Bacterial Urinary Tract Infection (UTI)

Important Notes

- Change in mental status alone, without other signs and symptoms of UTI, is NOT sufficient to diagnose UTI
- Cloudy or foul smelling urine does NOT mean UTI is present
- Pyuria either in the setting of negative urine cultures or in patients with asymptomatic bacteriuria usually requires no treatment. If pyuria persists, consider other causes (e.g. interstitial nephritis or cystitis, fastidious organsims)
- Follow-up urine cultures and/or urinalysis are only warranted for ongoing symptoms. They should NOT be acquired routinely to monitor for response to therapy.

Diagnosis

Specimen collection

- The urethral area should be cleaned with an antiseptic cloth and the urine sample should be collected midstream or obtained by fresh catheterization. Specimens collected using a drainage bag or taken from a collection hat are not reliable and should not be sent.

Interpretation of the urinalysis and urine culture

- Urinalysis and urine cultures must be interpreted together in the context of symptoms
- **Urinalysis/microscopy**
  - Dipstick
    - Nitrites indicate bacteria in the urine
    - Leukocyte esterase indicates white blood cells in the urine
    - Bacteria: presence of bacteria on urinalysis should be interpreted with caution and is not generally useful
  - Pyuria (more sensitive than leukocyte esterase): > 10 WBC/hpf or >27 WBC/microliter
- **Urine culture**
  - If U/A is negative for pyuria, positive cultures are likely contamination
  - Most patients with UTI will have ≥100,000 colonies of a uropathogen. Situations in which lower colony counts may be significant include: patients who are already on antibiotics at the time of culture, symptomatic young women, suprapubic aspiration and men with pyuria.

Asymptomatic bacteriuria

- Positive urine culture ≥ 100,000 CFU/mL with no signs or symptoms
- Do not obtain routine urine cultures in asymptomatic patients except in pregnant women during early pregnancy or in patients about to undergo urologic procedures in which mucosal bleeding is expected (NOT urinary catheter placement)
- Asymptomatic bacteriuria is common: 1–5% of premenopausal women, 3–9% of postmenopausal women, 40–50% of long-term care residents and 9–27% of women with diabetes.

Acute cystitis

- Dysuria, urgency frequency, suprapubic pain **PLUS** pyuria (>10 WBC/hpf) **PLUS** positive urine culture ≥ 100,000 CFU/mL
- **Uncomplicated**: female, no urologic abnormalities, no stones, no catheter
- **Complicated**: male gender, possible stones, urologic abnormalities, pregnancy

Acute pyelonephritis

- Fever, flank pain **PLUS** pyuria (>10 WBC/hpf) **PLUS** positive urine culture ≥100,000 CFU/mL
- Many patients will have other evidence of upper tract disease (i.e., leukocytosis, WBC casts, or abnormalities upon imaging)
- **Uncomplicated**: female, no urologic abnormalities, no stones, no catheter
- **Complicated**: male gender, possible stones, urologic abnormalities, pregnancy

Urosepsis

- Urinary source of infection with signs and symptoms of sepsis

Microbiology

- *E. coli* (75-95%) is the most frequent organism
- *Staphylococcus saprophyticus* (5-15%) is seen in young females who are sexually active
- Other Gram-negative organisms: *Proteus mirabilis*, *Klebsiella pneumoniae*, *Enterobacter* spp., *Pseudomonas* spp.
  - Frequency of these organisms increases in patients with structural abnormalities in the urinary tract, presence of nephrostomy tubes, hospital and long-term care facility patients
- *Enterococcus* spp. can be a contaminant or colonizer, particularly in patients with urinary catheters or multiple organisms growing in urine culture.
- *S. aureus* is rarely isolated from the urinary tract as uropathogen in patients without indwelling catheters. Presence of *S. aureus* may indicate dissemination from the blood or other deep tissue; negative blood cultures should be confirmed in patients without catheters or other urinary tract instrumentation.

Treatment

Asymptomatic Bacteriuria

No treatment unless the patient is:

- Pregnant
- About to undergo a urologic procedure in which mucosal bleeding on a case-by-case basis (NOT urinary catheter placement)
- Consider treatment in renal transplant and neutropenic patients

Treatment Notes

- Treatment does not decrease asymptomatic bacteriuria or prevent subsequent development of UTIs
- Treatment is associated with increased risk of development of future UTIs that are antibiotic resistant and adverse events related to antibiotic use

Acute Cystitis

Uncomplicated

- Nitrofurantoin (Macrobid®) 100 mg PO Q12H for 5 days
  OR
- Cefadroxil* 1 g PO daily for 5 days
  OR
- Cephalexin* 500 mg PO Q6H for 5 days
  OR
- Cefuroxime* 250 mg PO Q12H for 5 days
  OR
- Cefdinir* 300 mg PO Q12H for 5 days
  OR
- TMP/SMX 1 DS tab PO Q12H for 3 days
  OR
- IV option: Cefazolin 1 g IV Q8H for 3 days

*Use Cefazolin susceptibility as a surrogate to predict susceptibilities for Cefadroxil, Cephalexin, Cefuroxime, Cefdinir for *E. coli*, *K. pneumoniae*, and *P. mirabilis.* For susceptibility interpretation for other organisms consult ID pharmacist.

Complicated

- Same regimens as above except duration is 7–14 days based on clinical response and underlying risk factors

Treatment Notes

- UTIs in men are traditionally considered complicated. UTIs in men in the absence of obstructive pathology (e.g., BPH, stones, strictures) are uncommon. Please critically evaluate your diagnosis of UTI in male patients.
- Oral therapy is preferred and should be given unless patient is unable to tolerate oral therapy
- If IV β-lactams are used empirically for 3 days, no additional therapy is needed for uncomplicated cystitis
- If IV β-lactams are used empirically for < 3 days or treating complicated cystitis, the patient can be switched to an appropriate oral beta-lactam and duration of IV therapy should be counted towards total duration of therapy
- Oral Fosfomycin can be used if susceptible for Gram-negative MDR organisms (susceptibilities must be requested)

Acute Pyelonephritis

Community-acquired

- Ceftriaxone 1 g IV Q24H
  OR
- Ertapenem 1 g IV Q24H (if history of ESBL)
  OR
- Severe PCN allergy: Aztreonam 1 g IV Q8H **OR** Gentamicin

Duration: 7–14 days

Hospitalized > 48H

- Cefepime 1 g IV Q8H
  OR
- Severe PCN allergy: Aztreonam 1 g IV Q8H **OR** Gentamicin

Duration: 7–14 days

Step-Down Therapy

Oral therapy should be used for pyelonephritis once susceptibilities are available.

- Ciprofloxacin 500 mg PO Q12H for 7 days
- TMP/SMX 1 DS PO Q12H for 7-10 days
- Cefadroxil* 1 g PO Q12H for 14 days
- Cefuroxime* 500 mg PO Q12H for 14 days
- Oral Fosfomycin can be considered if susceptible for Gram-negative MDR organisms (susceptibilities must be requested). Consult ID Pharmacist for dosing.

*Use Cefazolin susceptibility as a surrogate to predict susceptibility for Cefadroxil, Cefuroxime and Cefdinir for *E. coli*, *K. pneumoniae* and *P. mirabilis*. For susceptibility interpretation for other organisms consult ID Pharmacist.

Notes

- Days of empiric therapy should be counted towards total duration of therapy
- Longer durations may be required if associated with underlying urinary tract abnormalities

Urosepsis

- Cefepime 1 g IV Q8H
  OR
- PCN allergy: Aztreonam 1 g IV Q8H ± Gentamicin
- **Duration**: 7–10 days

Treatment Notes

- Oral Ciprofloxacin or TMP/SMX have excellent bioavailability and should be used as step-down therapy if organism is susceptible
- Oral β-lactams should not be used for bacteremia due to inadequate blood concentrations
- Duration of empiric IV therapy should be counted towards total duration of therapy

Treatment of Enterococcus

Enterococcus spp. can be a contaminant or colonizer, particularly in patients with urinary catheters or multiple organisms growing in urine culture. Patients should be treated only if symptomatic unless they meet criteria for treatment of asymptomatic bacteriuria. See asymptomatic bacteriuria section above.

E. faecalis

Almost all isolates are susceptible to Ampicillin

- Amoxicillin 500 mg PO Q8H
  OR
- Ampicillin 1 g IV Q6H
  OR
- PCN allergy: Nitrofurantoin 100 mg PO Q12H OR Tetracycline 500 mg PO Q6H if susceptible

E. faecium (often Vancomycin-resistant)

- **Uncomplicated UTIs**
  - Nitrofurantoin 100 mg PO Q12H if susceptible
    OR
  - Tetracycline 500 mg PO Q6H if susceptible
    OR
  - Fosfomycin 3 g PO once (susceptibility must be requested prior to its use)
- **Complicated UTIs**
  - Linezolid 600 mg PO Q12H
    OR
  - Fosfomycin 3 g PO every 2–3 days (max 21 days)

Treatment Duration

- Treatment duration is agent specific, see each treatment section above for duration

Management

Renal Excretion/Concentration of Selected Antibiotics

- **Good** (> 60%): aminoglycosides, Amoxicillin, Amoxicillin/clavulanate, Fosfomycin, Cefadroxil, Cefazolin, Cefepime, Cefuroxime, Cephlalexin, Ciprofloxacin, Colistin, Ertapenem, Trimethoprim/sulfamethoxazole, Vancomycin, Amphotericin B, Fluconazole, Flucytosine
- **Variable** (30–60%): Linezolid (30%), Doxycycline (29 - 55%), Ceftriaxone, Tetracycline (~60%)
- **Poor** (< 30%)**:** Azithromycin, Clindamycin, Cefdinir, Moxifloxacin, Oxacillin, Tigecycline, Micafungin, Posaconazole, Voriconazole

References

1. Boscia JA et al: Lack of association between bacteriuria and symptoms in the elderly. *Am J Med* 81:979, 1986 [PMID:3799658]

   Comment: In this survey of 72 elderly subjects (age 69 - 101 years), attempts were made to determine if bacteriuria without dysuria was asymptomatic. No differences in symptoms (either dysuria or overall well-being) were found when bacteriuric subjects compared their symptoms to when they were nonbacteriuric, suggesting that bacteruria without dysuria in elderly patients is largely asymptomatic.

2. Cai T et al: The role of asymptomatic bacteriuria in young women with recurrent urinary tract infections: to treat or not to treat? *Clin Infect Dis* 55:771, 2012 [PMID:22677710]

Comment: This large (n=699) randomized controlled trial evaluated treatment of asymptomatic bacteriuria in a young women (18-40 y/o) with recurrent UTIs (≥1 episode per year) and found that women who were treated were twice as likely to develop UTIs compared to those who were not treated at 12 month follow up. Asymptomatic bacteriuria maybe protective in young women with recurrent UTIs.

3. Cai T et al: Asymptomatic bacteriuria treatment is associated with a higher prevalence of antibiotic resistant strains in women with urinary tract infections. *Clin Infect Dis* 61:1655, 2015 [PMID:26270684]

Comment: This large study (n=550) demonstrates that treatment of asymptomatic bacteriuria leads to development of resistance and it does not prevent development of UTIs in the future. Patients who were treated were 4 times more likely to develop UTIs compared to those who were not treated with antibiotics (HR 4.36; SD 2.1, p=0.003).

4. Gupta K et al: International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: A 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. *Clin Infect Dis* 52:e103, 2011 [PMID:21292654]

Comment: 2010 IDSA guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women

5. McKenzie R et al: Bacteriuria in individuals who become delirious. *Am J Med* 127:255, 2014 [PMID:24439075]

Comment: Commentary on the association between bacteriuria and delirium. Authors suggest the following when assessing for true urinary tract infection: (1) use of the term "bacteriuria" or "asymptomatic bacteriuria" rather than UTI to encourage ongoing diagnostic evaluation, (2) consider careful monitoring rather than antibiotic administration and (3) Obtain urine cultures beforehand and stop treatment if culture is negative if the initial decision made is to treat with antibiotics.

6. Nicolle LE et al: Infectious Diseases Society of America guidelines for the diagnosis and treatment of asymptomatic bacteriuria in adults. *Clin Infect Dis* 40:643, 2005 [PMID:15714408]

Comment: 2005 IDSA guidelines for the management of asymptomatic bacteriuria.

7. Sousa R et al: Is asymptomatic bacteriuria a risk factor for prosthetic joint infection? *Clin Infect Dis* 59:41, 2014 [PMID:24723280]

Comment: In this large multicenter study (n=2,497) patients undergoing total hip or knee arthroplasty prevalence of asymptomatic bacteriuria was 12.1% and incidence of prosthetic joint infection was 1.7%. Patients who had asymptomatic bacteriuria were more likely to have prosthetic joint infection (OR, 3.23; 95% CI 1.67-6.27), but with unrelated pathogen. Treating asymptomatic bacteriuria did not decrease incidence of prosthetic joint infections (3.9% vs. 4.7%, p=0.78).