Carolina Antimicrobial Stewardship Program Guideline

Urinary Tract Infection Diagnosis & Management in Adolescents & Adults at UNC Medical Center

This guidance document provides best practice recommendations for the diagnosis and antimicrobial treatment of urinary tract infections (UTIs). These recommendations apply to adolescents (≥ 13 years of age) and adults.

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Key Points

- **Diagnosis**
  - Decision to workup for UTI (UA or urine culture) should be based on patient symptoms.
  - Inappropriate urine culture ordering often leads to misdiagnosis and unnecessary antibiotics.

- **Treatment of asymptomatic bacteriuria** is **NOT** recommended as it offers no benefit and may cause harm.

- **Bottom Line**: unnecessary testing and treatment of asymptomatic bacteriuria can lead to antibiotic resistance, adverse drug effects, and *C. difficile* infection.

Questions?
Page the Carolina Antibiotic Stewardship Program at 216-2398

This document is intended for educational purposes and does not replace the medical decision and diagnosis of a treating provider. Although we have made a good faith effort to provide accurate information as of the date of creation, we make no representation or warranty regarding its accuracy and have no obligation to update the guidelines as new medical information becomes available.
I. Diagnosis

Types of UTIs:

- **Urinary Tract Infection (UTI):**
  - **Cystitis:** infection of the bladder.
  - **Pyelonephritis:** infection involving the kidneys and upper urinary tract.
  - **Catheter-Associated UTI (CAUTI):** presence of an indwelling urinary catheter with signs and symptoms of UTI with positive urine culture and no other identified source of infection

- **Asymptomatic Bacteriuria (ASB):** isolation of bacteria in the urine at levels often regarded as clinically significant (i.e. > 100,000 CFU/mL) +/- pyuria, in patients without symptoms of UTI.

### Table 1: Symptoms suggestive of UTI

<table>
<thead>
<tr>
<th>Classification/Diagnosis</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASB</td>
<td>None!</td>
</tr>
<tr>
<td>Cystitis</td>
<td>Dysuria, new or worsening frequency or urgency, suprapubic pain</td>
</tr>
<tr>
<td>Pyelonephritis</td>
<td>Cystitis symptoms + chills, flank pain or tenderness, fever</td>
</tr>
<tr>
<td>CAUTI</td>
<td>Chills, flank pain or tenderness, fever</td>
</tr>
</tbody>
</table>

The following symptoms are **NOT** specific/suggestive of UTI*: malodorous or cloudy urine, increased urine sediment

Altered mental status (AMS) may be present in certain populations with UTI. Reference [AMS Algorithm](#).

*Consider alternative, non-UTI diagnosis, such as dehydration.

### Table 2: Urinalysis Interpretation

<table>
<thead>
<tr>
<th>UA Factor</th>
<th>Normal</th>
<th>Abnormal</th>
<th>Interpretation</th>
<th>Caveats</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>WBC</strong></td>
<td>&lt; 5</td>
<td>≥ 5</td>
<td>*Normal: UTI unlikely, negative predictive value &gt;90%</td>
<td>• Less sensitive in neutropenic patients (i.e. ANC &lt; 500 cells/μL).</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><em>Abnormal: nonspecific to UTI</em>; may occur in other conditions, including STIs or genital dermatitis.</td>
<td></td>
</tr>
<tr>
<td><strong>Leukocyte Esterase</strong></td>
<td>Absent</td>
<td>Present (any)</td>
<td>*Normal: UTI unlikely</td>
<td>• Less specific than WBC for UTI.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><em>Abnormal: nonspecific</em>. Indicates WBCs in urine.</td>
<td></td>
</tr>
<tr>
<td><strong>Nitrite</strong></td>
<td>Absent</td>
<td>Positive</td>
<td>*Normal: does not rule out UTI (low sensitivity)</td>
<td>• Certain bacteria do not produce nitrite, including <em>Enterococcus</em>.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>*Abnormal: indicates presence of certain bacteria, including <em>E. coli</em>. Does not differentiate between ASB, contamination, or infection.</td>
<td></td>
</tr>
<tr>
<td><strong>Bacteria</strong></td>
<td>Absent</td>
<td>Present</td>
<td>*Normal: no bacteria seen. Low sensitivity.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>*Abnormal: indicates presence of bacteria. Does not differentiate between ASB, contamination, or infection.</td>
<td></td>
</tr>
</tbody>
</table>

*Non-infectious causes of WBC and leukocyte esterase in urine include STIs, genital dermatitis, inflammatory and autoimmune disease (Kawasaki’s disease, systemic lupus erythematosus, etc.), presence or recent urinary catheter. Sometimes no cause is identified.
II. Algorithms

A. Urine Diagnostic Guide Algorithm

Start Here

Does the patient have clinical signs and symptoms suggestive of a UTI?

No indwelling catheter:
- Dysuria, new or worsening frequency or urgency, suprapubic pain
- Flank pain or tenderness

Indwelling urethral catheter present:
- New flank pain or tenderness
- Fever and rigors (exclude other causes first)

No

The following symptoms are NOT specific for UTI:
- Malodorous urine
- Cloudy urine
- Increased urine sediment
- Fails or altered mental status

Yes

Are the symptoms consistent with urinary infection? (If positive, initiate empirical antibiotic treatment)

Order UA¹ and obtain appropriate urine sample²

UA suggestive of UTI:
- WBC ≥ 5 (pyuria)
- Positive nitrite (if using urine dipstick)

Order urine culture and initiate antibiotics, as appropriate³

UA not suggestive of UTI:
- WBC < 5
- Negative nitrite (if using urine dipstick)

UTI unlikely, treatment not recommended

Is the patient hemodynamically unstable without alternative or obvious etiology?

No

Is the patient febrile (≥ 100.4°F) without other source of infection AND high-risk criteria below?

No

UTI Treatment Algorithm

AMS Algorithm

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1. If available, may order UA with reflex culture (Epic order available for ED and outpatients). Consider ordering UA and culture simultaneously in the following scenarios:
   a. Neutropenic (ANC ≤ 500 cells/μL)
   b. Hemodynamic instability (order prior to initiating empiric antibiotics)

2. Reference PolicyStat (Specimen Acceptability/Rejection Criteria - Micro Processing) for urine specimen criteria. If urine is collected from an indwelling Foley catheter, the specimen must be processed as “Catheterized Urine.” Urine specimens obtained from a Foley bag are never appropriate for adult patients and processing will therefore be rejected by the lab.

3. UTI Treatment Algorithm

4. AMS Algorithm

Developed by CASP; Meredith Gilliam, MD; Christine Kistler, MD; Donna Truoccolo, PharmD; Kyle Schuchter, PharmD
Approved by UNCMC Anti-infective P&T Subcommittee 5/2023; Updated 12/2023
B. Altered Mental Status Algorithm

Start Here
Acutely altered mental status or confusion

Acute AMS/delirium:
- Fluctuating or acute mental status change
- Consider use of evidence-based screening tools:
  - Floor patients: 4 A’s Test for Delirium¹
  - ICU patients: CAM-ICU²

Must be able to assess baseline mental status in order to distinguish acute from chronic

Assess for UTI-specific signs and symptoms

UTI-specific symptoms or clinically unstable
UTI-specific symptoms:
- Acute dysuria, new or worsening urgency/frequency
- Suprapubic pain
- Flank pain or tenderness

Clinical instability³:
- Hypotension requiring vaspressors
- Acute decompensation and inability to report symptoms

SEND urine for UA (with reflex culture if available)

UA findings:
- WBC ≥ 5 (pyuria)
- Positive nitrite (if using urine dipstick)

Consider UTI, treat accordingly⁴

UTI unlikely, treatment not recommended

Non-specific symptoms and clinical stability
Non-specific symptoms:
- Confusion or altered mental status
- Chronic dysuria, urinary incontinence, frequency
- Fever or leukocytosis without focal UTI symptoms

Deferring UTI-directed antibiotics. Assess and treat more likely causes.
Consider the following:
- Attempt hydration (oral or IV)
- Evaluate new/adjusted medications for adverse effects, drug-drug interactions, and polypharmacy
- Assess for other potential causes of AMS (hypoxia, electrolyte disturbances, constipation, etc.)
- Investigate other potential sources of infection

Symptoms persist:
- Consider work-up per UTI pathway

Assess response to treatment

Symptoms improve or other etiology found:
- UTI ruled out


1. 4 A’s Test for Delirium Screening or 3D-CAM
2. CAM-ICU (Confusion Assessment Method for the ICU)
3. Sepsis is a common ED diagnosis, based upon non-specific SIRS criteria (below). While many patients with sepsis are not considered “clinically unstable” per the criteria in the algorithm, prompt administration of antimicrobials and infectious work-up are often indicated. Urinalyses and urine cultures may be appropriate in this setting. However, if UTI is ruled-out, consider discontinuation of UTI-directed antibiotics in these patients.
   a. SIRS criteria: ≥ 2 of the following → Temp >38°C (100.4°F) or <36°C (96.8°F); HR > 90 bpm; RR > 20; or WBC >12,000/mm³, <4,000/mm³, or >10% bands
4. UTI Treatment Algorithm
C. UTI Treatment Algorithm

Start Here

**UA abnormal (WBC > 5 and/or nitrite) AND symptoms present**

- Does the patient have bacteriuria AND meet any of the following high-risk criteria?
  - Pregnant
  - Upcoming invasive urologic procedure (if screened)
  - Renal transplant ± 60 days post-transplant

**Yes**

- **Bladder Infection or Cystitis**
  - **Does the patient meet ALL of the following criteria?**
    - Non-pregnant, premenopausal female (if pregnant, see footnote?)
    - Immunocompetent
    - No functional or structural urological abnormalities (spinal cord injury, renal stones, urethral stents)

**No**

- **UTI + Systemic Symptoms or Pyelonephritis**
  - **1st Line Empiric Therapy:** choose one
    - Ceftaxone 2g IV q24h
    - Gentamicin 40mg IV daily dose per pharmacy consult
  - Consider patient’s previous urine culture isolates (if recent) and tailor empiric therapy to include coverage, as appropriate.

**No**

- **Don’t treat asymptomatic bacteriuria**

**Yes**

- **1st Line Empiric Therapy:** choose one
  - Nitrofurantoin 100mg PO bid for 5 days
  - Cephalexin 500mg PO TID for 5 days
  - Fosfomycin 3g PO for 1 dose
  - SMX-TMP 800-160mg PO bid for 3 days

- **2nd Line Empiric Therapy:** choose one
  - Ciprofloxacin 200mg PO bid for 3 days
  - Levofloxacin 250mg PO daily for 3 days

**Utilize shortest effective duration**

- **No bacteremia**
  - 1st Line Therapy
    - Levofloxacin 750 mg PO daily for 5 days
    - Ciprofloxacin 500 mg PO bid for 5-7 days
    - SMX-TMP 800-160 mg PO bid for 7 days
    - IV β-lactam for 7 days
  - If considering oral β-lactams as step-down therapy, total antibiotic duration should be extended to 7-10 days. Options include:
    - Ciprofloxacin 500 mg 3-4 times daily
    - Amoxicillin 500-1000 mg PO TID
    - Amoxiclav 875 mg PO bid

- **Bacteremia**
  - 1st Line Therapy
    - Levofloxacin 750 mg PO daily for 7 days
    - Ciprofloxacin 500-750 mg PO bid for 7 days
    - SMX-TMP 1000-3200 mg (2 DST tablets) PO bid for 7 days
    - IV β-lactam for 7 days
    - 10:14: all other agents

**Reference:**

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*CAUTI most often presents with systemic UTI symptoms that are indistinguishable from pyelonephritis*

1. UNC Antibiotic Dosing Guide (normal renal function, renal insufficiency, hemodialysis) and CRRT Dosing Guide
2. Gentamicin could serve as an effective, broad-spectrum, single dose option for cystitis in individuals with a history of a multi-drug resistant UTI or those with antimicrobial allergies or intolerances.
3. Fluoroquinolones have poor local susceptibility rates for the most likely uropathogens. Refer to UNC Antibiogram.
4. Utilize current UNC Antibiogram on CASP website, under CASP Resource page
5. Oral antibiotics should be considered for patients that meet the following criteria: able to tolerate enteral medication, signs of clinical improvement (defervesced, normal or down-trending WBC, etc.), and availability of an effective oral antibiotic (per confirmed susceptibility data or comparable spectrum of activity).
6. Shorter treatment durations of 7 days are recommended only for patients with gram-negative bacteremia that are considered uncomplicated (identified source, source control obtained, immunocompetent, clinical improvement within 72 hours of effective antibiotic treatment).
7. Recommendations for pregnant women requiring antimicrobial therapy for cystitis or asymptomatic bacteriuria are listed below:
   a. First line (regardless of trimester): β-lactam agents, such as amoxicillin +/- clavulanate or cephalaxin
   b. Second line:
      i. Any trimester: fosfomycin
      ii. Not at term (i.e. pre-38th week) and not near/at delivery: nitrofurantoin
   c. Contact pharmacy if considering alternative antibiotics in a pregnant patient, including SMX-TMP.
D. Urine Culture Interpretation Algorithm

1. **High risk groups warranting treatment of asymptomatic bacteriuria**: pregnant, upcoming invasive urologic procedure, ≤ 60 days post-renal transplant

2. **Antibiogram** – **UNC Medical Center Antibiogram**

3. **S. aureus** is not a common urinary pathogen. Its presence in the urine should raise the suspicion for hematogenous spread. Blood cultures should be obtained and other potential foci of infection should be evaluated (ed: renal abscess, etc.).

4. **Diagnostic Algorithm** for catheter retention or removal

5. **Fluconazole** requires renal adjustment for CrCl ≤ 50 ml/min (**UNC Antibiotic Dosing Guide**). Dosing for cystitis is 3 mg/kg (200mg) and for pyelonephritis is 3-6 mg/kg (200-400mg).

6. **Amphotericin B** requires pre-medication with IV fluid (NS), acetaminophen, and diphenhydramine. Bladder irrigation is discouraged due to limited data supporting clinical benefit; should only be used in consultation with CASP and/or pharmacy. Consider ID consult for all *C. krusei* or *C. glabrata* UTIs if considering treatment.
III. Frequently Asked Questions (FAQs)

1. A patient has a positive urine culture, but the UA is normal. Should this patient be treated with antibiotics?

No, this should not be treated with antibiotics. The absence of pyuria (>5 WBC/hpf on UA) has a high negative predictive value. A normal WBC on the UA is useful in ruling out a UTI. Asymptomatic bacteriuria is common in many patient populations and the prevalence increases with age. Screening and treatment is appropriate for pregnant women and patients prior to certain urologic procedures. Otherwise, asymptomatic bacteriuria should not be treated, as treatment offers no clinical benefit but does pose risk to the patient.

2. A patient has a positive UA (>5 WBC/hpf), but the urine culture has no growth. Should I treat this with antibiotics?

Pyuria alone is not an indication for treatment with antibiotics. Pyuria is a common finding and can be seen in many conditions including catheter use, interstitial nephritis, and sexually transmitted infections. Pyuria should be interpreted in conjunction with the urine culture and patient symptoms for the diagnosis of UTI.

3. A patient is sedated in the ICU or is non-verbal at baseline and can’t report symptoms. How do I know if this patient has a UTI?

When the usual lower urinary tract symptoms (dysuria, frequency, etc.) cannot be assessed, suspect UTI when other signs and symptoms of infection are present with no other identified cause (i.e. fever with no other identified cause). See AMS Algorithm and UA interpretation criteria for additional guidance.

4. If a patient appears septic and is unable to report symptoms (and has no other identified source of infection), should I send a UA with reflex to urine culture?

Yes, in this instance a reflex culture is appropriate because it is important to send the UA with reflex to culture prior to starting antibiotics, and antibiotics should be administered in a timely manner. Antibiotics should not be withheld while awaiting UA interpretation.

5. A patient has *E. coli* pyelonephritis with concurrent *E. coli* bacteremia. What should the treatment duration be?

Patients with pyelonephritis may translocate bacteria to the blood causing a bacteremia. This may happen without causing a sepsis-like picture. Patients should be treated for the same duration that they would have been treated for pyelonephritis, which is generally 7 days. If patient has rapid clinical response, repeat blood cultures to document clearance are not necessary.

References:

6. A patient has more than one bacteria growing in the same urine culture. How should I manage this patient?

This can be common for patients with indwelling Foley catheters and often represents colonization or contamination. This generally should not be treated with antibiotics. The presence of 3 or more species in the urine is suggestive of contamination and a new specimen should be obtained if a UTI is suspected. See Urine Culture Interpretation Algorithm.
7. In which patients would fosfomycin be an appropriate antimicrobial option?

- Fosfomycin could be considered for cystitis due to either *E. coli* or *E. faecalis*. Given that *E. coli* is the most common UTI pathogen, fosfomycin is an appropriate empiric option. The data to support fosfomycin for the treatment of UTI due to other organisms is lacking. However, if a patient is treated with fosfomycin and they clinically improve despite growing a resistant organism (i.e., *Klebsiella pneumoniae*), additional antimicrobial treatment is likely not necessary.
  - The microbiology lab at UNC is unable to perform fosfomycin susceptibility testing, thus all use is empiric.
- The recommended dose for cystitis is 3g PO as a single dose. Multidose regimens of 3g PO q48-72 hours for 2 doses can be considered for cystitis in patients other than young, healthy women. GI adverse effects are more common with these multidose regimens. Use caution in patients with impaired renal function (CrCl < 30 ml/min), as fosfomycin elimination may be prolonged.
- Fosfomycin should NOT be considered a preferred option for the treatment of pyelonephritis due to limited renal distribution. If considering fosfomycin for this indication or any indication other than cystitis, please contact CASP.

8. When can oral cephalosporins be used for UTIs caused by *Enterobacterales* based on the cefazolin susceptibility result?

- For cystitis due to *E. coli*, *K. pneumoniae*, or *P. mirabilis*, cefazolin is used as a surrogate to predict susceptibility to a variety of oral cephalosporins, including cephalexin.
- The typical cefazolin breakpoint for these organisms is ≤ 2 mcg/mL, but that breakpoint is increased to ≤ 16 mcg/mL for cystitis due to the excellent urinary penetration of oral cephalosporins.
- This means that an *E. coli* isolate from a urine culture with a cefazolin MIC of 8 mcg/mL will be reported as:

<table>
<thead>
<tr>
<th>Susceptibility</th>
<th>MIC SUSCEPTIBILITY RESULT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amoxicillin + Clavulanate</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>Resistant</td>
</tr>
<tr>
<td>Ampicillin + Sulbactam</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Cefazolin</td>
<td>Resistant</td>
</tr>
<tr>
<td>Cephalaxin</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>Resistant</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Levofoxacin</td>
<td>Resistant</td>
</tr>
<tr>
<td>Nitrofurantoin</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Piperacillin + Tazobactam</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Tobramycin</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Trimethoprim + Sulfamethoxazole</td>
<td>Susceptible</td>
</tr>
</tbody>
</table>

- Clinical interpretation of this resistance pattern should be based upon the patient’s diagnosis:
  - If cystitis: cephalexin is an appropriate therapeutic option. Cephalexin is preferred over cefdinir for susceptible isolates given favorable adverse effect profile, narrower spectrum of activity, and cost.
  - If pyelonephritis with or without concurrent bacteremia: Oral fluoroquinolones or TMP/SMX is preferred, but oral beta-lactams may be considered for step-down therapy in clinically improved patients. Refer to UTI Treatment Algorithm C (p.5) for dosing and duration recommendations.