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 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, recent antibiotic use, 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. Designating as complicated influences choice and duration of antibiotic.

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, spermicide use, diaphragm use, pregnancy, diabetes, and obesity.

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 situations 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, or 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, streptococci, enterococci, and staph saprophyticus. Fluoroquinolones are not recommended 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.

Initial Approval Date and Reviews:	**Most Recent Revision and Approval Date:**	**Next Scheduled Review Date:**
September 2020; September 2022, September 2024 Ambulatory Best Practice Committee	**September 2024**	September 2026 Ambulatory Quality Best Practice

RECOMMENDED DRUGS FOR SIMPLE CYSTITIS

Drug	Duration	Clinical Pearls
Nitrofurantoin monohydrate macrocrystals 100 mg twice a day ($17) *	**5 days**	First line Avoid in first trimester of pregnancy and at 38-42 weeks gestation Administer with food or milk Avoid concurrent administration of magnesium-containing compounds Avoid if CrCl < 30 ml/min May cause brown-colored urine
Amoxicillin/Clavulanate 500mg twice a day ($11) *	**5 days**	Second line May decrease effectiveness of oral contraceptives
Trimethoprim-sulfamethoxazole (TMP-SMX)160 mg/800 mg twice a day ($8) *	**3 days**	Second Line For patients with penicillin allergy Avoid in pregnancy May cause photosensitivity Maintain hydration to avoid renal stone formation
Fosfomycin 3gram sachet ($100) *	**Single dose**	Second line in first trimester of pregnancy and at 38-42 weeks gestation OR with severe pen and sulfa allergy Do not administer in dry form To administer, dissolve sachet contents in 3-4oz of cool water, stir, and take immediately.

For renal dosing adjustments, see the AMB UTI Treatment Orderset
*Average Wholesale Price for duration of treatment

Choice among 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. A urinary analgesic, phenazopyridine (200mg three times a day for 2 days if GFR > 50 mL/min), can also be prescribed for symptom control until the antibiotic starts to take effect.

If nitrofurantoin cannot be used, second line agents are listed in the table above and include the following: Amoxicillin-clavulanate, Trimethoprim-Sulfamethoxazole (TMP-SMX), and Fosfomycin. For renal dosing, see the AMB UTI Treatment Orderset.

(For antibiotic choice during pregnancy, see below under Special Populations)

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 complicated UTI may be seen 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 suspected (known 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. TMP-SMX is considered first line. It is advisable to give an initial dose of a long-acting parenteral antibiotic, such as ceftriaxone or an aminoglycoside in addition to other oral therapy while awaiting culture results. For renal dosing, see the AMB UTI Treatment Orderset.

DRUGS for PYELONEPHRITIS

Drug	Duration	Clinical Pearls
TMP-SMX 160 mg/800 mg bid ($3)	10 days	May cause photosensitivity Maintain hydration to avoid renal stone formation Avoid in pregnancy and patients with sulfa allergy
Ciprofloxacin 500 mg bid ($5)	7 days	**Boxed Warning** for tendon rupture, peripheral neuropathy, and CNS effects – reserve for second line use for patients with sulfa allergy or recent urine cultures with quinolone susceptible pseudomonas. Avoid in pregnancy Contraindicated if using tizanidine May cause photosensitivity Take at least 2 hours before or 6 hours after any compound that contains metal cations May prolong QT interval, especially when used with other medications that may prolong it
Levofloxacin 750 mg daily ($2)	7 days	**Boxed Warning** for tendon rupture, peripheral neuropathy, and CNS effects – reserve for second line use for patients with sulfa allergy or recent urine cultures with quinolone susceptible pseudomonas. Avoid in pregnancy May cause photosensitivity Take at least 2 hours before or 6 hours after any compound that contains metal cations May prolong QT interval, especially when used with other medications that may prolong it

Cefdinir 300 mg twice daily ($102)	10 days	Only if pregnant OR with recent urine cultures demonstrating cefazolin susceptibility Avoid in patients with cephalosporin or severe pen allergy Use only when first-line agents cannot be used Oral therapy should follow appropriate parenteral therapy

For renal dosing adjustments, see the AMB UTI Treatment Orderset
*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 (Relapse or Reinfection)

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

--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) or structural abnormality (such as kidney stone). 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 is 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.

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

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, or colo-vesicle fistula.

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 at 38-42 weeks gestation); fluoroquinolones and TMP-SMX are contraindicated. 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 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. In men 35 years and younger who may have concomitant urethritis or epididymitis, sexually transmitted infections, including Neisseria gonorrhea and Chlamydia trachomatis must be considered.

Prostatitis Type	Features	Treatment
Acute Prostatitis	**Fever, UTI symptoms, pelvic pain** **GNR on urine culture**	**TMP/SMX, Quinolone for 2-4 weeks**
Chronic Bacterial Prostatitis	**Low grade fever, UTI symptoms** **May be subtle or asymptomatic** **GNR isolated from post-massage urine or expressed prostatic secretions**	**Quinolone for 6 weeks** **May recur and require re-treatment** **TMP/SMX – as an alternative**
Chronic prostatitis/Chronic pelvic pain syndrome	**Pain, voiding difficulty** **Inflammatory/non-inflammatory** **Cultures neg** **Association with other pain syndromes**	**Alpha blocker +antibiotic (quinolone)** **Finasteride** **NSAID** **Psych support**
Asymptomatic inflammatory prostatitis	**Incidental finding on prostate biopsy**	

- **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 (acute dysuria, new or worsening

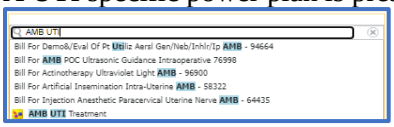
urgency or frequency, new incontinence, gross hematuria, or CVA or suprapubic tenderness) or signs of serious acute illness such as fever and alteration of consciousness. When non-specific signs and symptoms are accompanied by signs and symptoms of systemic infection or pyelonephritis, evaluation for 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.

- **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 have been initiated.

MedConnect Resources

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



Patient Education

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