Diagnosis and Treatment of Infections of the Urinary Tract in Adult Patients – Adult – Inpatient/Ambulatory Clinical Practice Guideline

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Executive Summary

Guideline Overview

This clinical practice guideline is designed to lead prescribers through the evaluation, diagnosis, and treatment of infections of the urinary tract (UTI). It will focus on difficult diagnostic and treatment scenarios and is intended for use throughout the continuum of care, including outpatient clinics, emergency department, and inpatient wards.

Key Revisions (Interim Update November 2016)

1. Additional comments to fluoroquinolones to limit use based on emerging FDA warnings and empiric therapies reordered.
2. Cefpodoxime replaced by cephalexin as empiric therapy given good UWHC susceptibility data.
3. Updated nitrofurantoin guidance to indicate that nitrofurantoin may be given to patients with CRCL as low as 30 mL/min with close monitoring for resolution of infection.

Key Practice Recommendations

1. In general, urinalysis is a poor predictor of UTI and it is probably indicated to be combined with clinical manifestations before the diagnosis of UTI is made or antimicrobial therapy initiated. (*Class IIa, Level C*)
   - 1.1. Urine color/clarity or odor should not be used alone to diagnosis or start antimicrobial therapy in any patient population. (*Class III, Level B*)
   - 1.2. Urine leukocyte esterase should not be used alone to diagnosis or to initiate antimicrobial therapy in any patient population. (*Class III, Level B*)
   - 1.3. Urine nitrates should not be used alone to diagnosis or to initiate antimicrobial therapy in any patient population. (*Class III, Level B*)
   - 1.4. The presence of bacteria in the urine on microscopic examination without UTI symptoms is NOT recommended for the diagnosis of UTI. (*Class III, Level B*)
2. Pyuria accompanying asymptomatic bacteriuria is NOT an indication for antimicrobial treatment in the general population.[1] (*Class III, Level A*).
   - 2.1. The choice to treat with antimicrobials should only be made after evaluation of the entire clinical picture, consideration for the reasons for pyuria, and identification as the urine as most likely source of infection (see *Diagnosis* section for recommendations for work up of difficult patients).
3. Diagnosis based on results of culture of urine specimen collected in a manner that minimizes contamination is reasonable. (*Class IIa, Level A*)[1]
   - 3.1. The clean-catch method is preferred for collection as it minimizes infection risk inherent in catheterization[2-5] (*Class IIa, Level B*), but specimens with more than five epithelial cells should be considered unreliable and are probably indicated for recollection by clean-catch or straight catheterization.
4. In all elderly patients, **acute mental status change and functional decline are nonspecific clinical manifestations of several circumstances**, including, but not limited to dehydration, hypoxia, or medication (including polypharmacy) adverse reactions. It is reasonable to correlate UTI diagnosis with other signs of systemic inflammation, including leukocytosis.[6] (*Class IIb, Level B*)
   - 4.1. It is may be reasonable to conclude UTI diagnosis in catheterized patients as a diagnosis of exclusion in the absence of localized urinary tract findings.[6] (*Class IIb, Level C*)
   - 4.2. In patients with a clinically suspected UTI, a change in urine character (color or odor) does not add to the diagnostic value. Therefore, urine color and odor should not be used alone to diagnose or start antimicrobial therapy (*Class III, Level B*).[7] However, these two symptoms are also frequently demonstrated in patients with asymptomatic bacteriuria.[8,9]
   - 4.3. Falls without localizing urinary symptoms were not associated with bacteriuria or pyuria.[8,9]
   - 4.4. Elderly patients, especially those with dementia or indwelling Foley catheters, have high rates of bacteriuria and may not have UTI symptoms[10]. Diagnosis of sepsis of a urinary source is NOT recommended in the absence of urinary symptoms because of bacteriuria. (*Class III, Level C*)
5. Nitrofurantoin 100 mg PO BID for five days is recommended as first line therapy for treatment of uncomplicated cystitis.[11] (*Class I, Level A*)
   - 5.1. More than 95% of *E.coli* isolates UWHC as sensitive to nitrofurantoin (UWHC Antibiogram).
   - 5.2. Patients with Stage IV or V kidney disease (CrCL <30 mL/min) should not receive nitrofurantoin.[12] (*Class III, Level A*)
   - 5.3. Patients with Stage III kidney disease (CrCL 31-59 mL/min), nitrofurantoin may be considered, but patients should be monitored closely for resolution of infection.[13,14] (*Class IIa, Level A*)

Treatment of specific organisms

Organism	Treatment Option	Notes
Mixed genitourinary flora in *non-catheterized* patient	Recollection	Generally represent poor specimen collection. Suggest recollection.
Mixed genitourinary flora in *catheterized* patient	Target predominate organism	If no predominating organism, likely colonization. With predominating organism, tailor treatment to said organism.
Staphylococcus saprophyticus	Amoxicillin/clavulanate 500/125 mg PO BID x 7 days OR Amoxicillin 500 mg PO TID x 7-10 days[A]	Second leading cause of UTI in young women. Alternative regimens include ciprofloxacin 250 mg PO BID x 3-7 days, trimethoprim/sulfamethoxazole 160/800 mg PO BID x7 days, or cephalexin 250 mg PO BID x 7-10 days.[A]
Coagulase-negative *Staphylococcus (*non-*saprophyticus)*	Vancomycin IV[B] Goal trough 10-15	Rarely pathogens in the urinary tract and generally represent poor specimen collection, unless from indwelling catheter.
Staphylococcus aureus	Tailored to antimicrobial susceptibilities	Rarely causes ascending infection de novo. Patients should have blood cultures drawn and hematogenous route investigated.
Enterococcus spp. (ampicillin-susceptible)	Amoxicillin 500 mg PO BID x 3-7 days[A]	Susceptibility testing should guide final therapy. Ampicillin susceptibility predicts piperacillin activity. Alternative regimen of vancomycin for patients with true penicillin or β-lactam allergy.
Enterococcus spp. (vancomycin-resistant)	Often asymptomatic and no treatment required. Tailor to antimicrobial susceptibilities. Duration of therapy: Remove catheter: 1-3 days Without catheter: 7-14 days	Frequent colonizer or cause of asymptomatic bacteriuria. Once GI colonization, eradication Is not possible and hence it may frequently appear in the urinary system. Alternative regimens (in preferential order) include nitrofurantoin, fosfomycin, doxycycline, tetracycline, daptomycin 4mg/kg, linezolid PO, or tigecycline.
Proteus spp.	Tailor to antimicrobial susceptibilities x 14 days	High propensity to produce renal calculi. Relapsing *Proteus* infections should prompt an evaluation for urinary calculi.
Anaerobic organisms	Empiric treatment NOT recommended	Rarely pathogens in the urinary tract and the microbiology lab will not routinely perform cultures.
Gardnerella vaginalis	Recollection	May be isolated from urine but rarely pathogenic. Investigate sample quality to assess pathogenicity.
Ureaplasma urealyticum	Recollection/special collection	May be isolated from urine but rarely pathogenic. Investigate sample quality to assess pathogenicity.
Mycoplasma hominis	Recollection/special collection	May be isolated from urine but rarely pathogenic. Investigate sample quality to assess pathogenicity.
Candida albicans	Fluconazole 100-400 mg PO daily x14 days[A]	Remove or replace catheter if appropriate.
Candida glabrata Low risk		Remove or replace catheter if appropriate.
Candida glabrata High risk (includes severely immunocompromised and febrile; renal transplant; patients with retained genitourinary hardware; and patients undergoing genitourinary procedure)	Remove or replace catheter. Treatment with fluconazole 400-800 mg IV/PO daily[A]	Most common organism in UW renal transplant patients; however, most were asymptomatic. Imaging of the kidneys and collection system should be performed Non-fluconazole antifungals and echinocandins should not be used for treatment. Bladder irrigation with amphotericin B 50 mg daily x 7-10 days.
Corynebacterium urealyticum	Vancomycin IV[B] Goal trough 10-15	Common in renal transplant population, otherwise investigate sample quality to assess pathogenicity. Consider urology consultation as this organism may cause encrusting pyelitis.

Companion Documents

- Renal Function-based Dose Adjustments – Adult – Inpatient Clinical Practice Guideline
- Catheter-Associated Urinary Tract Infection (CAUTI) – Adult – Inpatient Clinical Practice Guideline
- Antibiotics for the Treatment of Gram-negative Infections – Adult – Inpatient Clinical Practice Guideline
- UWHC Antibiogram
- Treatment of Patients with Reported Allergies to Beta-Lactam Antibiotics – Adult – Inpatient Clinical Practice Guideline
- Intravenous Vancomycin Use – Adult – Clinical Practice Guideline
- Preventative Health Care – Pediatric/Adult - Ambulatory

Pertinent UWHC Policies & Procedures

- Indwelling Urinary Catheter Removal – Inpatient – Adult Protocol [25]
- Bladder Management – Pediatric – Inpatient [8]
- Bladder Management – Inpatient – Adult Protocol [26]
- Acute Spinal Cord Injury Bladder Management – Adult – Inpatient [144]
- UWHC Policy 3.14AP: Sterile Intermittent Catheterization Program
- UWHC Policy 3.15AP: Sterile Intermittent Straight Catheterization for Bladder Decompression and/or Specimen Collection (Adult and Pediatric)
- UWHC Policy 3.18A: Replacement and Care of a Suprapubic Catheter
- UWHC Policy 3.28: Collecting a Urine Specimen from an Indwelling Urinary Catheter
- UWHC Policy 3.30: Continuous Bladder Irrigation (CBI) (Adult)
- UWHC Policy 3.31: Insertion, Removal and Maintenance of an Indwelling Urinary Catheter (IUC) (Adult and Pediatric)
- UWHC Policy 13.12: Basic Care Standards (Adult)

Patient Resources

- Health Facts for You #4286: Urinary Tract Infections: Information for Women
- Health Facts for You #5914: Urodynamic Testing
- Health Facts for You #7355: Urinary Catheters and Urinary Tract Infections
- Health Facts for You #7833: Urinary Catheters and Urinary Tract Infections (Spanish)

Scope

Disease/Condition

This clinical practice guideline is designed to lead prescribers through the evaluation, diagnosis, and treatment of infections of the urinary tract (UTI).

Clinical Specialty

All medical specialties

Intended Users

Physicians, Advanced Practice Providers, Nurses, and Pharmacists

Objective

To decrease number of urine cultures ordered per 1000 patient days.
To optimize antibiotic utilization for treatment of UTI.

Target Population

Patients with signs and symptoms of urinary tract infection cared for in outpatient clinics, the emergency department, and inpatient wards.

Interventions and Practices Considered

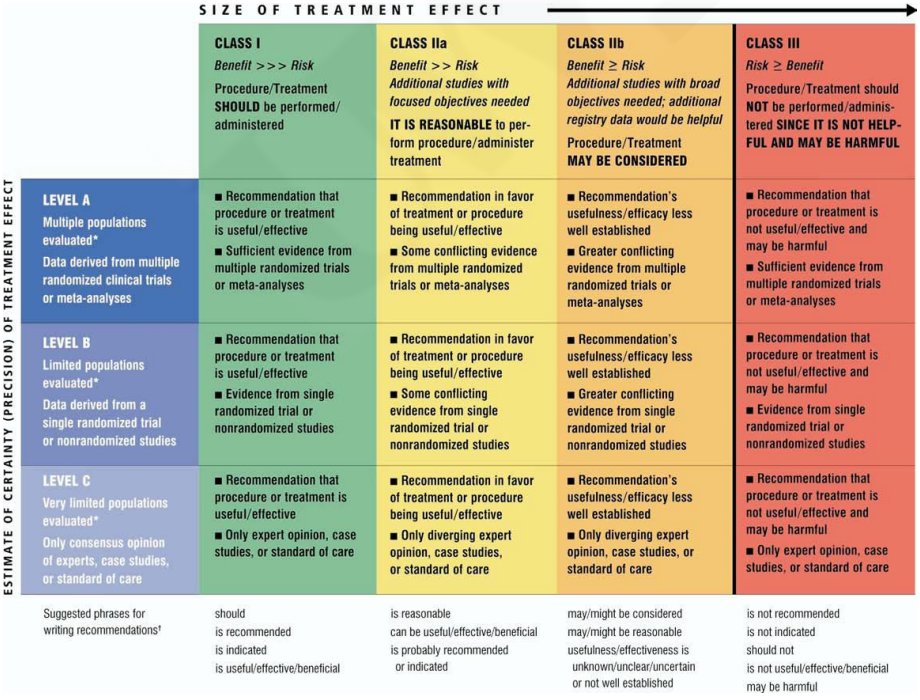
Diagnosis of urinary tract infections, treatment of urinary tract infections with antimicrobials, and avoidance of antimicrobial use in patients without urinary tract infection following evaluation.

Major Outcomes Considered

1. Successful treatment of urinary tract infections measured by successful infection resolution
2. Avoidance of antimicrobial use in patients without urinary tract infection

Methodology

Electronic database searches (i.e., PUBMED) were conducted and workgroup members to collect evidence for review. Expert opinion, clinical experience, and regard for patient safety/experience were also considered during discussions of the evidence. A modified Grading of Recommendations Assessment, Development and Evaluation (GRADE) developed by the American Heart Association and American College of Cardiology was used to assess the Quality and Strength of the Evidence in this Clinical Practice Guideline.[15]



Definitions (modified from Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases 7th ed.)

1. *Significant Bacteriuria*
   1.1. Greater than or equal to 10^5 bacteria per mL of voided urine
      1.1.1. In healthy women with acute cystitis , lower colony counts may represent significant bacteriuria
   1.2. Greater than or equal to 10^3 bacteria per mL of catheterized urine or symptomatic female
2. *Asymptomatic bacteriuria* – significant bacteriuria in patients without symptoms
3. *Cystitis* – syndrome involving dysuria, frequency, urgency, and occasionally suprapubic tenderness
   3.1. These symptoms may also be caused by urethritis (e.g. gonorrhea or Chlamydia) or non-infectious causes
4. *Acute pyelonephritis* – syndrome often involving flank pain, tenderness, and fever often associated with cystitis symptoms. Flank pain is not required for this diagnostic consideration.
   4.1. These symptoms may also be caused by non-infectious etiologies (e.g. renal infarction or calculus)
5. *Uncomplicated UTI* – infection in a structurally and neurologically NORMAL urinary tract
6. *Complicated UTI* – infection in a urinary tract with functional or structural abnormalities, including indwelling catheters and calculi
   6.1. Includes infections in **men**, pregnant women, children, and other patients who are hospitalized or in the health-care setting for extended periods of time
7. *Relapse* – recurrence of bacteriuria with the same infecting organism(s) caused by persistence of the organism(s) in the urinary tract
8. *Reinfection* – recurrence of bacteriuria with a different infecting organism than the original infecting bacterium. This may also be the same organism if it persisted in the vagina or feces.
9. *Sepsis of a urinary source* – Sepsis syndrome caused by UTI
10. *Chronic UTI* – persistence of the same organism for months or years with clinical relapses after treatment.
11. *Chronic bacteriuria* – persistence of one or more bacteria colonizing the urinary tract in the absence of clinical symptoms
12. *Recurrent UTI* – recurrence of episodes of uncomplicated or complicated UTI with the same or different organism beyond the expected frequency
13. *TMP-SMX* – Trimethoprim-sulfamethoxazole
14. *GU* – Genitourinary

Introduction

Infections of the urinary tract are one of the most common sites for bacterial infection and are the most common type of infection in the United States, utilizing $1.6 billion dollars in 2002.[16] The accurate diagnosis and treatment of urinary tract infections plays an important role in cost-effective medical care and appropriate antimicrobial utilization. Some patients receive antibiotic therapy when treatment is not indicated. The prevalence of bacteriuria in young non-pregnant women is 1-5%.[17,18] As patients age, the rate of asymptomatic bacteriuria increases.[10] The rate of bacteriuria in men is much lower, fewer than 0.1%.[19] **The presence of bacteria in the urine is not necessarily an indication for antimicrobial therapy.** Indications for treatment are discussed in the guideline below. Preventative care and prophylactic agents may reduce the risk of UTI and are discussed in the guideline as well. However, manipulation of the urinary tract via instrumentation of urinary tract increases the risk of developing UTI. One catheterization of the bladder results in UTI in 1% of ambulatory patients[20] and indwelling catheters with open drainage systems results in a UTI in nearly 100% of patients in three to four days.[21,22]

The incidence of asymptomatic bacteriuria increases with age (10% of males and ≥ 20% of females older than 65 years)[1,10,23-27] **and the overuse of antibiotics leads to antibiotic resistance and adverse effects, including risk of *C. difficile* infection.[28-32]** The choice to treat with antimicrobials should only be made after evaluation of the entire clinical picture and identification as the urine as most likely source of infection.

Recommendations

Diagnosis (see *Appendix 1*)

1. **Signs and symptoms – General principles**
   1.1. In patients with dysuria, frequent or urgent urination, suprapubic pain or tenderness a diagnosis of urinary tract infection,[33,34] sexually transmitted infection, or noninfectious cystitis should be strongly considered. [20,21] (*Class I, Level A*)
      1.1.1. Other diagnoses may need to be considered based on clinical presentation. (*Class IIb, Level C*)
   1.2. Vaginal symptoms (e.g. vaginitis, urethritis) should prompt alternative diagnoses.[33,34] (*Class I, Level A*) Queries must be made for these symptoms to avoid misdiagnosis.

1.3. Diagnosis based on results of culture of urine specimen collected in a manner that minimizes contamination is reasonable. (*Class IIa, Level A*)[1]
   1.3.1. The clean-catch method is preferred for collection as it minimizes infection risk inherent in catheterization[2-5] (*Class IIa, Level B*), but specimens with more than five epithelial cells should be considered unreliable and are probably indicated for recollection by clean-catch or straight catheterization.
1.4. Asymptomatic women: bacteriuria is defined as two consecutive voided urine specimens with isolation of the same bacterial strain with quantitative counts $\geq 10^5$ CFU/mL[1]
1.5. Men: a single clean-catch voided urine specimen with one bacterial species isolated with quantitative count $\geq 10^5$ CFU/mL.[1]
1.6. Catheterized men or women: a single urine specimen with one bacterial species isolated with quantitative count $\geq 10^2$ CFU/mL may be considered significant (since the natural history is for colony counts to increase to 10^5 CFU/mL in 48 to 72 hours).[35]
1.7. Paraplegic patients may only present with fever or hypothermia, increased spasticity, and/or autonomic dysreflexia.[36] Consideration of UTI diagnosis is reasonable with these signs and symptoms. (*Class IIb, Level B*)

2. **Clinical laboratory findings for the diagnosis of bacteriuria (not UTI) and decision to start antimicrobial therapy**
2.1. **In general, urinalysis is a poor predictor of UTI and it is probably indicated to be combined with clinical *manifestations before the diagnosis of UTI is made or antimicrobial therapy initiated. (Class IIa, Level C)***
2.2. Urine color/clarity or odor should not be used alone to diagnosis or start antimicrobial therapy in any patient population. (*Class III, Level B*)
   2.2.1. Visual inspection of urine clarity is not helpful in diagnosing UTI in women. This is not recommended.[37] (*Class III, Level B*)
   2.2.2. In patients with a clinically suspected UTI, a change in urine character (color or odor) does not add to diagnostic value. Therefore, urine color and odor should not be used alone to diagnose or start antimicrobial therapy (*Class III, Level B*).[7]
   2.2.3. Foul smelling and/or cloudy urine is not a reliable indicator of infection in catheterized patients and should NOT be an indication alone for testing the urine or starting antimicrobial therapy.[38] (*Class III, Level A*)
2.3. Urine leukocyte esterase should not be used alone to diagnosis or to initiate antimicrobial therapy in any patient population. (*Class III, Level B*)
   2.3.1. A dipstick leukocyte esterase test has high sensitivity and specificity (80-90% and 95-98%, respectively); however, a positive leukocyte esterase **alone** is NOT recommended for diagnosis of UTI.[39,40] (*Class III, Level B*)
   2.3.2. A negative leukocyte esterase in the presence of UTI symptoms may still prompt a urine culture if clinically suspected[39,40] (*Class IIa, Level B*), but also prompt a search for urethritis, vaginitis, or sexually transmitted infection.
   2.3.3. A negative leukocyte esterase AND a negative urine nitrate probably rules out infection in pregnant women, elderly patients, family medicine patients, and urology patients.[41] Alternative diagnosis investigation are probably indicated in this scenario (*Class IIb, Level B*)
2.4. Urine nitrates should not be used alone to diagnosis or to initiate antimicrobial therapy in any patient population. *(Class III, Level B)*
   2.4.1. Urine nitrate has low false-positive rate. Diagnosis of UTI can be indicated in a patient with elevated urine nitrate.[39,42] (*Level IIa, Level B*)
   2.4.2. A negative leukocyte esterase AND a negative urine nitrate probably rules out infection in pregnant women, elderly patients, family medicine patients, and urology patients.[41] Alternative diagnosis investigation are probably indicated in this scenario (*Class IIb, Level B*)
2.5. Quantitative urine WBC *should not be used alone* to diagnosis or to initiate antimicrobial therapy in any patient population. (*Class III, Level B*)
   2.5.1. In neutropenic or leukopenic patients, the WBC count may be low and reflex culture may not occur. The Microbiology Lab should be contacted and an order for urine culture ordered if urinary symptoms are present and urinary source of infection is suspected. (*Class IIb, Level C*)
   2.5.2. Patients with oliguria or anuria (including dialysis) usually have some degree of pyuria.
2.6. Urine Bacteria
   2.6.1. The presence of bacteria in the urine on microscopic examination without UTI symptoms is NOT recommended for the diagnosis of UTI.[42] (*Class III, Level B*)
   2.6.2. In patients *without* an indwelling catheter the following cutoffs should define clinically significant bacteriuria[6]:
      - $\geq 10^5$ CFU/mL of ≤ 2 species of microorganisms in voided culture
      - $\geq 10^2$ CFU/mL of any number of microorganisms in a straight cath culture

2.6.3. In patients *with* an indwelling catheter, ≥10^3 CFU/mL of any organism(s) defines clinical significant bacteriuria since this is predictive of higher numbers within 48 hours.[6]

2.7. Urine squamous epithelial cells

2.7.1. A good urine specimen has fewer than five epithelial cells per low power field on UA. Recollection or straight catheterization may be considered for poor specimens. (*Class IIb, Level C*)

2.8. Indications for urine culture in patients with a urinary catheter in place include[6,43-47] (*Class I, Level C*):

- new fever or rigors with negative clinical assessment for other more likely etiologies
- acute alteration of mental status with negative clinical assessment for other more likely etiologies
- suprapubic pain or tenderness
- acute gross hematuria
- costovertebral pain or tenderness to palpation
- increased spasticity or autonomic dysreflexia in patients with altered neurologic sensation
- alteration in medical condition (e.g. unexplained increase or decrease in WBC count) with negative clinical assessment for other more likely etiologies of a patient for whom fever may not be a reliable sign

2.9. Indications for urine culture in non-catheterized patients with pyuria or hematuria (without squamous epithelial cells on urinalysis) include (*Class I, Level C*):

- suspected pyelonephritis with classic signs and symptoms[48]
- symptoms of cystitis or prostatitis in the absence of STI[48]
- new fever or rigors after other more likely etiologies have been excluded
- acute alteration of mental status after other more likely etiologies have been excluded
- alteration in medical condition (e.g. unexplained increase or decrease in WBC count) of a patient for whom fever may not be a reliable sign
- rarely, as a test of cure when medically indicated

2.10. Inappropriate indications for urine culture include (*Class I, Level C*):

- abnormal urine quality (e.g. color, odor, turbidity)[37,38,44]
- routine component of "pan-culture" in fever workup until other etiologies have been excluded
- asymptomatic pyuria not meeting above criteria
- asymptomatic elderly, diabetic, or institutionalized patient not meeting criteria above
- **routine documentation of bacteriuria clearance**

3. **Dealing with altered mental status in the elderly**

3.1. In all elderly patients, **acute mental status change and functional decline are nonspecific clinical manifestations of several circumstances**, including, but not limited to dehydration, hypoxia, or medication (including polypharmacy) adverse reactions. It is reasonable to correlate UTI diagnosis with other signs of systemic inflammation, including leukocytosis.[6] (*Class IIb, Level B*)

3.1.1. It is may be reasonable to conclude UTI diagnosis in catheterized patients as a diagnosis of exclusion in the absence of localized urinary tract findings.[6] (*Class IIb, Level C*)

3.1.2. In patients with a clinically suspected UTI, a change in urine character (color or odor) does not add to the diagnostic value. Therefore, urine color and odor should not be used alone to diagnose or start antimicrobial therapy (*Class III, Level B)*.[7] However, these two symptoms are also frequently demonstrated in patients with asymptomatic bacteriuria.[8,9]

3.1.3. Falls without localizing urinary symptoms were not associated with bacteriuria or pyuria.[8,9]

3.2. Signs and symptoms usually associated with UTI are frequently absent in the catheterized patient.[45] **Foul smelling and/or cloudy urine is not a reliable indicator of infection and should NOT be an indication alone for testing the urine or starting antimicrobial therapy**.[38] (*Class III, Level A*)

3.3. Elderly patients, especially those with dementia or indwelling Foley catheters, have high rates of bacteriuria and may not have UTI symptoms[10]. Diagnosis of sepsis of a urinary source is NOT recommended in the absence of urinary symptoms because of bacteriuria. (*Class III, Level C*)

3.4. UTI diagnosis is reasonable when there are localizing genitourinary signs and symptoms and a positive urine culture result.[6,46] (*Class IIa , Level B*)

3.5. Diagnosis of UTI is reasonable by meeting the following clinical criteria (must meet both Criteria 1 and 2).[6,46] (*Class IIa, Level B*)

No Indwelling Catheter	With Indwelling Catheter
Criteria 1 (must have at least one subcriterion) • Acute dysuria or acute pain, swelling, or tenderness of the testes, epididymis, or prostate • Fever or leukocytosis AND localized urinary tract criteria (acute CVA pain/tenderness, suprapubic pain, gross hematuria, new or increased incontinence, urinary frequency or urgency)	Criteria 1 (must have at least one subcriterion) • Fever, rigors, or new-onset hypotension, with no alternative site of infection • Acute change in mental status or acute functional decline, with no alternative diagnosis AND leukocytosis • New-onset suprapubic pain or CVA pain/tenderness • Purulent discharge from around the catheter or acute pain, swelling, or tenderness of the testes, epididymis, or prostate
Criteria 2 (must have at least one subcriterion) • ≥ 10^5 CFU/mL of ≤ 2 species of microorganisms in voided culture • ≥ 10^2 CFU/mL of any number of microorganisms in a straight cath culture	Criteria 2 • Urinary catheter specimen culture with ≥10^5 CFU/mL of any organism(s) (Urinary catheter specimens should be collected following replacement of the catheter if the current catheter has been in place longer than14 days)

3.6. A UTI diagnosis is reasonable without localizing symptoms if a blood culture isolate is the same as the organism isolated from the urine and there is not alternate site of infection.[6](*Class IIa, Level B*)

3.7. In the absence of a clear alternative source of infection, fever or rigors with a positive urine culture result in the non-catheterized resident, or acute confusion in the catheterized patient will often be treated as UTI. However, evidence suggests that most of these episodes are likely not due to infection of the urinary tract.[6] (*Class IIb, Level B*)

3.8. Residents with intermittent or condom catheters are at lower risk for UTI and are probably in the same risk category as those with no indwelling catheter.[46] (*Class IIa, Level C*)

4. **Outpatient Visit – lab confirmation/screening**

4.1. In women with symptoms consistent with UTI and without a history of laboratory-confirmed UTI, an office visit with UA is recommended.[33] (*Class I, Level B*)

4.1.1. Women with frequent UTI recurrences and prior confirmation by diagnostic tests who are aware of their symptoms may be empirically treated.[33,34] (*Class I, Level B*)

4.2. Because of the small risk of iatrogenic introduction of bacteria into the bladder, urinary catheterization to obtain a specimen is NOT routinely recommended.[20,21] (*Class III, Level B*) However, with patients for whom the quality of a clean catch urine sample has or may be compromised (i.e. more than 10 epithelial cells), catheterization may be considered. (*Class IIb, Level C*)

5. **Special populations**

5.1. Pregnancy

5.1.1. Pregnant women should be screened for bacteriuria by urine culture at least once in early pregnancy, and they should be treated if the results are positive, assuming collection quality is adequate, regardless of symptoms.[33] (*Class I, Level A*)

5.2. Renal Transplant

5.2.1. In patients with a history of renal transplant it is reasonable to screen for bacteriuria by urine culture with every clinic visit during the early postoperative period for the first three to six months and to treat if the results are positive based on the renal transplant standard operating procedures. (*Class IIa, Level B*)

5.2.2. Candiduria in the renal transplant patient is likely a marker of severity of illness and treatment of asymptomatic candiduria does not appear to improve outcomes. Removal of the indwelling bladder catheter, if present, is reasonable.[49] (*Class IIb, Level B*)

5.3. Elderly, community dwelling patients

5.3.1. Screening for bacteriuria in the elderly, community dwelling patients, with or without indwelling catheter is not recommended.[50,51] (*Class III, Level B*)

5.3.1.1. Elderly patients in the community have a prevalence of asymptomatic bacteriuria of up to 19%[50], or higher in older age groups.

5.4. Patients from skilled nursing facilities or institutionalized patients

5.4.1. Screening for bacteriuria in elderly, institutionalized patients with or without indwelling catheter is not recommended.[50,51] (*Class III, Level A*)

5.4.1.1. Elderly patients in a long term care facility have a prevalence of asymptomatic bacteriuria of up to 50%.[51]

5.5. Up to 23% of patients with a short-term (fewer than two weeks) indwelling catheters have bacteriuria.[50] Up to 100% of patients with a long-term (longer than two weeks) indwelling catheters have bacteriuria.[52]

5.6. Diabetic women

5.6.1. Screening for bacteriuria in diabetic women is NOT recommended.[53] (*Class III, Level A*)

5.6.1.1. Up to 27% of women with diabetes have asymptomatic bacteriuria.[53]

Asymptomatic Bacteriuria

6. Pyuria accompanying asymptomatic bacteriuria is NOT an indication for antimicrobial treatment in the general population.[1] (*Class III, Level A*).
   6.1. The choice to treat with antimicrobials should only be made after evaluation of the entire clinical picture, consideration for the reasons for pyuria, and identification as the urine as most likely source of infection (see *Diagnosis* section for recommendations for work up of difficult patients).
7. **Pregnancy** - Pregnant women should be screened for bacteriuria by urine culture at least once in early pregnancy, and they should be treated if the results are positive regardless of symptoms.[33] (*Class I, Level A*)
   7.1. Antimicrobial treatment of asymptomatic bacteriuria decreases the risk of pyelonephritis in pregnant women by 9 to 20 fold.[54]
   7.2. Cephalexin is reasonable for treatment of asymptomatic bacteriuria in pregnancy since cephalosporins are considered among the safest treatments during pregnancy.[55] (*Class IIa, Level B*)
   7.3. Treatment with sulfonamides (trimethoprim-sulfamethoxazole (TMP-SMX) Pregnancy Category C) or nitrofurantoin (Pregnancy Category B) is reasonable at doses listed below given their historical use in pregnant women without issue. (*Class IIa, Level B*)
      7.3.1. TMP-SMX may interfere with folic acid metabolism. No well-controlled studies exist in pregnant women; however, a retrospective study of 186 pregnancies showed a reduced incidence of congenital abnormalities in women receiving TMP-SMX.[56] The use of TMP-SMX in pregnant women is cautioned given theoretical detriments. (*Class III, Level B*).
      7.3.2. Nitrofurantoin use in pregnant women should be avoided when the onset of labor is imminent because of the possibility of hemolytic anemia due to immature erythrocyte enzyme systems. Use of nitrofurantoin after 38 weeks is contraindicated.[57] (*Class III, Level B*)
   7.4. Fosfomycin (Pregnancy Category B) has been used safely and effectively in the treatment of bacteriuria in pregnant women[58,59] and may be considered for the treatment of resistant organisms. [45,46] (*Class IIa, Level B*)
   7.5. A meta-analysis was unable to determine an optimal duration of anti-infective therapy.[60] Therefore, a single-dose, three-day, four-day, or seven-day treatment regimen may be considered. (*Class IIa, Level A*)
8. The incidence of asymptomatic bacteriuria increases with age (10% of males and 20% of females older than 65 years)[1,10,23-27] and the overuse of antibiotics leads to antibiotic resistance, exposes patients to potential side effects, and has not been shown to reduce mortality[28-31]; therefore, treatment for patients without symptoms is NOT recommended (*Class III, Level B*)
9. The treatment or prophylaxis of asymptomatic bacteriuria may be considered in patients with an urinary stent.[61] (*Class IIb, Level B*)
   9.1. Urinary stents in place for fewer than 2 weeks have not demonstrated an increased rate of colonization.[61]
10. **Acute kidney injury and chronic renal failure**
   10.1. In healthy women, E.coli bacteriuria is not associated with a decline in renal function or with the development of end-stage renal failure.[62]
   10.2. UTI and pyelonephritis are rarely considered on the differential diagnosis of acute kidney injury.[63] Patients with AKI and bacteriuria should be considered for pyelonephritis IF the clinical picture supports infection of the urinary tract. (*Class IIb, Level C*)
   10.3. Antibiotics should be considered in a patient with clinical signs of UTI and AKI.[1,48]
   10.4. In patients with chronic renal failure, 27% have bacteriuria and 38% have pyuria; however, only 7% had symptomatic UTI.[64] No significant correlation was found between bacteriuria and urine output. Pyuria was significantly more frequent in oliguric or hemodialysis patients. Therefore, in oliguric patients with chronic renal failure, asymptomatic bacteriuria is common and the patient should be evaluated for systemic symptoms before beginning antimicrobial therapy.

Empiric and Definitive Treatment of Uncomplicated Cystitis

11. **The therapeutic options below are listed in their preferred order.**
12. The optimal therapy depends on many factors and each medication has risks and benefits which must be considered when choosing treatment

13. The choices below may be used for the empiric treatment of uncomplicated cystitis. Definitive treatment should be guided by susceptibility results. (*Class IIb, Level C*)
    13.1. Fosfomycin susceptibility testing is limited based on limited approval by the FDA; however, resistance rates in *E.coli* [65] and other multi-drug resistant organisms is low.[66]

14. **Nitrofurantoin**
    14.1. Nitrofurantoin 100 mg PO BID for five days is recommended as first line therapy for treatment of uncomplicated cystitis.[11] (*Class I, Level A*)
        14.1.1. More than 95% of *E.coli* isolates UWHC as sensitive to nitrofurantoin (UWHC Antibiogram).
    14.2. Patients with Stage IV or V kidney disease (CrCL <30 mL/min) should not receive nitrofurantoin.[12] (*Class III, Level A*)
    14.3. Patients with Stage III kidney disease (CrCL 31-59 mL/min), nitrofurantoin may be considered, but patients should be monitored closely for resolution of infection.[13,14] (*Class IIa, Level B*)
    14.4. In the case of diagnostic uncertainty with regards to pyelonephritis, nitrofurantoin should not be chosen since tissue concentrations are minimal.[67] (*Class III, Level A*)

15. **Trimethoprim-sulfamethoxazole (TMP-SMX)**
    15.1. TMP-SMX 160-800 mg PO BID for three days is recommended for the treatment of outpatient uncomplicated cystitis. (*Class I, Level A*)
        15.1.1. TMP-SMX doses may need to be adjusted for renal function. See *Renal Function-based Dose Adjustments – Adult – Inpatient Clinical Practice Guideline*.
        15.1.2. Recommendation for use is based on resistance rates of uropathogens at UWHC during the past year. If the local resistance rate exceeds 20%, use is not recommended. (*Class III, Level C*)
        15.1.3. The current rate of outpatient *E.coli* urine-isolated resistance is 18% (data provided from UWMF clinics and EXCLUDES urology and transplant clinics).
        15.1.4. The current rate of inpatient, common Gram-negative urine isolates (*Enterobacter cloacae, E. coli, Klebsiella oxytoca, Klebsiella pneumoniae, Proteus mirabilis,* and *Pseudomonas aeruginosa)* resistant to TMP-SMX is 24%.

16. **Fluoroquinolones**
    16.1. Ciprofloxacin 250 mg PO twice daily or levofloxacin 250 mg PO daily for three days is reasonable for the treatment of uncomplicated cystitis (*Class IIb, Level A*); however fluoroquinolone-associated collateral damage as manifested by increased resistance rates is an important issue to consider when choosing fluoroquinolone treatment over alternatives.[68]
        16.1.1. The current rate of fluoroquinolone resistance in outpatient *E.coli* urine isolates is 10% (data provided from UWMF clinics and EXCLUDES urology and transplant clinics).
        16.1.2. The current rate of inpatient, common Gram-negative urine isolates (*Enterobacter cloacae, E. coli, Klebsiella oxytoca, Klebsiella pneumoniae, Proteus mirabilis,* and *Pseudomonas aeruginosa)* resistant to fluoroquinolones is 19%.
    16.2. Levofloxacin may also be considered for the treatment of concomitant lower respiratory tract infection and urinary tract infection as an inpatient.
    16.3. Ciprofloxacin and levofloxacin doses may need to be adjusted for renal function. See *Renal Function-based Dose Adjustments – Adult – Inpatient Clinical Practice Guideline*.
    16.4. Moxifloxacin should not be used for UTI treatment because it achieves very low urine levels.[69] (*Class III, Level B*)

17. **β-lactam antibiotics**
    17.1. Short course (three days) of β-lactam antibiotics are generally less effective than other antimicrobials used for short course therapy and should not be used as first-line agents for short course therapy unless the patient is unable to receive alternatives listed above.[48] (*Class III, Level A*).
        17.1.1. Cefpodoxime 100 mg PO BID demonstrated equivalent clinical and microbiological outcomes as trimethoprim/sulfamethoxazole at day four through seven. [70]
            17.1.1.1. Cephalexin is reasonable as empiric therapy given high susceptibility rates at UW Health. (*Class IIa, Level C*)
        17.1.2. When the antimicrobial susceptibility of the bacteria is known at treatment initiation, amoxicillin 500mg PO BID or cephalexin 500mg PO BID for seven days (if susceptible) is as effective as agents listed above and are reasonable. (*Class IIa, Level B*)
        17.1.3. If a β-lactam agent is chosen, therapy for a full seven-day course is probably recommended.[48] (*Class IIa, Level A*)
    17.2. β-lactam antibiotic doses may need to be adjusted for renal function. See *Renal Function-based Dose Adjustments – Adult – Inpatient Clinical Practice Guideline*.

18. **Fosfomycin**
    18.1. Fosfomycin 3 g PO once is recommended for treatment of uncomplicated cystitis.[71] (*Class I, Level B*)
    18.2. Fosfomycin 3 g PO every 72 hours for 3 doses is reasonable for treatment of complicated cystitis without bacteremia.[71] (*Class IIa, Level B*)
        18.2.1. Under unusual circumstances, repeat dosing for durations longer than seven days may be considered for treatment of virulent, multi-drug resistant bacteria. (*Class IIa, Level C*)
    18.3. Fosfomycin has broad spectrum of activity against Gram-negative and Gram-positive organisms including vancomycin-resistant *Enterococcus* (VRE) and extended spectrum β-lactamases (ESBL) and is effective for the treatment such infections in the urinary tract.[72]
    18.4. In the case of diagnostic uncertainty with regards to pyelonephritis or with potential bacteremia, fosfomycin should generally not be chosen since serum concentrations are minimal.[73] (*Class III, Level A*).

Treatment of Complicated UTI

19. In general, broader spectrum empiric treatment followed by a tailoring of therapy based on culture and susceptibility results may be reasonable. (*Class IIb, Level C*)
20. If the patient is moderately ill without a history of resistant uropathogens and without recent fluoroquinolone use, ciprofloxacin or levofloxacin monotherapy is reasonable[74,75] (*Class IIa, Level B*), although the recent 20% outpatient resistance rates at UWHC and UWMF suggests this monotherapy strategy may not be appropriate.
    20.1. UWHC and UWMF outpatient clinics generally have lower fluoroquinolone resistance rates than inpatient wards
    20.2. UWHC Hospital resistance rates may approach 20%.
21. If the patient is severely ill, it is reasonable to select broad-spectrum Gram-negative coverage based on the relevant UWHC Antibiogram.[74,75] (*Class IIa, Level B*)
    21.1. See *Treatment of Acute Pyelonephritis* section for management approach.
    21.2. Combination initial empiric therapy of a fluoroquinolone and ceftriaxone may be considered. (*Class IIb, Level C*)
22. Surgical intervention to correct an anatomic abnormality or alleviate the functional abnormality can be beneficial, especially for severely ill patients.[44,74,75] (*Class IIb, Level B*)
23. The duration of therapy for complicated UTI is prolonged, and should be seven days for a rapid response or ten to fourteen days for delayed response.[44,75] (*Class I, Level A*)

Treatment of Acute Pyelonephritis

24. **General Principles**
    24.1. In patients with symptoms consistent with pyelonephritis, a urine culture should be obtained and sent for culture. Treatment should be tailored as soon as possible to the infecting organism.[48] (*Class I, Level C*)
        24.1.1. Outpatient *E.coli* resistance at UWHC for calendar year 2011 was 10% to ciprofloxacin and 18% for trimethoprim/sulfamethoxazole (data provided from UWMF clinics and EXCLUDES urology and transplant clinics).
        24.1.2. The current rate of inpatient, common Gram-negative urine isolates (*Enterobacter cloacae, E. coli, Klebsiella oxytoca, Klebsiella pneumoniae, Proteus mirabilis,* and *Pseudomonas aeruginosa)* resistant to TMP-SMX is 24%.
    24.2. The choices below may be used for the empiric treatment of pyelonephritis. Definitive treatment guided by susceptibility results may be considered. (*Class IIa, Level B*)
    24.3. Nitrofurantoin and fosfomycin should not be used for the treatment of pyelonephritis as described in Section #14 and Section #18.[67,73]

25. **Outpatient treatment options**
    25.1. **Fluoroquinolone**
        25.1.1. Oral ciprofloxacin 500 to 750 mg PO BID for seven days or levofloxacin 500 to 750 mg PO daily for five days, with or without an initial IV dose, is recommended for therapy not requiring hospitalization.[48] (*Class I, Level A*)
            25.1.1.1. Ciprofloxacin and levofloxacin doses may need to be adjusted for renal function. See *Renal Function-based Dose Adjustments – Adult – Inpatient Clinical Practice Guideline*.
        25.1.2. Ceftriaxone 1 gram IV or aminoglycoside (IV/IM), such as tobramycin or gentamicin 5 mg/kg, (may be dose adjusted for renal function) may be reasonably substituted for the IV fluoroquinolone.[48] (*Class IIa, Level B*)

26. **Inpatient treatment options**
    26.1. **Based on current antibiogram resistance rates, initial empiric, strong consideration for combination therapy may be reasonable.** (*Class IIb, Level C*)
    26.2. **Ceftriaxone**

26.2.1. Since the susceptibility prevalence is greater than 90%, treatment of pyelonephritis with ceftriaxone 1 g IV every 24 hours is recommended.[76] (*Class IIa, Level B*)
26.2.1.1. Two gram doses are unnecessary and not recommended. (*Class III, Level C*)
26.2.2. Treatment should continue until pathogen susceptibilities are known and targeted therapy initiated.[48] (*Class I, Level C*)

26.3. **Aminoglycosides**
26.3.1. Once-daily tobramycin or gentamicin is effective for the treatment of pyelonephritis.[48] (*Class I, Level C*)
26.3.1.1. Patients with recent exposure to fluoroquinolones or β-lactams may be considered for empiric aminoglycoside therapy instead of a fluoroquinolone.[77] (*Class IIb, Level C*)
26.3.1.2. Aminoglycoside dosing recommendations can be found in the *Antibiotics for the Treatment of Gram-negative Infections – Adult – Inpatient Clinical Practice Guideline*.
26.3.2. Treatment should continue until pathogen susceptibilities are known or for up to five days, whichever is shorter and targeted therapy initiated.[48] (*Class I, Level C*)
26.3.3. Short courses of aminoglycosides (fewer than five days) are unlikely to result in nephrotoxicity when dosed appropriate for renal function.[78] (*Class I, Level B*)

26.4. **Fluoroquinolones**
26.4.1. Ciprofloxacin 400 mg IV or 500 to 750 mg PO every 12 hours for seven to ten days is appropriate and recommended for patients unable to tolerate β-lactam therapy.[79] (*Class I, Level A*)
26.4.1.1. Ciprofloxacin and levofloxacin doses may need to be adjusted for renal function. See *Renal Function-based Dose Adjustments – Adult – Inpatient Clinical Practice Guideline*.
26.4.2. If fluoroquinolones are used empirically, a dose of either ceftriaxone or aminoglycoside may be considered due to high levels of resistance.[48] (*Class IIb, Level C*)
26.4.3. Levofloxacin is a reasonable alternative..
26.4.4. Moxifloxacin should NOT be used for the treatment of pyelonephritis or UTI due to low urinary concentration.[80] (*Class III, Level B*)

26.5. **Trimethoprim/sulfamethoxazole (TMP-SMX)**
26.5.1. TMP/SMX 160/800 mg BID for fourteen days is effective if the pathogen is known to be susceptible.[79] (*Class I, Level A*)
26.5.1.1. TMP/SMX dose may need to be adjusted for renal function. See *Renal Function-based Dose Adjustments – Adult – Inpatient Clinical Practice Guideline*.
26.5.2. If TMP/SMX is used empirically, a dose of either ceftriaxone or aminoglycoside is reasonable due to levels of resistance of approximately 20%.[48] (*Class IIa, Level C*)

27. **Duration of therapy**
27.1. The duration of therapy for acute pyelonephritis in otherwise healthy, adult women of seven to ten days is effective, especially if a fluoroquinolone is used.[81,82] (*Class I, Level B*)
27.2. Immunocompromised patients or patients with genitourinary devices may be considered for longer durations of therapy. (*Class IIb, Level C*)
27.3. Oral TMP/SMX is recommended for fourteen days. [79] (*Class I, Level A*)
27.4. Oral β-lactam therapy is reasonable for ten to fourteen days.[76] (*Class IIa, Level B*)

Diagnosis and Prevention of Catheter-Associated Urinary Tract Infection (CA-UTI)

28. Unlike clean-catch specimens, no definitive quantitative number of bacteria defines significant bacteriuria. A quantitative count of $\geq 10^3$ CFU/mL should define significant bacteriuria in catheterized patients.[35,44] (*Class I, Level C*)
29. Cultures should be obtained from a freshly placed catheter whenever possible.[44] (*Class I, Level B*)
30. Cultures should NOT be obtained from the drainage bag.[44] (*Class III, Level C*)
31. Screening for bacteriuria in asymptomatic patients is NOT recommended for either short-term catheterized patients or long-term catheterized patients.[44] (*Class III, Level A*)
32. Signs and symptoms usually associated with UTI are frequently absent in the catheterized patient.[45] **Foul smelling and/or cloudy urine is not a reliable indicator of infection and should NOT be an indication alone for antimicrobial therapy**.[38] (*Class III, Level A*)
33. Alternative symptoms, such as pain or discomfort over the kidney or bladder, fever, urinary spasticity, autonomic hyperreflexia/dysreflexia, malaise, lethargy, or sense of unease can be beneficial for the diagnosis of CA-UTI.[44] (*Class IIa, Level C*)
34. Urinary catheters removal as soon as clinically appropriate is reasonable.[2,4,5,83,84] (*Class IIa, Level A*)
34.1. Protocols allowing nursing staff to insert and remove urinary catheters without physician orders include *Bladder Management – Inpatient – Adult Protocol [26]* and *Indwelling Urinary Catheter Removal – Inpatient – Adult Protocol [25]*.

35. While systemic antimicrobial administration reduced the rate of catheter-associated bacteriuria during the first four days after catheterization, the incidence of bacteriuria normalized thereafter.[85,86] Systemic antimicrobials resulted in an increased incidence of resistant organisms and are NOT recommended. (*Class III, Level B*)
36. In all elderly patients, acute mental status change and functional decline are nonspecific clinical manifestations of several circumstances, including, but not limited to dehydration, hypoxia, and polypharmacy adverse reactions. UTI diagnosis in correlation with other signs of systemic inflammation, including leukocytosis may be considered.[6] (*Class IIb, Level B*)
    36.1. It is may be reasonable to conclude UTI diagnosis in catheterized patients as a diagnosis of exclusion in the absence of localized urinary tract findings [6] (*Class IIb, Level C*)
37. Elderly patients, especially those with dementia or indwelling Foley catheters, have high rates of bacteriuria and may not have UTI symptoms.[10] Diagnosis of sepsis of a urinary source is NOT recommended in the absence of urinary symptoms because of bacteriuria. (*Class III, Level C*)
38. Antimicrobial prophylaxis at the time of urinary catheter removal can be beneficial for patients with short-term urinary catheters (equal to or fewer than fourteen days).[87] (*Class IIa, Level A*)
    38.1. Nitrofurantoin, TMP/SMX, or ciprofloxacin or levofloxacin may be reasonable choices. (*Class IIb, Level C*)

Treatment in Special Populations

39. **Peri-procedural (GU, OB/GYN) with bacteriuria**
    39.1. Treatment is recommended before transurethral resection of the prostate (TURP)[88] (*Class I, Level A*) and before other urologic procedures with anticipated mucosal bleeding.[89] (*Class IIa, Level B*).
    39.2. Generally, catheter irrigation with antiseptics have demonstrated no benefit reducing rates of catheter-associated bacteriuria[90,91]; however, in men undergoing transurethral procedures, antiseptic irrigation with chlorhexidine or povidone-iodine reduced the rate of catheter-associated bacteriuria by 22-24%.[92,93] Irrigation in select patient populations, such as those undergoing GU procedures can be beneficial. (*Class IIa, Level B*)
    39.3. In patients with known urinary organisms and risk factors for surgical infection (as listed below), a single dose of either ciprofloxacin 500 mg PO or TMP/SMX 160/800 PO may be given at the time of urinary catheter removal.[44] (*Class IIb, Level B*)
        39.3.1. Risk factors for surgical infection: advanced age, anatomic anomalies of the urinary tract, poor nutritional status, smoking, chronic corticosteroid use, immunodeficiency, externalized catheters, colonized endogenous/exogenous material, distant coexistent infection, prolonged hospitalization
    39.4. In patients undergoing a GU surgical procedure, a urine culture is typically collected in advance.
        39.4.1. If asymptomatic bacteriuria is found, the sample should be investigated for contamination and a repeat sample ordered if time permits (more than three days until surgery). (*Class IIb, Level C*)
            39.4.1.1. Contamination includes five or more epithelial cells or identification of skin flora.
        39.4.2. When possible, treatment should be guided by culture susceptibility results (*Class IIb, Level C*)
        39.4.3. Cultures positive for *Lactobacillus,* coagulase-negative *Staphylococcus,* or *Staphylococcus* non-*saprophyticus* often do not require treatment and are considered skin or vaginal flora. (*Class III, Level C*)
        39.4.4. If a potential non-enterococci uropathogen is identified, treatment with nitrofurantoin 100 mg PO BID for five days may be considered. (*Class IIb, Level C*)
            39.4.4.1. Alternatives include TMP/SMX160/800mg PO BID for three days or ciprofloxacin 250 mg PO BID for three days. (*Class IIb, Level C*)
            39.4.4.2. If an enterococcus uropathogen is identified, treatment should be initiated with amoxicillin 500 mg TID for three days (two days prior to procedure and one day post-procedure) may be considered. (*Class IIb, Level C*)
    39.5. Doses may need to be adjusted for renal function. See *Renal Function-based Dose Adjustments – Adult – Inpatient Clinical Practice Guideline*.

40. **Urologic patients undergoing urodynamic testing**
    40.1. The use of antibiotics reduces the rate of bacteruria but does not reduce the rate of symptomatic UTI in patients undergoing urodynamic testing. Therefore, it is reasonable to reserve prophylactic antibiotic use for patients with risk factors for complications and avoid antibiotic use in patients with risk for adverse drug reaction.[94] (*Class I, Level B)*
        40.1.1. Risk factors for complications associated with UTI following urodynamic testing include prolonged catheter use and presence of prosthetic joint. (*Class I, Level C*)
        40.1.2. If the patient has a catheter, performs intermittent self-catheterization, or uses a condom catheter, prophylactic antibiotics prior to testing are reasonable. (*Class IIa, Level C*)
    40.2. It is reasonable to choose antibiotics based on recent urine cultures. (*Class IIb, Level C):*
        40.2.1. For cultures obtained within the past 30 days:
            40.2.1.1. When possible, treatment guided by culture susceptibility results may be considered. (*Class IIb, Level C*)

40.2.1.2. If the culture includes enterococcus, not VRE, amoxicillin 500 mg PO TID for three days (two days prior to procedure and one day post-procedure) may be reasonable. (*Class IIb, Level C*)
40.2.1.3. In patients with penicillin intolerance, nitrofurantoin 100 mg PO BID for three days (two days prior to procedure and one day post-procedure) may be reasonable. (*Class IIb, Level C*)
40.2.2. If urine cultures were not obtained and resulted in the past 10 days:
40.2.2.1. First-line therapy may be considered as ciprofloxacin 250 mg PO BID for three days (two days prior to procedure and one day post-procedure). (*Class IIb, Level C*)
40.2.2.2. Alternative therapy that may be considered includes TMP/SMX 160/800 mg PO BID or nitrofurantoin 100 mg PO BID (both given for three days (two days prior to procedure and one day post-procedure). (*Class IIb, Level C*)
40.2.3. Doses may need to be adjusted for renal function. See *Renal Function-based Dose Adjustments – Adult – Inpatient Clinical Practice Guideline*.

Treatment of Specific Organisms

41. Mixed genitourinary (GU) flora
41.1. Non-catheterized patient
41.1.1. Mixed GU flora or *Gardnerella vaginalis* in the non-catheterized patient generally represent poor specimen collection. Recollection should be considered rather than requesting microbiologic workup. (*Class IIb, Level C*)
41.2. Catheterized patient
41.2.1. Mixed GU flora without a predominate organism generally represent colonization and do not require treatment (*Class IIb, Level* C) unless the patient meets criteria listed in *Treatment of Catheter-associated Urinary Tract Infection*.
41.2.2. Mixed GU flora with a predominating organism should be treated with antibiotics targeted to the predominating organism and according to principles described in *Treatment of Catheter-associated Urinary Tract Infection.*
41.2.2.1. It may be necessary to ask the microbiology lab to do sensitivity testing on the predominant uropathogen if the culture has multiple organisms.

42. Coagulase-negative *Staphylococcus*
42.1. *S. saprophyticus* is the second-leading cause of UTI in young women.[48]
42.1.1. Amoxicillin/clavulanate 500/125 mg PO BID for seven days or amoxicillin 500 mg PO TID for seven to ten days are reasonable first-line agents.[48] (*Class IIa, Level C*)
42.1.2. Alternative agents that may be considered include ciprofloxacin 250 mg PO BID for three to seven days, levofloxacin 250 mg daily for three to seven days, TMP/SMX 800/160 mg PO BID for seven days or cephalexin 250 mg PO BID for seven to ten days (*Class IIb, Level C*).
42.1.3. Doses may need to be adjusted for renal function. See *Renal Function-based Dose Adjustments – Adult – Inpatient Clinical Practice Guideline*.
42.2. Non-*S.saprophyticus* species, including coagulase-negative *Staphylococcus*, are rarely pathogens in the urinary tract and generally represent poor specimen collection, unless collected from an indwelling catheter or nephrostomy tube. Investigation into the quality of the sample may be reasonable to assess the likelihood of pathogenicity. (*Class IIb, Level C*)
42.2.1. Vancomycin is may be considered as empiric therapy given the high rate of methicillin-resistance in coagulase-negative *Staphylococcus*. (*Class IIa, Level C*)
42.2.2. Vancomycin dose should be adjusted based on renal function. See *Intravenous Vancomycin Use – Adult – Clinical Practice Guideline*.

43. *Staphylococcus aureus*
43.1. Rarely does *S. aureus* cause ascending infection *de novo*.[95-97]
43.1.1. Patients with *S. aureus* cultured in the urine, especially without an indwelling catheter, should have blood cultures drawn and a hematogenous route investigated. (*Class I, Level A*) *S aureus* may colonize chronic indwelling catheters.
43.2. Empiric therapy with vancomycin may be reasonable and definitive treatment of *S. aureus* bacteriuria tailoring to the antimicrobial susceptibility testing results may be considered. (*Class IIb, Level C*)
43.2.1. Vancomycin dose should be adjusted based on renal function. See *Intravenous Vancomycin Use – Adult – Clinical Practice Guideline*.

44. *Enterococcus* spp. and vancomycin-resistant *Enterococcus* (VRE)

44.1. Differentiation of colonization, asymptomatic bacteriuria, and UTI is important in the treatment of VRE bacteriuria. Once colonizing the GI tract, eradication is not possible, and hence it may frequently appear in the urinary system.[44,98]
  44.1.1. VRE UTI is generally associated with urinary catheters and may be considered complicated UTI.[98] (*Class IIb, Level B*)
  44.1.2. It may be reasonable to treat for seven to fourteen days of therapy, with every effort made to remove the catheter.[44] (*Class IIb, Level B*)
44.2. Susceptibility testing should guide therapy, but generally ampicillin or amoxicillin are recommended as the drugs of choice for ampicillin-susceptible *Enterococcus*.[99] (*Class I, Level B*)
  44.2.1. Piperacillin (as a component of Zosyn) is expected to have activity against ampicillin-susceptible *Enterococcus* similar to amoxicillin and may be considered an alternative. (*Class I, Level C*)
    44.2.1.1. Vancomycin may be considered for patients with severe β-lactam intolerance in patients with non-VRE pathogen. (*Class I, Level C*)
  44.2.2. Emerging evidence suggests that the resistance interpretation may not be important in the treatment of VRE UTIs.[100] It may be reasonable to consider treatment with amoxicillin regardless of susceptibility reporting because the drug achieves very high urinary concentrations. (*Class IIb, Level B*)
44.3. Many patients with VRE bacteriuria are asymptomatic and not treating may be considered.[98] (*Class IIb, Level B*)
  44.3.1. Some asymptomatic patients who recently have had urinary catheters may be considered for one to three doses of antibiotics after the catheter is removed. (*Class IIb, Level C*)
44.4. Alternative therapies for the treatment of VRE UTI include that may be considered are: nitrofurantoin, fosfomycin, doxycycline, tetracycline, linezolid or levofloxacin, depending on susceptibilities. These are preferred agents, if susceptible, as they are oral, safe, and cost effective. (*Class I, Level C*)
44.5. Daptomycin 4 mg/kg ideal body weight IV daily or linezolid 600 mg PO or IV every 12 hours may be considered based on susceptibility testing and patient characteristics but are less preferred as they are IV administered, may cause side effects, and are more expensive. (*Class IIb, Level C*)
44.6. Doses may need to be adjusted for renal function. See *Renal Function-based Dose Adjustments – Adult – Inpatient Clinical Practice Guideline*.

45. *Proteus* spp.
  45.1. Given the propensity of *Proteus* spp. to produce renal calculi and the difficulty of eradicating stones, extended treatment durations (up to fourteen days) may be considered. (*Class IIb, Level C*)
  45.2. In relapsing *Proteus* infection, urinary calculi evaluation is probably indicated.[101] (*Class IIa, Level C*)

46. Anaerobic organisms
  46.1. Anaerobic organisms are rarely pathogens in the urinary tract and the Microbiology Laboratory will not culture urine for anaerobes.[102]
  46.2. Empiric treatment against anaerobic organisms is not recommended.[102] (*Class III, Level B*)

47. *Gardnerella vaginalis, Ureaplasma urealyticum, and Mycoplasma hominis*
  47.1. These organisms may be isolated from the urine, but rarely are pathogenic. Special culture techniques are necessary for isolation, and the Microbiology Laboratory should be contacted.[103]
  47.2. Treatment may be considered in high-risk patients or patients with symptomatic UTI.[103] (*Class IIb, Level C*)
  47.3. Sample quality investigation may be considered to assess pathogenicity likelihood. (*Class IIb, Level C*)

48. *Candida* spp.
  48.1. Therapy is not recommended, unless the patient is at high risk of dissemination (severely immunocompromised patients with fever, renal transplant patients, patients with retained hardware in the genitourinary system, patients undergoing a genitourinary surgical procedure).[104] (*Class I, Level C*)
  48.2. The catheter should be either removed or replaced prior to starting antifungal therapy whenever possible.[104] (*Class I, Level A*)
  48.3. In asymptomatic patients, imaging of the kidneys and collecting system to exclude abscess, fungal ball, or urologic abnormality may be reasonable.[104] (*Class IIb, Level B*)
    48.3.1. Surgical debridement[105], sterile water irrigation[106], percutaneous debulking[107], or streptokinase irrigation[106] can be beneficial. (*Class IIa, Level B*)
  48.4. *Candida glabrata* was the most commonly identified organism in renal transplant patients at UWHC and most patients were asymptomatic. Most candiduria resolved after removal of the indwelling bladder catheter within one week of diagnosis.
    48.4.1. In general, non-renal transplant patients, treatment with antifungals was not associated with improved survival[49] and therefore, antifungal treatment is not recommended (*Class III, Level B).*
      48.4.1.1. "Treatment" should consist of catheter replacement. (*Class I, Level C*)

48.4.1.2. Elimination of the predisposing factors (including obstruction, catheter presence) is recommended first before antifungal therapy is initiated.[104] (*Class I, Level C*)

48.4.2. However, in renal transplant patients with an indwelling Foley catheter, catheter replacement may be considered before starting antifungal therapy. (*Class IIb, Level C*)

48.5. Treatment of *Candida* spp. cystitis should be with fluconazole 100-800 mg IV/PO daily for fourteen days.[108-110] (*Class I, Level A*)

48.5.1. Non-fluconazole antifungals (itraconazole, voriconazole, and posaconazole) and the echinocandins (micafungin, caspofungin, anidulafungin) are not effective for cystitis treatment due to low urinary concentrations of active drug.[104,110] (*Class III, Level A*)

48.5.2. High-dose fluconazole (400-800 mg or renal-equivalent dosing) is reasonable for the treatment of *Candida glabrata* cystitis.[110] (*Class IIa, Level B*)

48.5.3. Flucytosine is a highly effective anti-fungal agent for treatment of candiduria and may be considered when fluconazole is not feasible (patient tolerance, drug-drug interactions, resistance, etc.) (*Class IIb, Level C*)

48.5.3.1. Prolonged treatment may be limited by toxicity.[111,112] Treatment should be limited to seven to ten days due to risk of resistance when used as a single agent. (*Class IIb, Level B*)

48.5.4. Bladder irrigation with amphotericin-B 50 mg daily for seven to ten days may be considered in patients with an indwelling catheter or for patients with fluconazole-resistant organism, such as *Candida krusei* and *Candida glabrata*, but effectiveness is not well established.[113] (*Class IIb, Level B*)

48.5.5. Intravenous treatment with amphotericin with conventional amphotericin product, not the liposomal product is reasonable. (*Class IIa, Level B*)

48.5.5.1. The liposomal product does not achieve sufficient urinary concentrations.[114] Short courses of low-dose therapy leave amphotericin concentrations present in the urine for up to one week after short-course therapy or longer for prolonged courses.[115]

48.6. Treatment of *Candida* spp. pyelonephritis with fluconazole 400 mg IV or PO daily for fourteen days is reasonable.[110] (*Class IIa, Level B*)

48.6.1. Echinocandins are highly metabolized in the liver with minimal active drug found in the urine and use for UTI treatment is not routinely recommended. Use of an echinocandin for renal parenchyma treatment may be considered under the direction of an Infectious Diseases specialist. (*Class IIb, Level C*)

48.6.2. The prolonged treatment course for fungal pyelonephritis limits the use of flucytosine due to toxic effects of cumulative exposure. In patients requiring flucytosine, a dose of 25 mg/kg IV every 6 hours with renal insufficiency adjustment (if necessary) is recommended.[111] (*Class I, Level B*).

48.6.2.1. Due to the propensity for resistance development with long-term flucytosine monotherapy, the addition of a second agent, such as conventional amphotericin B, can be beneficial.[112] (*Class IIa, Level B*)

48.7. Candiduria in the critically ill patient may be an indication of disseminated candidiasis and prompt evaluation to differentiate colonization from infection may be considered. (*Class IIb, Level C*)

48.7.1. Further treatment of invasive *Candida* spp. infections with subsequent candiduria should be guided by Infectious Disease consult.

48.8. Antifungal doses may need to be adjusted for renal function. See *Renal Function-based Dose Adjustments – Adult – Inpatient Clinical Practice Guideline*.

49. *Corynebacterium urealyticum*

49.1. *C. urealyticum* is common in the renal-transplant population[116] and it is reasonable to consider in the presence of ureteral stent, alkaline urine pH, previous UTI, or recent antibiotic therapy.[117] (*Class IIa, Level B*)

49.1.1. If isolated in a non-renal transplant patient, sample quality investigation may be considered to assess pathogenicity likelihood. (*Class IIb, Level C*)

49.2. *C. urealyticum* treatment with a glycopeptide-based (e.g. vancomycin) therapy is reasonable.[116] (*Class IIa, Level B*)

49.2.1. Vancomycin doses may need to be adjusted based on renal function. See *Intravenous Vancomycin Use – Adult – Clinical Practice Guideline*.

49.3. *C. urealyticum* is frequently a cause of encrusting pyelitis Urology consultation may be considered. (*Class IIb, Level C*)

Prevention Strategies

50. Antibiotic prophylaxis is not recommended but may be considered on a case-by-case basis in patients with recurrent UTI. (*Class III, Level C*)

51. Vaginal/urine pH acidification may be considered to reduce the colonization of some uropathogenic bacteria.(*Class IIb, Level C*)

51.1. Cranberry juice

51.1.1. Cranberry product manufacturing is unregulated by the FDA and products are considered an herbal supplement by the UWHC Pharmacy and Therapeutics Committee. Therefore, cranberry products will not be purchased by the UWHC pharmacy department or prescribed routinely to patients.

51.1.2. Clinical studies have shown no reduction in catheter-associated urinary tract infections with cranberry products.[118,119] The use of cranberry-based products effectiveness is not well established. (*Class IIb, Level B*)

51.2. Methenamine

51.2.1. Methenamine use is contraindicated in patients with calculated creatinine clearance of below 50 mL/min due to decreased excretion and serum accumulation leading to toxicity.[120] (*Class III, Level B*)

51.2.1.1. Methenamine activity is dependent on urine pH and urine more acidic that a pH of six with the addition of ascorbic acid to increase the effectiveness of formaldehyde can be beneficial.[121] (*Class IIa, Level B*)

51.2.2. The use of methenamine in the catheterized patient is probably safe, but efficacy is reduced because of limited dwell time in the bladder. Clinical studies have shown no reduction in catheter-associated urinary tract infections.[118] Therefore, the use of methenamine may be reasonable on a case-by-case basis. (*Class IIb, Level B*)

51.3. Ascorbic acid

51.3.1. Ascorbic acid effectively acidifies urine pH and has demonstrated reductions in UTIs in pregnant women and can be effective for UTI prophylaxis. [122] (*Class IIa, Level B*)

51.3.2. It is reasonable to consider ascorbic acid use with methenamine as ascorbic acid acidifies urine.[121] (*Class IIa, Level B*)

52. Use of the contraceptive nonoxynol-9 is not recommended.[21] (*Class III, Level B*)

53. Estrogen replacement therapy, especially vaginal hormone replacement therapy, may be considered to reduce the recurrence of UTIs in women where hormone replacement therapy is otherwise indicated.[123,124] (*Class IIa, Level B*)

53.1. This treatment should be considered for post-menopausal, as well as surgically and medically menopausal women, unless otherwise contraindicated.[124,125] (*Class I, Level A*)

54. Systemic antimicrobials (including antifungal agents) given at the time of catheter placement, replacement, or removal is not recommended as fever associated with catheter manipulation is transient, unless the patient has a genitourinary procedure with risk factors listed in *Treatment in Special Populations*.[126,127] (*Class III, Level B*)

55. Probiotics (lactobacilli preparations) have been studied for prevention of UTI and provided no clear benefit.[128] Probiotic use for UTI prophylaxis is not recommended. (*Class III, Level A*)

Therapeutic Monitoring Strategies

56. It is not recommended to perform repeat urinalysis to confirm clinical or microbiologic response. (*Class III, Level C*)

57. Bacteriologic response should occur within 48 hours for cystitis and within 72 hours for complicated UTI or pyelonephritis. Fever is common for 72 hours in patients with complicated UTI and pyelonephritis.

57.1. If no response occurs by 48-72 hours, alternative therapy may be considered. (*Class IIb, Level C*)

57.2. In genitourinary procedure patients with known urinary organisms and risk factors for surgical infection (listed below), a single dose of either ciprofloxacin 500 mg PO or TMP/SMX 160/800 mg PO at the time of urinary catheter removal is reasonable.[129] (*Class IIa, Level B*)

57.2.1. Risk factors for surgical infection: advanced age, anatomic anomalies of the urinary tract, poor nutritional status, smoking, chronic corticosteroid use, immunodeficiency, externalized catheters, colonized endogenous/exogenous material, distant coexistent infection, prolonged hospitalization.

Figure 1. Diagnosis of UTI in the 18-65 year old, non-catheterized patient

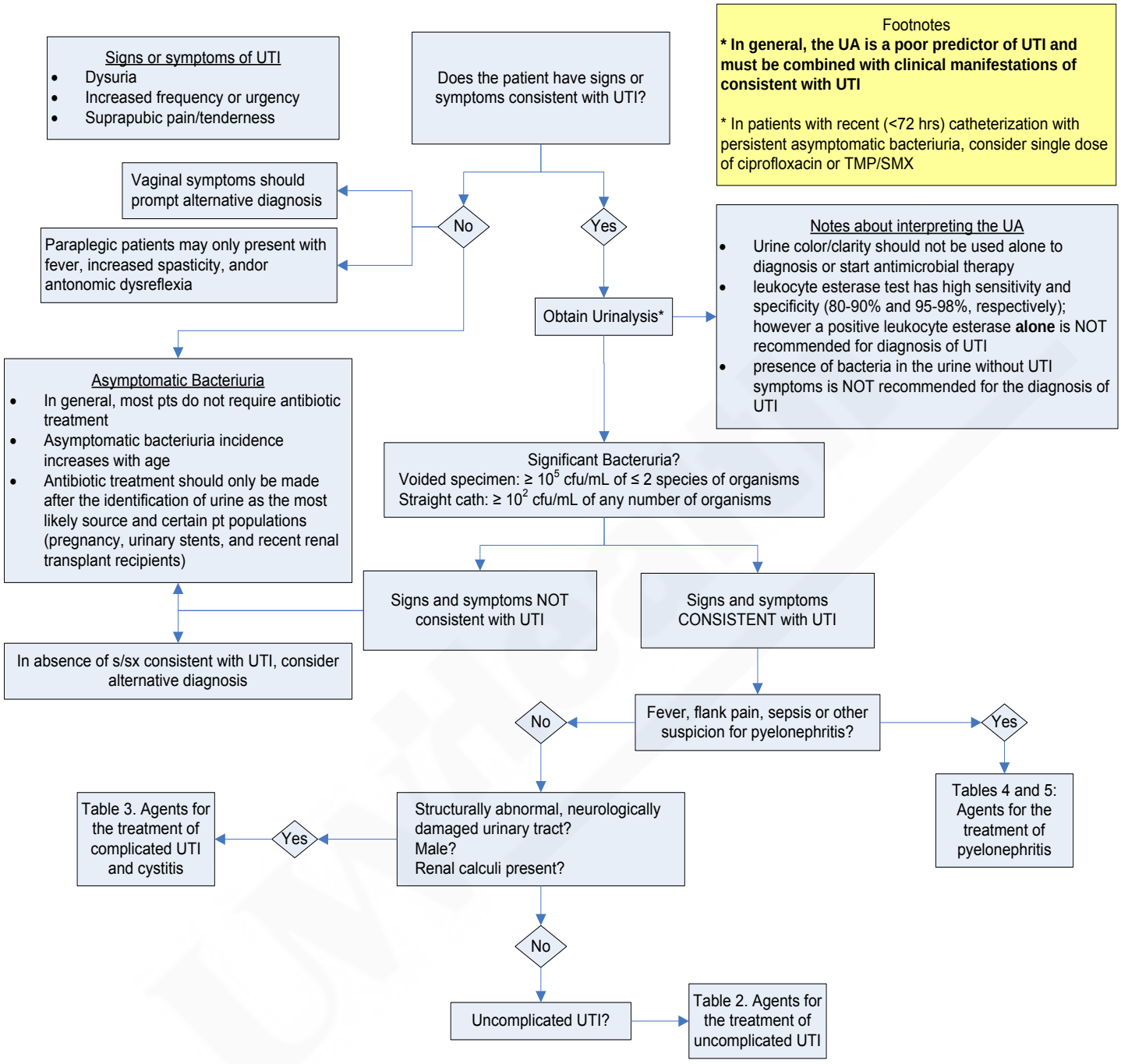


Figure 2. Diagnosis of UTI in the elderly and/or institutionalized catheterized and non-catheterized patient

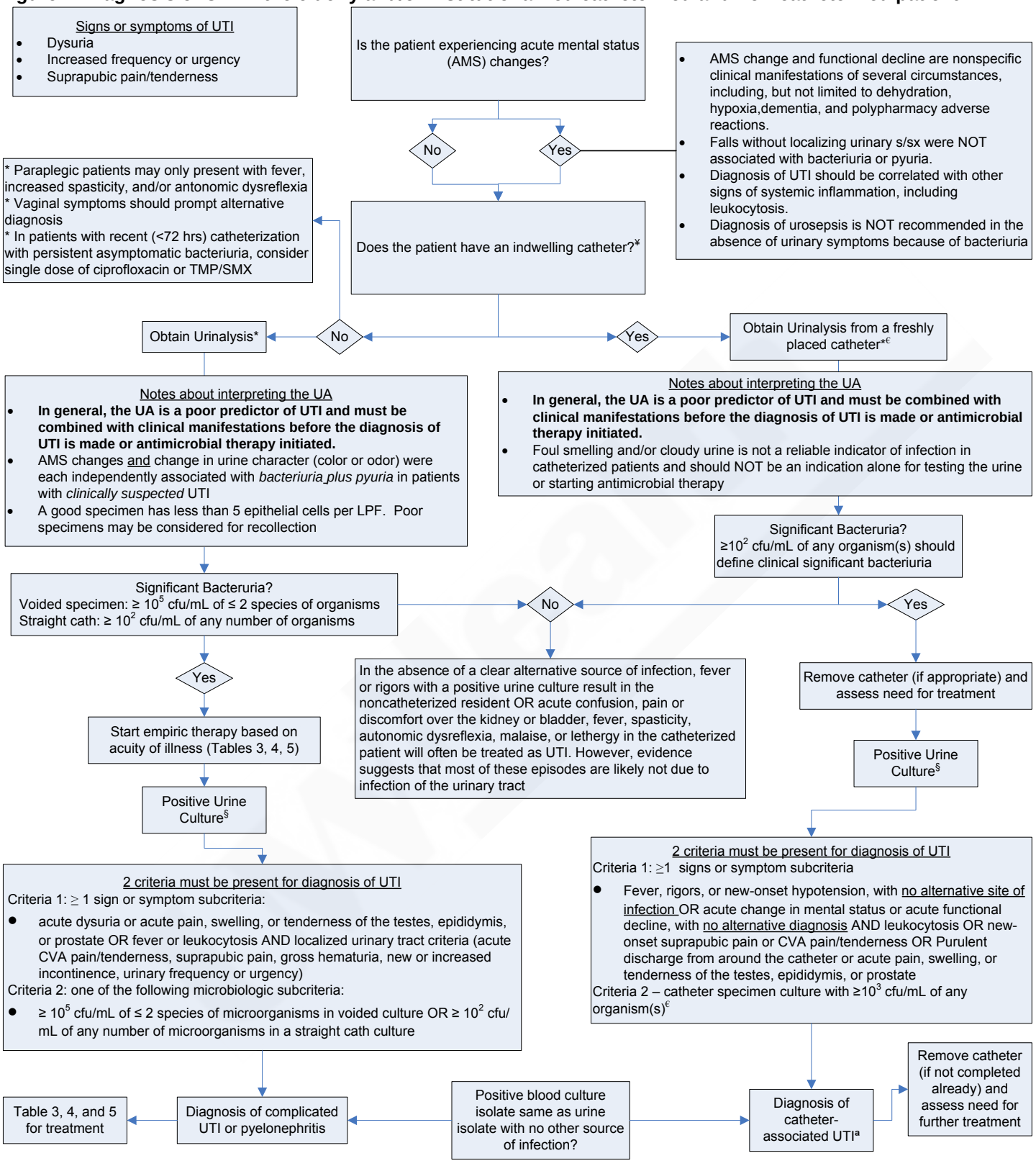


Figure 2 Footnotes

* Signs and symptoms usually associated with UTI are frequently absent in the catheterized patient. **Foul smelling and/or cloudy urine is not a reliable indicator of infection and should NOT be an indication alone for testing the urine or starting antimicrobial therapy.**

¥ Residents with intermittent or condom catheters are at lower risk for UTI and should be considered in the same risk category as those with no indwelling catheter.

€ Catheter specimens should be collected following replacement of the catheter if the current catheter has been in place >14 days.

§ Reference *Table 6* for guidance regarding interpretation of some organisms.

[a] Diagnosis of UTI in the catheterized patient should always be a diagnosis of exclusion in the absence of localized urinary tract findings.

Figure 3. Urinary tract infection management in abdominal solid organ transplant patients

	Asymptomatic bacteriuria	Symptomatic UTI[A]	
Clinical Features	No urinary symptoms	<u>Cystitis symptoms</u> • dysuria • urinary frequency • urinary urgency • elevated creatinine	<u>Pyelonephritis symptoms</u> • cystitis symptoms • suprapubic pain • pain at graft site • costovertebral angle tenderness or pain • fever, malaise
Urinalysis and Culture Findings	<u>"Positive" Urinalysis findings:</u> > 5 WBC/HPF, < 2 squamous epithelial cells/HPF, bacteria present *Pyuria (>5 WBC) or bacteriuria does not confirm diagnosis of UTI. Absence of pyuria or bacteriuria questions the diagnosis of UTI. Urinalysis collections with squamous epithelial cells present consider straight catheterization specimen to increase quality.* "<u>Significant" bacterial growth on urine culture</u>: • Men: clean-catch urine specimen with $>10^5$ CFU/mL of a single organism • Women: two clean-catch urine specimens more than 24 hours apart with $>10^5$ CFU/mL of a single organism • Straight catheterization sample: $>10^2$ CFU/mL of a single organism <u>Relative organism frequency</u> 70% of uropathogens are Gram-negative organisms, most frequently *E. coli* <u>Common nonpathogenic bacteria for which no treatment is necessary</u> • Non-saprophyticus, coagulase-negative *Staphylococcus* species (unless hardware is in place) • *Lactobacillus* species • *Gardnerella vaginalis* • *Corynebacterium non-urealyticum* • Mixed flora may represent poor collection methods		
Management	<u><3 months post-transplant</u> • No empiric antibiotics • Await final culture results to start therapy of five to seven day antibiotic course <u>>3 months post-transplant</u> • No treatment unless associated rise in creatinine	<u>Mild cystitis without concern for systemic infection</u> • If GFR >40 mL/min, nitrofurantoin 100 mg PO BID for 7 days • If GFR <40 mL/min or concern for drug-resistant isolates, fosfomycin 3 g PO x 1 dose • Deescalate to narrowest spectrum antimicrobial based on culture results when available <u>Moderate/severe infection or mild cystitis with concern for possible pyelonephritis or urinary hardware in place (e.g. stents, nephrostomy tubes)</u> • Empiric ciprofloxacin 500 mg PO BID[B] • Treat for 14 days • For patients with previous culture history, use historical results to guide empiric therapy • Deescalate to narrowest spectrum antimicrobial based on culture results when available <u>Patients allergic or intolerant to the above agents</u> • Amoxicillin/clavulanic acid 875 mg PO BID[B] • 3rd generation oral cephalosporin (cefpodoxime 200 mg BID)[B] • TMP/SMX DS (160/800 mg) BID (although likelihood of resistance is increased if previously received for prophylaxis post-transplant)[B]	

[A] In cases of multiple symptomatic UTIs, patients may require referral to Urology and/or Infectious Disease

[B] Doses should be adjusted for renal function. See *Renal Function-based Dose Adjustments – Adult – Inpatient Clinical Practice Guideline*

Table 1. Agents for the treatment of uncomplicated UTI/cystitis[A,B]

	Drug	Dose and Duration	Notes
EMPIRIC Therapies	**Nitrofurantoin**	100 mg PO BID x 5 days	CrCL <30mL/min: contraindicated CrCL 30-50 mL/min: use with caution and monitor for symptom resolution Not for use in pyelonephritis
	Trimethoprim/ Sulfamethoxazole[C]	160/800 mg PO BID x 3 days	Caution is advised in patients receiving for prophylaxis since likelihood of resistance is high
	Cefpodoxime[C,D]	100 mg PO BID x 7 days	Consider change to narrow spectrum β-lactam when susceptibilities are known
	Ciprofloxacin, Levofloxacin[C]	Ciprofloxacin: 250 mg PO BID x 3 days Levofloxacin: 250 mg PO daily x 3 days	Caution is advised due to increased rates of *Clostridium difficile* infection and other super-infections associated with fluoroquinolone use Moxifloxacin should not be used for treatment due to low urinary concentrations
DEFINITIVE Therapies	**Amoxicillin[C]**	500 mg PO BID x 7 days	Active against ampicillin-susceptible *Enterococcus spp.* Use when susceptibilities are known, not for empiric use
	Cephalexin[C,D]	500 mg PO BID x 7 days	Use when susceptibilities are known, not for empiric use
	Fosfomycin	3 g PO ONCE	Susceptibility testing is limited based on FDA approval; however, *E.coli* resistance rates are low Has in-vitro activity against VRE (vancomycin-resistant *Enterococcus* spp.) and ESBL (extended spectrum β-lactamase producing bacteria) organisms Not for use in pyelonephritis

[A] These agents are listed in their preferred order. The optimal therapy depends on many factors and each medication has risks and benefits which must be considered when choosing treatment.
[B] Definitive therapy should be guided by susceptibility testing and results.
[C] Doses should be adjusted based on renal function. See *Renal Function-based Dose Adjustments – Adult – Inpatient Clinical Practice Guideline.*
[D] Cefdinir, Cefixime, Cefuroxime, or Cefpodoxime may be considered as alternative if necessary for insurance coverage or if for other clinical reason.

Table 2. Agents for the treatment of complicated UTI/cystitis[A,B]

Moderately ill, no history of resistant uropathogens, no recent fluoroquinolone use, local resistance rates exceed 10%		
Ciprofloxacin[C]	500 mg PO BID	May start therapy with 400 mg IV Q12H until patient is tolerating orals
Moderately ill, *with* a history of resistant uropathogens or recent fluoroquinolone use		
Ceftriaxone +/- ciprofloxacin[C]	1 g IV Q24H +/- IV or PO ciprofloxacin BID	
Severely ill patients should be treated following the recommendations in *Table 4. Pyelonephritis*		

[A] In general, empiric treatment should have a broader spectrum of antibiotics followed by a tailoring of therapy based on culture and susceptibility results. Surgical intervention to correct the anatomic abnormality or alleviate the functional abnormality should be considered, especially for severely ill patient.

[B] The duration of therapy for complicated UTI is prolonged, generally 7 days for a rapid response or 10-14 days for delayed response.

[C] Doses should be adjusted based on renal function. See *Renal Function-based Dose Adjustments – Adult – Inpatient Clinical Practice Guideline*.

Table 3. Agents for the treatment of acute pyelonephritis – outpatient[A,B]

Drug	Dose and Duration	Notes
Ciprofloxacin[C]	500 mg PO BID x 7-10 days	Give first dose ciprofloxacin/levofloxacin 400/500mg IV ONCE
Levofloxacin[C]	750 mg PO daily x 5 days or 500 mg PO daily x 7-10 days	
Ceftriaxone	1 g IV Q24H	Alternative to one-time dose of IV fluoroquinolone
Tobramycin or Gentamicin[D]	5 mg/kg (adjusted body weight) IV Q24H	

[A] A urine culture should be collected and sent for culture in all patients with suspected pyelonephritis. Empiric therapy should be tailored as soon as possible to the infecting organism.

[B] Nitrofurantoin and fosfomycin should not be used for the empiric treatment of pyelonephritis with suspected bacteremia/sepsis because they do not achieve sufficient systemic bloodstream concentrations.

[C] Doses should be adjusted based on renal function. See *Renal Function-based Dose Adjustments – Adult – Inpatient Clinical Practice Guideline*.

[D] Doses should be adjusted based on renal function. See *Antibiotics for the Treatment of Gram-negative Infections – Adult – Inpatient Clinical Practice Guideline*.

Table 4. Agents for the treatment of acute pyelonephritis – inpatient[A,B,C,D]

Drug	Dose and Duration	Notes
Ceftriaxone	1 g IV Q24H x 10-14 days	Continue therapy until susceptibility is known.
Tobramycin or Gentamicin[E]	5 mg/kg (adjusted body weight) IV Q24H	Consider in patients with recent fluoroquinolone or β-lactam use Short courses of therapy (< 5 days) are unlikely to result in nephrotoxicity
Ciprofloxacin[E]	400 mg IV BID x 7-10 days	If used empirically, a dose of either ceftriaxone or aminoglycoside should be considered due to high rates of resistance
Trimethoprim/ Sulfamethoxazole[F]	160/800 mg PO BID x 14 days (may be given IV if unable to take oral medication)	If used empirically, a dose of either ceftriaxone or aminoglycoside should be considered due to high rates of resistance.

[A] A urine culture should be collected and sent for culture in all patients with suspected pyelonephritis. Empiric therapy should be tailored as soon as possible to the infecting organism.

[B] Nitrofurantoin and fosfomycin should not be used for the empiric treatment of pyelonephritis with suspected bacteremia/sepsis because they do not achieve sufficient systemic bloodstream concentrations.

[C] Immunocompromised patients or patients with GU devices may be considered for longer duration of therapy.

[D] These agents are listed in their preferred order. The optimal therapy depends on many factors and each medication has risks and benefits which must be considered when choosing treatment.

[E] Doses should be adjusted based on renal function. See *Antibiotics for the Treatment of Gram-negative Infections – Adult – Inpatient Clinical Practice Guideline*.

[F] Doses should be adjusted based on renal function. See *Renal Function-based Dose Adjustments – Adult – Inpatient Clinical Practice Guideline*.

Table 5. Treatment of specific organisms

Organism	Treatment Option	Notes
Mixed genitourinary flora in *non-catheterized* patient	Recollection	Generally represent poor specimen collection. Suggest recollection.
Mixed genitourinary flora in *catheterized* patient	Target predominate organism	If no predominating organism, likely colonization. With predominating organism, tailor treatment to said organism.
Staphylococcus saprophyticus	Amoxicillin/clavulanate 500/125 mg PO BID x 7 days OR Amoxicillin 500 mg PO TID x 7-10 days[A]	Second leading cause of UTI in young women. Alternative regimens include ciprofloxacin 250 mg PO BID x 3-7 days, trimethoprim/sulfamethoxazole 160/800 mg PO BID x7 days, or cephalexin 250 mg PO BID x 7-10 days.[A]
Coagulase-negative *Staphylococcus (non-saprophyticus)*	Vancomycin IV[B] Goal trough 10-15	Rarely pathogens in the urinary tract and generally represent poor specimen collection, unless from indwelling catheter.
Staphylococcus aureus	Tailored to antimicrobial susceptibilities	Rarely causes ascending infection de novo. Patients should have blood cultures drawn and hematogenous route investigated.
Enterococcus spp. (ampicillin-susceptible)	Amoxicillin 500 mg PO BID x 3-7 days[A]	Susceptibility testing should guide final therapy. Ampicillin susceptibility predicts piperacillin activity. Alternative regimen of vancomycin for patients with true penicillin or β-lactam allergy.
Enterococcus spp. (vancomycin-resistant)	Often asymptomatic and no treatment required. Tailor to antimicrobial susceptibilities. Duration of therapy: Remove catheter: 1-3 days Without catheter: 7-14 days	Frequent colonizer or cause of asymptomatic bacteriuria. Once GI colonization, eradication Is not possible and hence it may frequently appear in the urinary system. Alternative regimens (in preferential order) include nitrofurantoin, fosfomycin, doxycycline, tetracycline, daptomycin 4mg/kg, linezolid PO, or tigecycline.
Proteus spp.	Tailor to antimicrobial susceptibilities x 14 days	High propensity to produce renal calculi. Relapsing *Proteus* infections should prompt an evaluation for urinary calculi.
Anaerobic organisms	Empiric treatment NOT recommended	Rarely pathogens in the urinary tract and the microbiology lab will not routinely perform cultures.
Gardnerella vaginalis	Recollection	May be isolated from urine but rarely pathogenic. Investigate sample quality to assess pathogenicity.
Ureaplasma urealyticum	Recollection/special collection	May be isolated from urine but rarely pathogenic. Investigate sample quality to assess pathogenicity.
Mycoplasma hominis	Recollection/special collection	May be isolated from urine but rarely pathogenic. Investigate sample quality to assess pathogenicity.
Candida albicans	Fluconazole 100-400 mg PO daily x14 days[A]	Remove or replace catheter if appropriate.
Candida glabrata Low risk		Remove or replace catheter if appropriate.
Candida glabrata High risk (includes severely immunocompromised and febrile; renal transplant; patients with retained genitourinary hardware; and patients undergoing genitourinary procedure)	Remove or replace catheter. Treatment with fluconazole 400-800 mg IV/PO daily[A]	Most common organism in UW renal transplant patients; however, most were asymptomatic. Imaging of the kidneys and collection system should be performed Non-fluconazole antifungals and echinocandins should not be used for treatment. Bladder irrigation with amphotericin B 50 mg daily x 7-10 days.
Corynebacterium urealyticum	Vancomycin IV[B] Goal trough 10-15	Common in renal transplant population, otherwise investigate sample quality to assess pathogenicity. Consider urology consultation as this organism may cause encrusting pyelitis.

[A] Doses should be adjusted based on renal function. See *Renal Function-based Dose Adjustments – Adult – Inpatient Clinical Practice Guideline*.

[B] Vancomycin should be adjusted based on renal function. See *Intravenous Vancomycin Use – Adult – Clinical Practice Guideline*.

Table 6. Prevention Strategies

Therapy	Notes
Antimicrobial Agents	Discouraged due to concern for development of antimicrobial resistance. May be considered on a case-by-case basis.
Cranberry Juice	Unregulated product by the FDA, therefore, manufacturing standards and quality vary. No data to support reduction of catheter-associated UTI.
Methenamine	Contraindicated in patients with CrCL <50mL/min. Urine pH should be measured and be maintained <6. Efficacy depends on dwell time and therefore use in catheterized patients is unknown.
Ascorbic Acid	Reduces pH of urine and has shown to reduce UTIs in pregnant women. Consider use with methenamine
Vaginal Estrogen	Consider only when hormone replacement therapy is indicated. Consider in post-menopausal, surgically and medically menopausal women.
Vaginal pH reduction	May be considered to reduce the colonization of some uropathogenic bacteria.
Nonoxynol-9	NOT recommended.
Lactobacillus probiotics	NOT recommended.

Table 7. Candidates for screening Urinalysis[A]

UA screening suggested/recommended	UA screening NOT recommended
• **18-65 yo symptomatic women without a history of UTI** • **Pregnant women early in pregnancy** • **Early renal transplant recipients**	• 18-65 yo symptomatic women with frequent recurrences and prior lab confirmed UTI • Asymptomatic elderly, community dwelling patients • Asymptomatic LTCF or institutionalized patients • Asymptomatic diabetic women

[A] Because of the risk of iatrogenic UTI, catheterization is not recommended. However, in patients where the quality of sample has or may be compromised (>5 epithelial cells), catheterization may be considered.

UWHealth Implementation

Benefits/Harms of Implementation

- Implementation of this guideline will standardize the care of patients treated for urinary tract infections.
- Utilization of this guideline drives prescribing towards narrow spectrum agents. This reduces antimicrobial pressure on the bacterial biomass and reduces the emergence of bacterial resistance.

Implementation Strategy

- This guideline will be disseminated to clinical staff and available electronically.
- This guideline will serve as a resource for clinical inservices.

Implementation Tools/Plan

- This clinical practice guideline will be posted for reference in UConnect.
- Links to this clinical practice guideline will be available electronically at point of use sites.

Disclaimer

CPGs are described to assist clinicians by providing a framework for the evaluation and treatment of patients. This Clinical Practice Guideline outlines the preferred approach for most patients. It is not intended to replace a clinician's judgment or to establish a protocol for all patients. It is understood that some patients will not fit the clinical condition contemplated by a guideline and that a guideline will rarely establish the only appropriate approach to a problem.

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Appendix 1. Diagnosis of Urinary Tract Infection – Top Ten Myths

Lucas Schulz, PharmD, BCPS; Robert Hoffman, MD; Jeffrey Pothof, MD; Barry Fox, MD

For further reading consider:

1. Trautner BW, Grigoryan L, Petersen NJ, et al. Effectiveness of an Antimicrobial Stewardship Approach for Urinary Catheter-Associated Asymptomatic Bacteriuria. *JAMA Intern Med*. 2015;175(7): 1120-1127.
2. Kalra R, Kraemer RR. Urinary catheterization -- when good intentions go awry: a teachable moment. *JAMA Intern Med*. 2014;174(10): 1547-1548.

The diagnosis of UTI is not a laboratory defined diagnosis. The diagnosis should be based on clinical symptoms combined with supportive laboratory information, if obtained.

Myth 1: The urine is cloudy and smells bad. My patient has a UTI.
Truth 1: Urine color and clarity or odor should not be used alone to diagnose or start antibiotic therapy in any patient population.

a. Visual inspection of urine clarity is not helpful in diagnosing UTI in women.[37]
    a. 100 female patients at a university hospital had their urine tested by reading newsprint through the sample. The sensitivity, specificity, and positive and negative predictive values were 13.3%, 96.5%, 40.0%, and 86.3% respectively.
b. *Foul smelling urine is an unreliable indicator of infection in catheterized patients*, and usually dependent on a patients hydration status and concentration of urea in the urine.[1,38]

Myth 2: The urine has bacteria present. My patient has a UTI. Also see Myth 8.
Truth 2: The presence of bacteria in the urine on microscopic examination without UTI symptoms is NOT recommended for the diagnosis of UTI due to the possibility of contamination and asymptomatic bacteriuria[42]

a. UTI is not a laboratory defined diagnosis. Diagnosis should be based on clinical symptoms. The bacterial thresholds (below) should usually be present in patients with a UTI; however, the absence of bacteria does not rule out UTI in patients with clinical symptoms.
b. In patients *without* an indwelling catheter the following cutoffs should define significant bacteriuria[6]
    i. $\geq 10^5$ CFU/mL of ≤ 2 species of microorganisms in voided culture
    ii. $\geq 10^2$ CFU/mL of any number of microorganisms in a straight cath culture
c. In patients *with* an indwelling catheter, $\geq 10^3$ CFU/mL of any organism(s) should define significant bacteriuria[6] since this is predictive of higher colony counts of 10 to the fifth within 48 hours[130]

Myth 3: My patient's urine sample has >5 squamous epithelial cells per low powered field and the culture is positive. Because the culture is positive, I can disregard the epithelial cell count and treat the UTI.
Truth 3: A good specimen has less than 5 epithelial cells per low power field on UA. Poor specimens should be considered for recollection or straight catheterization should be performed.

Myth 4: The urine has positive leukocyte esterase. My patient has a UTI and needs antibiotics.
Truth 4: Urine leukocyte esterase ***should not be used alone*** to diagnosis or start antimicrobial therapy in any patient population.

a. A dipstick leukocyte esterase test has high sensitivity and specificity for the presence of quantitative pyuria, 80-90% and 95-98%, respectively; **however** a positive leukocyte esterase **alone** is NOT recommended for diagnosis of UTI.[39,40]Pyuria or bacteriuria alone is not an indication for antimicrobial therapy
b. On rare occasions, a negative leukocyte esterase in the presence of UTI symptoms may still prompt a urine culture if clinically suspected[39,40] but especially prompt a search for urethritis, vaginitis, or sexually transmitted infection.

Myth 5: My patient has pyuria. They must have a UTI.
Truth 5: Quantitative urine WBC ***should not be used alone*** to diagnosis or start antimicrobial therapy in any patient population

a. In neutropenic or leukopenic patients, the WBC count may be artificially low and reflex culture may not occur. The microbiology lab should be contacted and an order for urine culture ordered if urinary symptoms are present and urinary source of infection is suspected.
b. Borderline WBC counts of 6-10 may reflect the patient's state of hydration. Patients with oliguria or anuria (dialysis) usually have some degree of pyuria.
c. Non-infectious conditions, such as sexually transmitted infections or non-infectious cystitis may give pyuria.

Myth 6: The urine has nitrates present. My patient has a UTI.
Truth 6: Urine nitrates ***should not be used alone*** to diagnosis or start antimicrobial therapy in any patient population.

a. Urine nitrate has a high true-positive rate for bacteriuria, but bacteriuria, as noted above in Myth 2, does not define a clinically significant UTI Diagnosis of UTI should be considered in a patient with elevated urine nitrate in the presence of clinical signs and symptoms of UTI.[39,42]
b. A negative leukocyte esterase AND a negative urine nitrate largely rule out infection in pregnant women, elderly patients, family medicine, and urology patients.[41] Alternative diagnosis should be thoroughly investigated in this scenario.
c. In an analysis of the negative predictive value for pathogenic bacteria using the combined nitrite and leukocyte esterase dipstick analysis, the combination of a negative leukocyte esterase and negative nitrite test demonstrated an NPV of 88% (CI: 84%-92%).
d. If both leukocyte esterase AND nitrite analyses are positive, the sensitivity for bacteriuria was 48% (CI: 41%-55%), and specificity was 93% (CI: 90%-95%).[131] See Myth 2

Myth 7: All findings of bacteria in a catheterized urine sample should be diagnosed as a UTI.
Truth 7: Virtually 100% of patients with an indwelling Foley catheter are colonized within 2 weeks of placement with 2-5 organisms. Colony counts of a catheter may define bacteriuria but must be taken in a clinical context for making a diagnosis of UTI.

a. 98% of chronically catheterized patients had bacteriuria and 77% were polymicrobial. The mean interval between new episodes of bacteriuria was 1.8 weeks.[52]
b. Bacteriuria and pyuria in chronically catheterized patients should **only** be treated in the presence of signs and **symptoms of infection** (e.g. fever, leukocytosis, suprapubic pain and tenderness. Dysuria is obviously unassessable). Pyuria or bacteriuria alone is not an indication for antimicrobial therapy.
c. Patients with intermittent or condom catheters are at lower risk for UTI and should be considered in the same risk category as those with no indwelling catheter.[46]
d. While antibiotics may delay the onset of bacteriuria in catheterized patients, this strategy ultimately selects for resistant microorganisms. Prophylactic anti-infectives are not recommended for patients with chronic catheters, but may be considered for short-term use by urology specialists

Myth 8: Bacteriuria results in urinary tract infections and should be treated with antibiotics.
Truth 8: Bacteriuria does NOT establish a diagnosis of a UTI and does NOT necessarily require initiation of antimicrobial therapy for asymptomatic bacteriuria.

a. The prevalence of bacteriuria in elderly institutionalized patient *without* indwelling catheters varies from 25-50% for women and 15-49% for men and increases with age.[10] Bacteriuria and pyuria in the elderly is, to a large degree, an expected finding.
b. Symptomatic UTI is substantially less common than asymptomatic bacteriuria.
c. Asymptomatic bacteriuria has not been associated with long-term negative outcomes, such as pyelonephritis, sepsis, renal failure or hypertension.[51]
d. The overuse of antibiotics leads to antibiotic resistance and potential side effects.[28,29,31]
e. Pyuria, leukocyte esterase, or nitrate, individually, accompanying asymptomatic bacteriuria are NOT necessarily an indication for antimicrobial treatment in the general population.[1] Some exceptions include: pregnancy[33] and patients with urinary tract stenting[61]
f. Recent evidence suggests that in younger women with true recurrent UTI, that bacteriuria may be "protective" for future UTI with more pathogenic organisms.[132]

Myth 9: Falls and acute altered mental status changes in the elderly patient are usually caused by UTI.

Truth 9: Altered mental status and falls in the elderly are caused by many factors. Other signs and symptoms of UTI, especially dysuria (when able to assess) should be present to make the diagnosis of UTI in non-catheterized patients. Symptoms of active infection in a catheterized patient are obviously more difficult to assess.[45]

a. Elderly patients with acute mental status changes accompanied by bacteriuria and pyuria *without clinical instability or other signs or symptoms of UTI* can reasonably be observed for resolution of confusion for 24-48 hours without antibiotics[133,134], while searching for other causes of confusion.
    1. In all elderly patients, acute mental status change and functional decline are non-specific clinical manifestations of several circumstances, including, but not limited to dehydration, hypoxia, and poly-pharmacy adverse reactions. Diagnosis of UTI should be correlated with others signs of systemic inflammation,
b. In the non-catheterized patient, acute changes in mental status was associated with *bacteriuria plus pyuria* in patients with *clinically suspected* UTI.[7]
    1. However, these two findings are also frequently demonstrated in elderly patients with asymptomatic bacteriuria and attribution of altered mental status to bacteriuria can result in failure to identify the true cause. [25,26,135] Falls without localizing urinary symptoms were not associated with bacteriuria or pyuria.[8,9]
c. Elderly patients, especially those with dementia or indwelling Foley catheters, have high rates of bacteriuria and may NOT have UTI symptoms[10]. Diagnosis of infection/sepsis of a urinary source with simple bacteriuria is not recommended unless other infectious sources have been excluded and patients meet urine criteria suspicious for infection. Diagnosis of UTI in the catheterized patient should always be a diagnosis of exclusion by investigating other causes for altered mental status in the absence of localized urinary tract findings.[6]

Myth 10: The presence of yeast or candida in the urine, especially in patients with indwelling urinary catheters, indicates a candida UTI and needs to be treated.

a. The occurrence of candiduria in the catheterized patient is common, especially in the ICU and most often reflects colonization or asymptomatic infection. Treatment of candida in the urine should only occur in rare situations, such as clear signs and symptoms of infection and no alternative source of infection
b. Treatment of asymptomatic candiduria in non-neutropenic catheterized patients has *usually not* been shown to be valuable [136]
c. “Treatment” of candiduria should first include replacement/removal of urinary tract instruments.
d. Except in selected highest risk transplant recipients, or immuno-compromised hosts who are receiving steroids, or clinical scenarios for patients at high risk of systemic candidiasis, candiduria has a low incidence of systemic complications , and conservative observation is usually indicated.
e. Isolation of candida in the urine of non- catheterized patients should second raise concerns about vaginal or external contamination. If a reliable specimen is repeatedly obtained with yeast, and the patient is symptomatic, consideration of anti-fungal therapy may be warranted.

References for Appendix 1. Diagnosis of Urinary Tract Infection – Top Ten Myths

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