

Urinary Tract Infections (UTI)

Microbiology

- Common UTI pathogens include *E. coli*, *Klebsiella*, and other gram-negative coliform bacilli
- Less common cause of UTI includes *Enterococcus*
- Patients who are hospitalized with long-term urinary catheters are at increased risk for *Staphylococcus aureus* and *Pseudomonas*
- ESBL-producing organisms are becoming increasingly common and exhibit ceftriaxone resistance. Consider ESBL coverage in severely ill patients, known prior ESBL colonization, recent broad-spectrum antimicrobial use, or recent travel to endemic areas (Central America, Sub-Saharan Africa, Mediterranean, Middle East, South Asia).

Terminology

- Acute cystitis – infection of the bladder
 - Complicated cystitis – cystitis with presence of risk factors for therapeutic failure or recurrence
- Acute pyelonephritis – infection of the kidney(s)
 - Complicated pyelonephritis – presence of emphysematous pyelonephritis, renal parenchymal abscess, perinephric abscess, or papillary necrosis

Diagnosis

General:

- Cloudy or malodorous urine is not diagnostic for UTI, and should NOT be used as an indication for urine culture or antimicrobial therapy

UTI without urinary catheter:

- Acute cystitis presents with dysuria, frequency, urgency, hematuria, and/or suprapubic pain.
- Acute pyelonephritis presents with fever, chills, nausea, vomiting, and/or flank pain. Patients may or may not have cystitis symptoms. Bacteremic UTI's are generally considered to be pyelonephritis. The term "urosepsis" is imprecise, the majority of such patients with confirmed UTI will be managed the same as pyelonephritis.

UTI in presence of urinary catheter:

- Patients with catheter-associated UTI (CA-UTI) often lack typical UTI symptoms. Symptoms that are compatible with CA-UTI include
 - New fevers or rigors without other source
 - Pelvic discomfort, suprapubic tenderness, flank pain or tenderness
 - Acute gross hematuria
- Patients with urinary catheters often have pyuria, thus pyuria is not specific for CA-UTI. Conversely, the absence of pyuria is helpful as this strongly suggests an alternative diagnosis other than CA-UTI.
- Asymptomatic bacteriuria is common in catheterized patients.
- In suspected CA-UTI, collect urine culture from voided midstream urine if catheter can be discontinued. If catheter cannot be discontinued, collect urine culture from a freshly replaced catheter. Collect urine culture prior to initiation of antimicrobial therapy whenever possible.

UTI in men:

- UTIs in men are always considered complicated. A thorough search for BPH, stones, and strictures must be undertaken. Chronic pelvic symptoms, or recurrent UTIs with the same organism, should trigger assessment for bacterial prostatitis. Urology and/or Infectious Diseases consultation recommended.

UTI in patients with spinal cord injury:

- Patients with spinal cord injury often lack typical UTI symptoms. Symptoms compatible with UTI in this patient population include
 - New fevers or rigors without other source
 - Increased spasticity, autonomic dysreflexia, or sense of unease

EMPIRIC THERAPY
Patients WITHOUT a urinary catheter

Severity		Duration (days) ²
Asymptomatic bacteriuria	NONE – Exceptions: <ul style="list-style-type: none"> • Pregnancy (see below) • Prior to urologic procedure where bleeding/trauma is expected 	
Acute cystitis		
Uncomplicated <ul style="list-style-type: none"> • female • no urologic abnormalities • no stones • no catheter 	<i>First Line:</i> nitrofurantoin (MacroBID) 100 mg PO BID x 5 days (CrCl>40 only) <i>Second Line:</i> TMP/SMX 1 DS tab PO BID x 3 days OR amoxicillin-clavulanate 875-125 mg one tab PO BID x 5 days <i>Third Line:</i> cefixime 400 mg PO daily x 5 days OR ciprofloxacin 500 mg PO BID x 3 days OR fosfomycin 3 g PO once	3 – 5
Complicated (any of) <ul style="list-style-type: none"> • male • urologic abnormalities • stones • pregnancy (see below) 	Same regimens as above given for 7 days. Note: fosfomycin dosing is 3 g PO every 3 days x 3 doses <i>Consider imaging ± urological referral</i>	7
Pregnancy	Same regimens as above, except: <ul style="list-style-type: none"> • Ciprofloxacin is <i>contraindicated</i> in pregnancy • Nitrofurantoin should be avoided after 38 weeks gestation • TMP/SMX should be avoided in 1st trimester and after 32 weeks gestation 	7
Acute pyelonephritis		
Not severely ill Oral therapy	<i>First Line:</i> amoxicillin-clavulanate 875-125 mg one tab PO BID OR cefixime 400 mg PO daily <i>Second Line:</i> TMP/SMX 1 DS tab PO BID OR ciprofloxacin 500 mg PO BID	7 – 10
Not severely ill Intravenous therapy	ceftriaxone 1 g IV q24h <i>If severe beta-lactam allergy:</i> gentamicin 5 mg/kg IV q24h ¹	7 – 10
Severely ill (sepsis, septic shock)	piperacillin-tazobactam 3.375 g IV q6h <i>If known or suspected ESBL:</i> meropenem 500 mg IV q6h +/- ampicillin 1 g IV q6h if enterococcus suspected <i>If severe beta-lactam allergy:</i> gentamicin 7 mg/kg IV q24h ¹	7 – 10
Oral step-down if organism is susceptible and patient clinically improving.		
<i>First Line</i> amoxicillin 500 mg PO TID cephalexin 500 mg PO QID TMP/SMX 1 DS tab PO BID	<i>Second Line</i> amoxicillin-clavulanate 875-125 mg one tab PO BID cefixime 400 mg PO daily	<i>Third Line</i> ciprofloxacin 500 mg PO BID
First line agents preferred, use second or third line agents <u>only</u> if resistance or intolerance. In rare circumstances where cultures are negative but a high suspicion remains, choose from second line agents		

Doses may require adjustment in renal insufficiency.

¹ For aminoglycoside dosing, refer to dosing reference (such as Lexicomp) or discuss with clinical pharmacist. Use caution if CrCl<30.

² See “Oral Step-Down & Duration” section below for details.

Patients WITH a urinary catheter		
Severity		Duration (days) ²
Asymptomatic bacteriuria	NONE – Exceptions: <ul style="list-style-type: none"> • Pregnancy • Prior to urologic procedure where bleeding/trauma is expected Remove catheter if possible	
Catheter-associated UTI (CA-UTI)		
REMOVE (or replace) CATHETER WHENEVER POSSIBLE		
Symptomatic CA-UTI	First Line: amoxicillin-clavulanate 875-125 mg one tab PO BID OR cefixime 400 mg PO daily Second Line: TMP/SMX 1 DS tab PO BID OR ciprofloxacin 500 mg PO BID	7 – 10
Febrile or systemically unwell	ceftriaxone 1 g IV q24h <i>If severe beta-lactam allergy: gentamicin 5 mg/kg IV q24h¹</i>	7 – 10
Severely ill (sepsis, septic shock)	piperacillin-tazobactam 3.375 g IV q6h <i>If known or suspected ESBL: meropenem 500 mg IV q6h +/- ampicillin 1 g IV q6h if enterococcus suspected</i> <i>If severe beta-lactam allergy: gentamicin 7 mg/kg IV q24h¹</i>	7 – 10
Oral step-down if organism is susceptible and patient clinically improving.		
<u>First line</u> amoxicillin 500 mg PO TID cephalexin 500 mg PO QID TMP/SMX 1 DS tab PO BID	<u>Second Line</u> amoxicillin-clavulanate 875-125 mg one tab PO BID cefixime 400 mg PO daily	<u>Third Line</u> ciprofloxacin 500 mg PO BID
First line agents preferred, use second or third line agents <u>only</u> if resistance or intolerance. In rare circumstances where cultures are negative but a high suspicion remains, choose from second line agents		
Can consider 3 day treatment course in female patient ≤ 65 years old with lower tract infection who have catheter promptly removed.		

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². See “Oral Step-Down & Duration” section below for details.

Oral Step-Down & Duration

- Acute cystitis
 - Oral regimen preferred from outset in most patients. If started on parenteral agent, switch to oral agent as soon as feasible.
- Acute pyelonephritis
 - Oral step-down if organism is susceptible and patient clinically improving (afebrile, improving symptoms)
 - Step-down to oral beta-lactam is appropriate after 1-3 days of parenteral beta-lactam including in bacteremic UTI. Complete total 7-10 day treatment course.
 - If step-down to TMP/SMX, treat for 7-10 days total
 - If step-down to ciprofloxacin or levofloxacin, treat for 5-7 days total
- Catheter-associated UTI
 - Oral step-down if organism is susceptible and patient clinically improving (afebrile, improving symptoms)
 - Treat for 7 days if prompt resolution of symptoms
 - Treat for 10 days if delayed response
 - Can consider 3 day treatment course in female patient ≤ 65 years old with lower tract infection who have catheter promptly removed.
- Renal parenchymal abscess, perinephric abscess, or emphysematous pyelonephritis often requires longer duration of therapy. Urology & Infectious Diseases consultation recommended.
- How about bacteremia?
 - Duration of therapy in setting of bacteremic pyelonephritis (“urosepsis”) is no different than cases without bacteremia
- Follow-up urine culture as a test of cure is not recommended unless patient has not responded to therapy or is pregnant.

Microbe-Specific Issues

Treatment of UTI due to *Enterococcus*:

- *E. faecalis* is almost universally (~99%) susceptible to ampicillin. Options include:
 - amoxicillin 500 mg PO TID
 - ampicillin 1 g IV q6h
 - nitrofurantoin (cystitis only, do NOT use if CrCl < 40mL/min).
- *E. faecium* is commonly resistant to vancomycin, options include:
 - nitrofurantoin (cystitis only, do NOT use if CrCl < 40mL/min)
 - doxycycline
 - fosfomycin (cystitis only)
 - linezolid
 - vancomycin (if susceptibility confirmed)

Treatment of UTI due to ESBL-producing organisms:

- ESBLs are beta-lactamase enzymes that confer resistance to penicillins, cephalosporins, and aztreonam.
- If susceptible, options for therapy include:
 - piperacillin-tazobactam or amoxicillin-clavulanate
 - TMP/SMX
 - ciprofloxacin
 - nitrofurantoin and fosfomycin – cystitis only (INEFFECTIVE in pyelonephritis or bacteremia)