



## Management of Urinary Tract Infections in Adult Clinical Practice Guideline

*These guidelines are provided to assist physicians and other clinicians in making decisions regarding the care of their patients. They are not a substitute for individual judgment brought to each clinical situation by the patient's primary care provider in collaboration with the patient. As with all clinical reference resources, they reflect the best understanding of the science of medicine at the time of publication but should be used with the clear understanding that continued research may result in new knowledge and recommendations.*

### **Prevalence**

Urinary tract infections are the most common bacterial infections in the outpatient setting and account for about 6 million office visits yearly. They are most often diagnosed in women and are common in both young sexually active women and post-menopausal women.

### **Complicated vs Uncomplicated**

UTI's can be categorized as uncomplicated or complicated. Uncomplicated UTI's are episodes of cystitis and pyelonephritis in healthy non-pregnant females with no abnormalities of the urinary tract. Other UTIs are considered complicated because the risk of treatment failure or poor outcome is higher. Included in this category are UTI's in men, patients with neurogenic bladder, patients with kidney stones or other urologic abnormalities, patients who are pregnant and those who are immunocompromised including patients post renal transplant. Other classifications of UTI's exist, with complicated UTI's including all urinary tract infections that have spread beyond the bladder and uncomplicated encompassing localized infections even in patients with underlying urologic abnormalities.

### **Simple cystitis**

Cystitis typically presents with dysuria and or urgency, frequency, suprapubic pain, or hematuria without systemic symptoms. Onset is usually sudden. It is often recurrent, with 27% of women who develop one UTI experiencing a recurrence within 6 months. Women with one recurrence are more likely to experience subsequent recurrences. Cystitis has been associated with sexual activity and spermicide use.

Diagnosis can usually be made based on typical symptoms even without examination and testing. The probability of cystitis is > 90% in women who have dysuria and frequency without vaginal discharge or irritation. Urine dipstick testing for leukocyte esterase (enzyme released by WBC's) and nitrites (produced when bacteria reduce nitrates to nitrites) can be helpful in situation where symptoms are atypical with sensitivity and specificity of 75% and 82% respectively. Urine cultures are not indicated unless there is a risk for resistance (e.g., those who received antibiotics, from nursing home) and patients with risks for more serious infections like underlying urologic abnormalities, immunocompromising conditions, and poorly controlled diabetes.

Antibiotics should be selected that are active against the common pathogens: E coli, other Enterobacteriaceae and staph saprophyticus. Fluoroquinolones are not first line drugs for simple cystitis due to the prevalence of resistant organisms in the community, concerns that use will lead to resistant organisms, as well as safety concerns associated with this class of drugs.

### **FIRST LINE DRUGS FOR SIMPLE CYSTITIS**

<b>Drug</b>	<b>Duration</b>	<b>Clinical Pearls</b>
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<b>TMP/SMX 160 mg/800 mg twice a day</b> (\$8)	<b>3 days</b>	Halve dose for CrCl 15-30 mL/min Use with caution at 25-50% of recommended dose if CrCl <15mL/min May cause photosensitivity Maintain hydration to avoid renal stone formation Avoid using if there is a regional prevalence of >20% resistance
<b>Nitrofurantoin monohydrate macrocrystals 100 mg twice a day</b> (\$17)	<b>5 days</b>	Administer with food or milk Avoid concurrent administration of magnesium-containing compounds Avoid if CrCl < 30 ml/min May cause brown-colored urine
<b>Fosfomycin 3gram sachet</b> (\$100)	<b>Single dose</b>	Do not administer in dry form To administer, dissolve sachet contents in 3-4oz of cool water, stir, and take immediately.

\*Average Wholesale Price for duration of treatment

Choice among first line agents depends on patient factors (drug allergy history, possibility of pregnancy, drug availability and local resistance patterns if known). If a patient has received one of these in the prior three months, a different antibiotic should be chosen. Nitrofurantoin rarely selects for resistant organisms but is not effective in pyelonephritis and should not be chosen if pyelonephritis is suspected. Likewise, Fosfomycin should be avoided if early pyelonephritis is suspected. For those patients with risk factors, it is reasonable to treat them with longer duration of up to 7 days. A urinary analgesic, phenazopyridine, can also be prescribed for symptom control until the antibiotic starts to take effect.

If first line agents cannot be used, second line agents include the following:

- Beta lactams: amoxicillin-clavulanate 500 mg bid, cefpodoxime 100 mg bid, cefdinir 300 mg bid and cefadroxil 500 mg bid for 5-7 days
- Fluoroquinolones: ciprofloxacin 250 mg BID or extended release 500 mg daily or levofloxacin 250 mg daily for 3 days. Note that Moxifloxacin attains lower urinary level and should not be used.

### **Acute pyelonephritis/Complicated UTI managed in the outpatient**

Acute pyelonephritis typically presents with bladder irritative symptoms (frequency, urgency, and dysuria) associated with systemic symptoms (fever, chills, nausea, vomiting, back or flank pain). The spectrum of disease severity is wide, ranging from mild to life threatening. Sicker patients are more likely to be bacteremic, though the presence of positive blood cultures does not change antibiotic choice or duration.

Most episodes of acute pyelonephritis are caused by E coli though other gram-negative organisms, gram positive organisms and candida account for some infections. Extended spectrum B lactamase-producing Enterobacteriaceae causing cystitis to have increased frequency especially with recent antimicrobial use or health-care facility exposure. Bacteria typically reach the kidney in an ascending fashion, though hematogenous spread can also be the cause, particularly if Staph aureus or candida is found.

The diagnosis should be confirmed by a positive urine culture (> 10,000 CFU/ml - threshold for symptomatic patients). Imaging is indicated on presentation if obstruction or abscess is infected (known

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or suspected urolithiasis, sepsis, or new decrease in GFR). Imaging is also indicated in patients who deteriorate clinically or who fail to improve after 48-72 hrs.

Antibiotic choice should take into consideration the most likely pathogen, recent antibiotic use by the patient, drug allergies and interactions, and local resistance patterns if known. Note that nitrofurantoin and Fosfomycin, used in simple cystitis, are inappropriate choices for pyelonephritis since they do not reach adequate levels in the kidney or bloodstream. Fluoroquinolones are considered first line. It is advisable to give an initial dose of a long-acting parenteral antibiotic, such as ceftriaxone, ertapenem or an aminoglycoside in addition to other oral therapy while awaiting culture results when either the patient can't take fluoroquinolones or if there is a suspicion of a multi-drug resistant infection.

### DRUGS for PYELONEPHRITIS

Drug	Duration	Indication	Clinical Pearls
<b>Levofloxacin 750 mg daily (\$2)</b>	5-7 days	Gram neg rods	<b>Boxed Warning</b> for tendon rupture, peripheral neuropathy, and CNS effects – reserve for last line use Avoid using if regional uropathogen resistance area is >10% Dosing interval is every 48 hours if CrCl 20-49mL/min Administer one 750 mg dose followed by 500 mg every 48 hours if CrCl <20 mL/min Hydrate adequately to prevent crystalluria Space administration of any compounds containing metal cations by at least 2 hours May cause photosensitivity May prolong QT interval, especially when used with other medications that may prolong it
<b>Ciprofloxacin 500 mg bid or 1000 mg extended release daily (\$5)</b>	5-7 days	Gram neg rods	<b>Boxed Warning</b> for tendon rupture, peripheral neuropathy, and CNS effects – reserve for last line use Avoid using if regional uropathogen resistance area is >10% Adjust dose based on renal function – dose or interval changed depending on labs and formulation being used Contraindicated if using tizanidine Do not crush any formulation May cause photosensitivity Take at least 2 hours before or 6 hours after any compound that contains metal cations
<b>TMP-SMX 160 mg/800 mg bid (\$3)</b>	7-10 days	Gram neg rods	Halve dose for CrCl 15-30 mL/min

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			Use with caution at 25-50% of recommended dose if CrCl <15mL/min May cause photosensitivity Maintain hydration to avoid renal stone formation
<b>Amoxicillin-clavulanate 875 mg amoxicillin and 125 mg clavulanate bid (\$141)</b>	7-10 days	Enterococci and some Gram- negative rods	Do not use if CrCl <30 mL/min or patient is on hemodialysis Absorption decreased on empty stomach – take at start of meal May decrease effectiveness of oral contraceptives Use only when first line agents cannot be used
<b>Cefdinir 300 mg twice daily (\$102)</b>	10-14 days	Active against Gram negative rods	Administer once daily if CrCl < 30 mL/min Use only when first-line agents cannot be used Oral therapy should follow appropriate parenteral therapy
<b>Cefadroxil 1gm twice daily (\$100)</b>	10-14 days	Active against Gram negative rods	Administer every 24 hours if CrCl <25ML/min Administer every 36 hours if CrCl <20mL/min Use only when first-line agents cannot be used Oral therapy should follow appropriate parenteral therapy
<b>Cefpodoxime 200 mg twice daily (\$237)</b>	7-10 days	Active against many resistant Gram neg rods	Administer every 24 hours if CrCl<30 mL/min Administer tablet with food Suspension may be given without regard to food Use only when first-line agents cannot be used Oral therapy should follow appropriate parenteral therapy

Adapted from Acute pyelonephritis in Adults NEJM 2018

\*Average Wholesale Price for maximum duration of treatment

A close follow-up with either face to face or telephone visit should be done within 48-72 hours after initiation of treatment.

Indications for hospitalization include vomiting or nausea with inability to keep down oral antibiotics, volume depletion requiring more than mild fluid resuscitation, hypotension, unstable comorbid conditions, immunosuppression, unreliable home situation, and need for drainage of an infectious focus.

### **Recurrent UTI**

Recurrent UTI is defined as having 2 or more UTIs within 6 months or 3 or more within 1 year.

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Relapse is a recurrent UTI that happens with the same organism within 2 weeks of the initial infection which suggest that the infecting organism was resistant to the antibiotic chosen or that there is a persistent focus (such as subclinical pyelonephritis). A urine culture should be performed, and treatment should be started with a broader spectrum agent such as a quinolone and treated for presumed upper UTI for 7-10 days.

Reinfection, which is more common, is a recurrent UTI that happens more than 2 weeks after the initial infection and are caused by bacterial strain separate from the original one. Some women may be genetically pre-disposed to colonization with pathogenic bacterial strains. For recurrences within 6 months, treatment with a different first line agent should be considered particularly if the original agent was trimethoprim-sulfamethoxazole, because of the increased chance of resistance

Multiple strategies to prevent or manage recurrent episodes of cystitis exist and can be separated into non-pharmacologic and pharmacologic.

<b>Nonpharmacologic strategies</b>
<b>Reduce frequency of intercourse</b>
<b>Eliminate use of spermicides</b>
<b>Increase fluid intake (increase by 1.5 liters over baseline)</b>
<b>Urinate after intercourse</b>
<b>Cranberry, D Mannose, and probiotics have limited clinical efficacy but are often not discouraged</b>
<b>Pharmacologic strategies</b>
<b>Patient initiated treatment at onset of symptoms</b>
<b>Postcoital antimicrobial prophylaxis—single dose as soon as possible after intercourse</b>
<b>Continuous antimicrobial prophylaxis—daily bedtime dose</b>
<b>Vaginal estrogen for post-menopausal women</b>

Data supporting the effectiveness of the non-pharmacologic strategies is sparse. Pharmacologic prophylaxis, however, is ~ 95% effective in preventing recurrences. It should be limited to women with three recurrences in the past 12 months or two or more in the past 6 months.

Urologic work up is low yield and should be limited to situations in which the patient has persistent hematuria, multiple recurrences with the same strain of organism, complicated UTI with failure to improve in 48-72 hours or if there are other clues to structural abnormalities such as infection with proteus mirabilis.

**Special populations**

- **Pregnant women**—30-40% of pregnant women will have asymptomatic bacteriuria and are at risk for symptomatic UTI and adverse pregnancy outcomes. Asymptomatic bacteriuria as well as symptomatic UTI should be treated with antibiotics safe in pregnancy The safest antibiotics are amoxicillin-clavulanate, cephalosporins, and nitrofurantoin (avoid in first trimester and near term); fluoroquinolones are contraindicated, and trimethoprim-sulfamethoxazole can only be used safely during second trimester. Resolution should be confirmed by repeat urine culture.
- **Men**—The spectrum of UTI in men includes urethritis, cystitis, pyelonephritis, and prostatitis (acute and chronic). UTIs in men should be confirmed by urine culture. Evaluation for structural abnormalities by imaging (CT or US) and cystoscopy should be undertaken in older men and for

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recurrences or if structural abnormalities are suspected (persistent hematuria, for example). Prostatitis may be acute, chronic, or asymptomatic, and bacterial prostatitis requires a lengthy course of an antibiotic that can penetrate prostatic tissue. Gram-negative uropathogens account for about 80% of acute prostatitis infections, in men 35 years and younger who may have concomitant urethritis or epididymitis, sexually transmitted infections, including *Neisseria gonorrhoea* and *Chlamydia trachomatis* must be considered.

Prostatitis Type	Features	Treatment
<b>Acute Prostatitis</b>	<b>Fever, UTI symptoms, pelvic pain GNR on urine culture</b>	<b>TMP/SMX, Quinolone for 6 weeks</b>
<b>Chronic Bacterial Prostatitis</b>	<b>Low grade fever, UTI symptoms May be subtle or asymptomatic GNR isolated from post-massage urine or expressed prostatic secretions</b>	<b>Quinolone for 6 weeks May recur and require re-treatment TMP/SMX – as an alternative</b>
<b>Chronic prostatitis/Chronic pelvic pain syndrome</b>	<b>Pain, voiding difficulty Inflammatory/Non-inflammatory Cultures neg Association with other pain syndromes</b>	<b>Alpha blocker +antibiotic (quinolone) Finasteride NSAID Psych support</b>
<b>Asymptomatic inflammatory prostatitis</b>	<b>Incidental finding on prostate biopsy</b>	

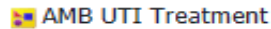
- Elderly**—Asymptomatic bacteriuria (defined as  $\geq 10^5$  CFU/ml on urine culture in a patient without symptoms) is common in elderly patients and associated with an increased risk of symptomatic UTI. There is no evidence, however, that treating asymptomatic bacteriuria reduces the development of symptomatic UTI. Hence, asymptomatic bacteriuria should not be treated. Diagnosing symptomatic UTI in the elderly can also be difficult for many reasons: chronic incontinence, making it hard to know which symptoms are new; cognitive impairment which may make history taking difficult; and nonspecific symptoms such as falls, change in functional status, and change in mental status that may be incorrectly attributed to a urinary tract infection. Urine testing should be limited to patients with classic UTI symptoms or signs of serious acute illness such as fever and alteration of consciousness. When non-specific signs and symptoms are accompanied by signs and symptoms of systemic infection or pyelonephritis, evaluation for acute complicated UTI with urine studies, in addition to general infectious work-up, is appropriate.
- Post renal transplant**—Urinary tract infections in the post-transplant patient are associated with acute cellular rejection, graft loss, impaired graft function, and death. Asymptomatic bacteriuria should be treated in the post-renal transplant patient. Urine cultures should be obtained in all patients with symptomatic UTI to guide therapy.

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- **Catheter-associated UTI** – patients with neurogenic bladder requiring intermittent catheterization, indwelling Foley or suprapubic catheter have a high risk of recurrent infections. Some patients like spinal cord injury patients might be difficult to diagnose since their clinical presentation is atypical. Urine testing and culture on properly collected specimen is recommended on all patients suspected of UTI. Most patients will present with systemic symptoms like fever hence are treated as complicated UTI. Empiric antibiotic choice should be tailored to results of past culture, use of prior antibiotics, prevalence of resistance and allergies. Those that require indwelling Foley should have it replaced once antibiotics has been initiated.

**MedConnect Resources**

A UTI specific power plan is present in MedConnect to facilitate appropriate treatment orders:



**Patient Education**

[https://www.uptodate.com/contents/urinary-tract-infections-in-adults-the-basics?search=urinary%20tract%20infection&topicRef=8063&source=see\\_link](https://www.uptodate.com/contents/urinary-tract-infections-in-adults-the-basics?search=urinary%20tract%20infection&topicRef=8063&source=see_link)

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