

Urinary Tract Infections (UTI)

MICROBIOLOGY

- **Most common:** *E. coli*
- **Less common:** *Klebsiella*
- **Rare pathogens:** *Enterococcus*, *S. saprophyticus*, *Proteus* and other gram-negative coliforms.
- **Catheter-associated UTI:** increased risk for *Staphylococcus aureus* and *Pseudomonas*.
- **ESBL-producing organisms:** resistant to ceftriaxone. 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).

CLASSIFICATION

Acute simple cystitis	Acute UTI confined to the bladder: - Dysuria, frequency, urgency, hematuria, and/or suprapubic pain - No signs or symptoms of upper tract or systemic infection.
Acute complicated UTI	Acute UTI accompanied by signs or symptoms of extension of infection beyond bladder: - Fever, chills, rigors, significant fatigue or malaise, nausea, vomiting - Flank pain, CVA tenderness - Pelvic or perineal pain in men Patients may or may NOT have cystitis symptoms. Bacteremic UTI and “urosepsis” are managed the same as acute complicated UTI
Special populations with unique features	Pregnant women Renal transplant recipients

DIAGNOSIS

- **Pyuria** >5 WBC per high-powered field on urine microscopy OR
- **Positive leukocyte esterase** as a surrogate
 - ! the absence of pyuria strongly suggests an alternative diagnosis other than UTI
 - ! cloudy or malodorous urine is NOT diagnostic for UTI< and should NOT be used as an indication for urine culture or antimicrobial therapy
- **Collect urine culture PRIOR to initiation of antimicrobial therapy whenever possible.**

UTI without urinary catheter (see table above)

Catheter-associated UTI (CA-UTI)

- Typically present as acute complicated UTI: fevers or rigors without other source, flank pain or CVA tenderness
- May occasionally present with acute simple cystitis with no complicated UTI findings: pelvic discomfort, suprapubic tenderness, or acute gross hematuria.
- **Asymptomatic bacteriuria is common in catheterized patients (~100% after 1 month of catheterization).**
- 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.

UTI in men

- 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

- 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

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 Simple Cystitis		
Non-Pregnant Females & Males	First Line: nitrofurantoin (MacroBID) 100 mg PO BID x 5 days (CrCl>30 only) Second Line: TMP/SMX 1 DS tab PO BID x 3 days OR amoxicillin-clavulanate 875-125 mg one tab PO BID x 5 days Third Line: cefixime 400 mg PO daily x 5 days OR ciprofloxacin 500 mg PO BID x 3 days OR fosfomycin 3 g PO once (Males: 3 g PO every 3 days x 3 doses)	<u>Females</u> 3 – 5 <u>Males</u> 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 Complicated UTI (Acute Pyelonephritis, Febrile UTI, or Catheter-Associated UTI)		
Not severely ill <i>Oral therapy</i>	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 Consider initial one-time dose of parenteral agent below Confirm empiric therapy once urine culture results available	<u>Females</u> 7 <u>Males</u> 10 – 14
Not severely ill <i>Intravenous therapy</i>	ceftriaxone 1 g IV/IM q24h <i>If severe cephalosporin allergy: gentamicin 7 mg/kg IV/IM q24h¹</i> Oral step-down once patient clinically improving and culture results available	
Severely ill (sepsis, septic shock)	piperacillin-tazobactam 3.375 g IV q6h <i>If known or suspected ESBL: meropenem 500 mg IV q6h</i> <i>If severe penicillin allergy: meropenem 500 mg IV q6h</i> Oral step-down once patient clinically improving and culture results available	
Oral step-down for complicated UTI if organism is susceptible and patient clinically improving.		
First Line	Second Line	Third Line
amoxicillin 500 mg PO TID cephalexin 500 mg PO QID TMP/SMX 1 DS tab PO BID	amoxicillin-clavulanate 875-125 mg one tab PO BID cefixime 400 mg PO daily	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 "Aminoglycoside Dosing and Therapeutic Monitoring" chapter in ASP Handbook.

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

ORAL STEP-DOWN & DURATION

- *Acute simple cystitis*
 - Oral regimen preferred from outset in most patients. If started on parenteral agent, switch to oral agent as soon as feasible.
- *Acute complicated UTI* (Acute Pyelonephritis, Febrile UTI, or Catheter-Associated UTI)
 - If started on parenteral agent, switch to oral agent once patient clinically improving and culture results available.
 - **Treat females for 7 days, males for 10-14 days.**
 - Can consider 3 day treatment course in female patient ≤ 65 years old with catheter-associated UTI who have catheter promptly removed.
- *Renal parenchymal abscess, perinephric abscess, or emphysematous pyelonephritis* often requires longer duration of therapy. Urology & Infectious Diseases consultation recommended.
- *Renal transplant patients with UTI* may require different durations than those recommended above. Infectious Diseases or Nephrology consultation recommended.
- *How about bacteremia?*
 - Duration of therapy in setting of bacteremic pyelonephritis 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 < 30mL/min).
- *E. faecium* is commonly resistant to vancomycin, options include:
 - nitrofurantoin (cystitis only, do NOT use if CrCl < 30mL/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 – acute simple cystitis only
 - TMP/SMX
 - ciprofloxacin
 - nitrofurantoin and fosfomycin – acute simple cystitis only (INEFFECTIVE in pyelonephritis or bacteremia)