunistic pathogen and can be difficult to treat secondary to its lipopolysaccharide outer membrane, fimbriae, and its antibiotic-resistant plasmids.

*Proteus mirabilis* is a gram-negative rod that, like *E coli*, possesses fimbriae to help attach to urinary tract epithelium. It also has the ability to produce urease which converts urea into ammonia. This leads to alkalization of the urine and facilitates struvite stone formation.

*Klebsiella pneumoniae* is an encapsulated gram-negative rod that aside from causing pneumonia (predominantly in alcoholics), causes UTI. It is capable of producing extended-spectrum  $\beta$  lactamase (ESLBs), making this organism potentially resistant to penicillins and cephalosporins.

*Staphylococcus saprophyticus* is a coagulase-negative, gram-positive coccus that is the most common gram-positive agent causing UTIs and is most often found in young women.

### Diagnosis

Clinical symptoms of UTIs classically include urinary frequency, urgency, and dysuria; being cognizant of additional symptoms may help differentiate among various types of infection.

Suprapubic pain often accompanies cystitis.

Right or left upper quadrant abdominal pain or back pain may accompany pyelonephritis. Fever is also common in pyelonephritis but is generally not present in cystitis.

Costovertebral angle tenderness, or pain elicited by gentle percussion over the back in proximity to the kidneys, is often present in pyelonephritis and excludes a diagnosis of simple cystitis.

Physical exam findings may reveal abdominal tenderness. Significant guarding or rebound tenderness should lead the urgent care clinician to consider potentially more serious disorders, such as pelvic inflammatory disease, appendicitis, ectopic pregnancy, or a ruptured bowel and should warrant transfer to an emergency department for a more detailed work-up.

Urine dipsticks are the mainstay laboratory diagnostic for urgent care practitioners.

It is important to assure that a clean catch specimen is obtained. This is done by instructing the patient to spread her labia with

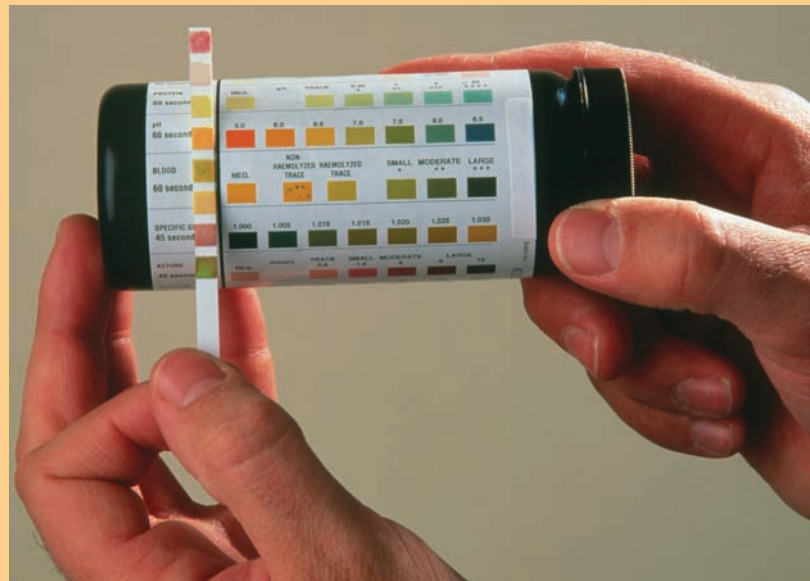
one hand and wipe with an antiseptic wipe from front to back. Then she should begin to urinate into the bowl and have the cup placed midstream. An adequate specimen may be obtained from menstruating women by having them place a fresh tampon just before the cleaning procedure described above.

Colorimetric test strips (**Figure 2**) have a very good sensitivity and specificity for blood, leukocyte esterase, and nitrite. UTI symptoms in the presence of leukocytes are adequate to make a diagnosis of UTI. Occasionally, low-volume pyuria (i.e., 1 WBC/HPF to 10 WBCs/HPF) may result in a false negative leukocyte esterase on dipstick.

In the face of strong clinical presentation, urine microscopy may be helpful; if not available, empiric therapy can be started. In approximately 10% of cystitis cases, gross or microscopic hematuria is present. This condition is known as hemorrhagic cystitis and is triggered by certain pathogens capable of greater penetration into the bladder wall and releasing hemolysins, causing bleeding.

Some species such as *Proteus* and occasionally *E coli* will convert nitrates normally found in the urine to nitrites. A finding of positive nitrites on urine dipstick is highly specific for a UTI but its absence does not exclude the diagnosis.

**FIGURE 2.**  
Multiple test colorimetric urine



Source: Saturn Stills / Photo Researchers, Inc.

A good practice is to always perform a urine pregnancy test in all women of childbearing years. All pregnant women with even asymptomatic bacteruria should be treated, and it is important to know pregnancy status when making an antibiotic selection.

Historically, urine cultures demonstrating  $10^5$  colony-forming units (CFUs) have been used to define infection; however, utilizing  $10^2$  CFUs in symptomatic women still yields an accurate diagnosis. Routine urine cultures in simple acute cystitis are probably unnecessary. Patients who have recurrent UTIs, failed recent antibiotic therapy, have been recently hospitalized, undergone urinary or vaginal instrumentation, or have had a Foley catheter in the previous two weeks may have a resistant or less common organism and a culture may be helpful in guiding therapy.

### Differential Diagnosis

Though frequency, urgency, and dysuria in the face of pyuria most often signal a UTI, these complaints and findings are also found in urethritis, bacterial and candidal vaginitis, genital herpes infection, and pelvic inflammatory disease. Since the causative agents of these entities may be different than those causing UTIs, it is important to distinguish the pathologies in order to select appropriate antibiotic therapy.



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It is also important to obtain a sexual history from the patient and to ask about related complaints such as vaginal discharge. The answers may prompt you to perform a pelvic exam to look for vaginal discharge, herpetic lesions, or uncover cervical motion or adnexal tenderness.

Additional considerations:

- Kidney stones may also present with dysuria and abdominal pain.
- It is more common to see hematuria (gross or microscopic) than pyuria.
- The presentation of classic renal colic is a severe flank pain that radiates to the lower quadrants or groin, is not changed by position, and is intermittent and often severe.
- Painless hematuria may be secondary to previous radiation therapy or be secondary to hemorrhagic cystitis.
- Always consider bladder cancer as a cause of hematuria and consider sending the urine for cytology or referring the patient promptly to a urologist.
- Appendicitis has been reported to irritate the ureter, causing some hematuria and pyuria. Patients presenting with RLQ pain, anorexia, fever and/or vomiting without CVA tenderness should be ruled out for appendicitis.

#### Treatment

Antibiotic therapy is the mainstay therapy for UTIs. Simple cystitis can be treated with oral antibiotics. Pyelonephritis may be selectively treated with oral antibiotics, but 10% to 15% of patients will require hospital admission for IV therapy. Outpatient therapy may be considered for patients with:

- no significant comorbidities such as diabetes or HIV
- little or no vomiting and able to tolerate PO fluids and meds
- pain controllable with oral medications
- good hydration status
- infection not complicated/associated with a kidney stone or GU system abnormality.

#### Pregnancy considerations

Pregnant women in the first trimester may be treated the same as non-pregnant woman. Those in the third trimester with pyelonephritis should be admitted. Typically, women in the second trimester require individualized care; either outpatient or hospitaliza-

tion can be appropriate, depending upon reliability of the patient and access to prompt follow-up.

Women who have frequent UTIs, especially in pregnancy, may benefit from being on a low-dose antibiotic for several months. Those women that seem to have recurrent infections after sexual intercourse often benefit from a single post-coital dose of an antibiotic.

Following is rationale for choosing among antibiotics commonly employed in the treatment of UTIs:

- **Fluoroquinolones** such as ciprofloxacin (Cipro) and levofloxacin (Levaquin) inhibit DNA synthesis by inhibiting DNA gyrase and are thus bactericidal. They have excellent coverage of most uropathogens and have the benefit of once- or twice-daily dosing. Another benefit: to date, this class seems to have fewer issues with resistance than others, though of course this may change over time.

On the other hand, fluoroquinolones are among the more expensive medications used to treat UTI, though ciprofloxacin has come down in price over the years. Consideration should be given to those patients without a prescription plan. Fluoroquinolones should not be used in pregnant women or in children.

- **Trimethoprim/sulfamethoxazole** (TMP/SMZ; Bactrim, Septra) blocks bacterial dihydrofolate reductase necessary to convert PABA into folic acid. It has been a commonly prescribed agent for patients not allergic to sulfa drugs.

TMP/SMZ has an advantage over other agents as it is inexpensive, but some areas of the country are noting *E coli* with increasing resistance—sometimes exceeding 20%. While we are not aware of a resource for such information, developing a relationship with a nearby hospital microbiology lab may allow you to obtain the annual antibiograms most labs generate; this gives the sensitivities of pathogens encountered in the institution.

- **Tetracyclines** such as doxycycline (Vibramycin) are bacteriostatic agents that inhibit protein synthesis by binding to the 30S ribosomal subunit. Doxycycline has very good activity against *E coli* and has the advantage of covering chlamydia and mycoplasma. These agents are commonly impli-

## Women prone to infection after intercourse may benefit from a post-coital dose of antibiotic.

cated in urethritis which can occasionally be mistaken for cystitis. They should not be used in pregnancy.

- **Nitrofurantoin** (Macrobid) is bactericidal in urine and works by inhibiting bacterial acetyl-coenzyme A, thus interfering with carbohydrate metabolism, and by inhibiting DNA and RNA synthesis, thus disrupting cell wall formation.

These multiple mechanisms may explain why this drug has developed very little resistance over the years. Nitrofurantoin has excellent clinical activity against *E coli* and *S Saprophyticus*. It also has some activity against *Enterococcus* and *Klebsiella* but not *Proteus* or *Pseudomonas*. This drug is especially useful in pregnancy, as it is rated Category B, but it is not approved for use in the treatment of pyelonephritis.

- **Cephalosporins**, such as the first-generation drug cephalexin (Keflex), inhibit bacterial cell wall synthesis. Because of its pregnancy category B rating, this class has great utility in pregnant women, however resistance rates to *E coli* are higher than with many of the other medications.

- **Penicillins** inhibit bacterial cell wall synthesis like the cephalosporins. Amoxicillin (Amoxil) had been a first-line therapy, but significant resistance to *E coli* has been noted and it is best reserved for treatment of *Enterococcus* and in pregnancy, where the organism is resistant to nitrofurantoin.

- **Fosfomycin** (Monurol) is in a unique class of antibiotics and works by inhibiting cell wall synthesis and by blocking bacterial adherence to epithelial cells. Fosfomycin offers the advantage of a single-dose regimen, which is a great benefit if compliance is thought to be a problem; however, reported cure rates are only about 80%.

Cranberry juice is considered an adjunctive therapy in the treatment and prevention of UTIs. Cranberry and blueberry juice, as well as some red wines, contain tannins which have been shown to decrease the binding ability of *E coli* to binding sites. The drug phenazopyridine (Pyridium) is an azo dye that acts as a bladder analgesic and decreases the urinary discomfort associated with cystitis. It should be used only for two days, as typically symptoms are improving by this point and be-

cause this drug may induce methemoglobinemia.

Patients with G6PD deficiency are at greater risk for hemolytic anemia.

In addition, patients should be warned that this drug will turn their urine, sweat, and tears orange in color.

Finally, contact lens users should be advised to switch to wearing glasses while on this medication.

Duration of treatment depends on the complexity of the infection and the drug selected. For simple, uncomplicated UTIs (i.e., no renal stone present, no urinary tract abnormalities, not recurrent and in a non-immunocompromised patient), a three-day course of trimethoprim/sulfamethoxazole or a fluoroquinolone has been shown to be as effective with less side effects as a seven- or 10-day course. Though single-dose regimens are effective for postcoital prophylaxis, recurrence rates are fairly high.

Doxycycline and nitrofurantoin require a seven- to 10-day course. Pyelonephritis should be treated for 10 to 14 days. TMP/SMZ should be used only if resistance patterns are favorable in your area (<20% to 25% resistance).

#### Follow-up

Typical, uncomplicated UTIs do not require follow-up

if symptoms are resolved. All patients should be told at discharge to return to the urgent care clinic or to their primary care physician if symptoms persist or do not improve. As noted previously, some cases will necessitate referral to a urologist or ED.

#### Prevention

Time devoted to educating patients on the causes of UTIs, as well as preventive measures, is well spent and likely to be appreciated.

Some women are predisposed to UTIs. Whether due to genetic or anatomical factors, however, women can reduce their risk by:

- voiding soon after sex (to "wash out" bacteria)
- voiding soon after a bath and avoiding prolonged soaking in a bath
- assuring adequate lubrication during sex, using a water-soluble lubricant such as K-Y jelly if needed, thus preventing abrasion to the protective barrier of the urethra
- making sure that wiping after urination and a bowel movement is from front to back; this keeps colonic bacteria from the anus away from the urethra
- voiding as soon as the urge is felt and not hold-



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ing urine, thus preventing pathogen replication, should urine become contaminated

- drinking plenty of water daily
- wearing cotton underwear and loose-fitting clothes, particularly in hot weather (to minimize a warm, moist environment and to prevent peri-urethral colonization)
- removing wet bathing suits promptly
- avoidance of feminine deodorant sprays/perfumes and douches (to prevent irritation of the urethra)
- drinking cranberry juice daily (to help prevent adherence of some bacteria).

### Summary

Urinary tract infections are common in the urgent care setting. It is important to remember the common causative organisms and appropriate antibiotic selections. Pyelonephritis is a more serious disorder that can be managed in an outpatient setting for select patients with good follow-up. Sometimes, urinary symptoms or positive urine dipsticks may indicate an infection that is not in the urinary system, such as a sexually transmitted infection, and can be much more serious and require different treatment. A good history

with review of systems and a physical exam should help make the distinction. ■

### Resources and Suggested Reading

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