

Urinary Tract Infection Update

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Abstract

Urinary tract infections are commonly treated in urgent care practice. Clinicians need to be aware of the advantages and limitations of diagnostic tests, as well as the proper empiric antibiotic treatment of these infections, in order to effect the best outcomes for patients. Several recent articles and a published guideline provide the most up-to-date information and form the basis of this review.

Introduction

Urinary tract infection (UTI) is a common problem diagnosed and treated in urgent care medicine practice. A 2010 report indicated that 3.1% of urgent care visits were for UTIs.¹ An estimated eight million episodes of UTI occur in the US each year² with one out of three women requiring treatment for UTI before age 24.³ Urinalysis and urine gram stain and culture may assist with diagnosis, but add to the cost of care and are not always necessary. UTIs can affect the lower urinary tract (cystitis) or upper tract (pyelonephritis). Similar to other acute infections, initial antibiotic treatment for cystitis is empiric. A variety of antibiotics is available for treating UTIs, but changing antibiotic sensitivities make appropriate empiric treatment a moving target over time. A recently published guideline⁴ by the Infectious Diseases Society of America and European Society for Microbiology and Infectious Diseases provides evidence-based recommendations for treating pre-menopausal, non-pregnant females with uncomplicated UTI. UTIs which occur in men, pregnant women, and patients with immunosuppression or urinary tract abnormalities, such as congenital malformations, uri-

nary calculi, recent urologic instrumentation, indwelling catheters, neurogenic bladder, and kidney transplant, are considered complicated and require more complex decision-making than will be reviewed in this update. Because the majority of UTIs are uncomplicated, however, this review should have broad application.

Symptomatology/Differential Diagnosis

Diagnosis of UTI in young healthy patients can usually be made clinically. Patients with cystitis typically present with any or all of the following: cloudy urine; abnormal urine odor; dysuria; urinary frequency, hesitancy, or urgency; suprapubic discomfort; gross hematuria.^{5,6} More severe symptoms are more predictive of UTI than milder ones,⁵ as is the presence of combinations of symptoms rather than just a single symptom.⁶ Complaints of vaginal discharge or vaginal irritation and the absence of dysuria or back pain reduce the likelihood of UTI.⁶ Pyelonephritis typically causes fever, chills, malaise, flank discomfort, nausea/vomiting, and/or abdominal pain, with or without concomitant lower urinary tract signs.

With cystitis, there may be no physical exam abnormalities or only mild suprapubic tenderness to palpation, while pyelonephritis typically causes a patient to look systemically ill in general, with costovertebral angle tenderness to percussion on physical exam in most cases. These patients may also have mild tenderness of the anterior upper quadrants of the abdomen overlying the kidneys. Though UTI is more common in women than men, symptoms and physical exam findings are usually similar in both sexes.

Older patients can present more of a diagnostic challenge and may have nonspecific symptoms such as malaise, fatigue, anorexia, or even fever or chills, without any of the more focal symptoms above to guide the clinician to the urinary tract as the source of the problem. UTI should be part of a fairly broad differential diagnosis for such patients.

Conversely, those with symptoms of UTI may uncommonly have other disorders. Patients with sexually transmitted infections, as well as urethritis, cervicitis, and vulvovaginitis from other causes, can present with symptoms similar to cystitis. Some patients with ureterolithiasis may have only mild flank pain or lower urinary tract symptoms. Pelvic inflammatory disease, appendicitis, and sigmoid diverticulitis are among the entities which have been misdiagnosed as acute cystitis. Interstitial cystitis is uncommon but often initially indistinguishable from acute infectious cystitis.

Generating a reasonable differential diagnosis for each patient and performing a careful history and physical examination with focused testing is the time-honored approach. Diagnoses such as those above – in addition to infection with a resistant organism or UTI combined with some element of urinary tract obstruction – should be considered in patients who do not improve promptly with usual empiric therapy. Of course, nonspecific symptoms like malaise, fatigue, anorexia, fever or chills can have many causes. Even with an abnormal urinalysis in hand, the careful clinician should avoid premature diagnostic closure, because urinary tract colonization is not uncommon in older patients and may be unrelated to a patient's presenting illness.

Diagnostic Testing

Urinalysis (UA) is a relatively simple, office-based test that can be used to evaluate patients with urinary complaints. In urgent care settings where UA is available, dipstick results rather than microscopic analysis may be more likely to be utilized. The different components of dipstick testing vary in their accuracy for predicting infection, with nitrite having the highest specificity (adjusted odds ratio of 6.36 in one study⁵) but poor sensitivity (i.e., it will be negative in many patients who have a UTI). The combination of dipstick-positive leukocyte esterase and blood may have the highest sensitivity (77%) and specificity (70%).⁵ Urinalysis results may also suggest diagnoses other than UTI or the need for additional history or examination, as when clue cells or trichomonads are found in a specimen.

Urine culture is traditionally the gold standard for diagnosing UTI, and, though a culture showing no growth essentially rules out UTI caused by the most common organisms, sensitivity and specificity will vary depending on the threshold colony count used and whether a specimen is obtained by catheterization or other methods. As well, the time required for culture results often exceeds the time to clinical cure with empiric treatment, and cultures can add significantly to the cost while not improving the quality of care in the majority of cases.

As with any clinical situation, diagnostic tests should be used when their results may improve management compared with not using them. The finding that, in patients with at least one UTI symptom, even a completely normal further history, physical exam, and dipstick UA cannot rule out UTI⁶ is often used as a rationale to not perform UA in patients with typical symptoms. Still, UA may have some use when there is diagnostic uncertainty, and, though it requires microscopy, findings of pyuria without bacteriuria increase the chance that a sexually transmitted infection rather than a UTI is present. An interesting study⁷ showed no significant difference in clinical outcomes whether patients were treated with antibiotics, in an immediate or delayed fashion, based on symptoms alone or based on UA results, though antibiotics were used less often if testing or delayed prescribing was employed. A cost effectiveness analysis⁸ showed that basing antibiotic treatment on dipstick testing was cost-effective, compared with treating immediately without testing, if avoiding a day of moderately severe symptoms was valued at \$15 (10 British pounds) or more. Though the monetary cost may not be directly paid by them, this is probably the case for most patients!

Urine culture ideally obtained before and without delaying antibiotics is recommended in patients with acute pyelonephritis⁴ and in the management of pediatric UTIs. Culture is also recommended in patients with complicated UTIs (men, pregnant women, and patients with immunosuppression or urinary tract malformations, urinary tract stones, recent urologic instrumentation, indwelling catheters, neurogenic bladder, and kidney transplant) and may also be helpful, while starting empiric therapy, in patients with a previous history of known resistant infections, failure of empiric antibiotics, or multiple recurrent UTIs. The yield of culture is lower in patients who are taking antibiotics at the time of testing.

Basic blood work (CBC, chemistry panel, blood culture) rarely helps decision-making for patients with uncomplicated UTI, and no useful role has been shown for erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP). Patients with suspected concomitant urinary tract obstruction or who show signs of severe systemic infection usually require prompt imaging with ultrasound or CT, and typically blood work is obtained for these patients and anyone else requiring hospitalization. CT without contrast is preferred for diagnosing urinary calculi and obstruction. Intravenous (IV) contrast may be used for a "CT urogram" and both IV and oral contrast is typically used in inflammatory disorders such as appendicitis or diverticulitis need to be excluded, though more recent evidence shows that unenhanced CT may be adequate.

Treatment Considerations

The main element of treatment for UTI in the United States is antibiotics; phenazopyridine may be prescribed as an adjunct to alleviate symptoms. An evidence-based guideline for the antimicrobial treatment of UTI in adults was published in March

2011 by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases⁴ and included interesting considerations, balancing the positives of likely efficacy with negatives, termed “collateral damage,” relating to the “ecological adverse effects of antimicrobial therapy.” The following recommendations come from that guideline.

Table 1: Antibiotic Treatment for Uncomplicated Acute Cystitis⁴

Nitrofurantoin 100 mg BID for 5 days
OR
Trimethoprim-sulfamethoxazole DS (160/800 mg) BID for 3 days (if prevalence of resistance is < 20%)
OR
Fosfomycin trometamol 3 gm single dose
OR
Pivmecillinam 400 mg BID for 5 days (not available in the United States)
If availability or allergy history precludes these choices, then use:
Fluoroquinolones for 3 days
OR
Beta-lactams (amoxicillin-clavulanate, cefdinir, cefaclor, or cefpodoxime-proxetil) for 3 to 7 days
Abbreviations: BID, twice a day; DS, double strength

Recommended treatment for patients with uncomplicated cystitis includes nitrofurantoin monohydrate macrocrystals (100 mg twice daily for five days) and trimethoprim-sulfamethoxazole (160/800 mg [1 double-strength tablet] twice-daily for three days) can be used when resistance prevalence to it is less than 20%. Fosfomycin trometamol (3 g in a single dose) is an option, though there is some evidence of decreased efficacy compared to the above regimens. Though not sold in the United States, pivmecillinam 400 mg twice a day for five days is an additional alternative, where available.

Three-day regimens of fluoroquinolones like ofloxacin, ciprofloxacin, and levofloxacin, are very effective but have higher rates of collateral damage, and the guideline authors recommend that these be reserved for more serious infections and only be considered alternates for uncomplicated acute cystitis.

Beta-lactam agents, including amoxicillin-clavulanate, cefdinir, cefaclor, and cefpodoxime-proxetil, in three- to seven-day regimens are appropriate choices if the other recommended agents cannot be used, though they have lower efficacy and a higher rate of adverse effects. There is less evidence to support the use of cephalexin and other beta-lactams than those above, though the guideline authors felt that they might be “appropri-

ate in certain settings,” while not elaborating on what those settings might be.

Amoxicillin and ampicillin are not recommended for patients with cystitis.

Table 2: Outpatient Antibiotic Treatment for Uncomplicated Acute Pyelonephritis⁴

If fluoroquinolone resistance prevalence is less than 10%
Ciprofloxacin 500 mg BID for 7 days, with or without an initial 400-mg dose of IV ciprofloxacin or 1 g of IV ceftriaxone or a consolidated 24-hour IV dose of an aminoglycoside
OR
Ciprofloxacin XR 1000 mg once daily for 7 days
OR
Levofloxacin 750 mg once daily for 5 days
If fluoroquinolone resistance prevalence is 10% or more, then use:
Ciprofloxacin 500 mg BID for 7 days, plus initial 1 g dose of IV ceftriaxone or a consolidated 24-hour IV dose of an aminoglycoside
OR
Ciprofloxacin XR 1000 mg once daily for 7 days, plus initial 1 g dose of IV ceftriaxone or a consolidated 24-hour IV dose of an aminoglycoside
OR
Levofloxacin 750 mg once daily for 5 days, plus initial 1 g dose of IV ceftriaxone or a consolidated 24-hour IV dose of an aminoglycoside
If infecting organism is known to be susceptible
Trimethoprim-sulfamethoxazole DS (160/800 mg) BID for 14 days, plus an initial 1 g dose of IV ceftriaxone or a consolidated 24-hour IV dose of an aminoglycoside
Only if above regimens are contraindicated
Oral beta-lactam (amoxicillin-clavulanate, cefdinir, cefaclor, or cefpodoxime-proxetil) for 10-14 days, plus an initial 1 g dose of IV ceftriaxone or a consolidated 24-hour IV dose of an aminoglycoside
Abbreviations: BID, twice a day; DS, double strength; g, gram; IV, intravenous; XR, extended release

To be managed as outpatients, individuals with pyelonephritis should be able to maintain their hydration and take oral antibiotics; fluoroquinolones are the primarily recommended. Oral ciprofloxacin (500 mg twice daily for seven days), with or without an initial 400-mg dose of intravenous (IV) ciprofloxacin (or 1 g of IV ceftriaxone or a consolidated 24-hour dose of an

aminoglycoside) can be used for outpatients if fluoroquinolone resistance prevalence is less than 10%. There is no rate of resistance at which a definite recommendation could be made to use something other than a fluoroquinolone. If, however, resistance is known or thought to exceed 10%, then a single initial dose of 1 g of ceftriaxone or a consolidated 24-hour dose of an aminoglycoside should be given IV prior to starting outpatient oral therapy with ciprofloxacin 500 mg twice daily. Other oral fluoroquinolone regimens (ciprofloxacin extended-release 1000 mg once a day for seven days or levofloxacin 750 mg for five days) are alternatives and may be given without consideration of an initial IV dose unless fluoroquinolone resistance prevalence exceeds 10%. In this case, as with the above situation, a single initial IV dose of 1 g of ceftriaxone or a consolidated 24-hour dose of an aminoglycoside should start treatment.

Oral trimethoprim-sulfamethoxazole (160/800 mg [1 double-strength tablet] twice-daily for 14 days) may be used, but only if the infecting organism is known to be susceptible. Patients receiving this regimen should all receive a starting IV dose of a long-acting antibiotic, e.g., 1 g of ceftriaxone or a consolidated 24-hour dose of an aminoglycoside. The guideline authors give a weaker recommendation to use oral beta-lactams (e.g., amoxicillin-clavulanate, cefdinir, cefaclor, and cefpodoxime-proxetil) due to lower effectiveness. These should be taken for 10-14 days and may be considered in situations where there are contraindications to the other treatment options. All patients with pyelonephritis treated with oral beta-lactams should receive a starting IV dose of a long-acting antibiotic as above.

Disposition Decisions

Patients with uncomplicated infections and normal, stable vital signs, who can maintain good oral intake and who are capable of taking oral antibiotics and reliable follow-up are candidates for outpatient management. Men, pregnant women, and patients with immunosuppression, urinary tract malformations, renal/ureteral stones, recent urologic instrumentation, indwelling catheters, neurogenic bladder, and kidney transplant who otherwise fit the above criteria may be treated as outpatients, if urine cultures can be obtained, and after consultation and close, scheduled follow-up with the appropriate specialty can be arranged. Urgent care clinicians should consider sending all other patients to the emergency department for extended observation, with IV hydration and symptom management (as well as consideration of admission), if such is not available in the clinician's setting.

Resolution of symptoms is adequate proof of cure in cases of uncomplicated UTI, and testing for cure is not necessary. Patients should be advised that symptoms may persist for several days, but that adequate treatment should result in progressively decreasing symptoms. If symptoms fail to improve steadily or are not resolved by the time the antibiotic course is finished, then patients should seek re-evaluation.

Conclusion

UTI is a common disorder seen in urgent care practice. The clinician should use history, physical examination, and focused testing to confirm the diagnosis and evaluate, when appropriate, for other diagnoses or more complicated situations. Most patients with uncomplicated UTI can be effectively managed as outpatients using empiric antibiotics in accordance with the most recent guidelines and appropriate discharge instructions.

Review Highlights

- Urinalysis adds little information for patients with typical cystitis symptoms or when there is otherwise little diagnostic uncertainty.
- Consider a broader differential diagnosis as well as resistant infections or associated urinary tract obstruction in patients who do not improve promptly with usual empiric therapy.
- Be wary of the “slam dunk”: Before diagnosing a urinary tract infection and discharging an elderly patient who presents with nonspecific symptoms, evaluate for other important potential causes with a thorough history and physical exam and focused testing.
- Urine culture is not necessary for non-pregnant, premenopausal women with uncomplicated, acute cystitis.
- Urine culture is recommended for pediatric urinary tract infections, acute pyelonephritis, and complicated UTIs.
- Pre-treatment urine culture may be helpful when there is a previous history of known resistant infections, failure of empiric antibiotics, or multiple recurrent UTIs.
- Use recommended antibiotics to maximize the chance of cure and minimize “collateral damage.”

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