Continuing Education

Urinary Tract Infection: Urine Trouble

Authors:

Matt Cole, Pharm.D.
Harrison School of Pharmacy, Auburn University

Jonathan Le, Pharm.D.
Harrison School of Pharmacy, Auburn University

Frank Smith, Pharm.D.
Harrison School of Pharmacy, Auburn University

Corresponding Author:
Bernie Olin, Pharm.D.
Associate Clinical Professor and Director
Drug Information and Learning Resource Center
Harrison School of Pharmacy, Auburn University

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Learning Objectives:

- Recognize the predisposing risk factors to developing a UTI.
- Name the most common causative bacteria of UTIs.
- Identify the "gold standard" test for the diagnosis of UTIs.
- List the common and severe side effects of the antibiotics used in UTIs.
- Identify the appropriate therapy for a UTI when given a specific clinical situation.

Background/Epidemiology

Urinary tract infections (UTIs) are common bacterial infections that affect an estimated 150 million people worldwide and over 7 million people in the United States (U.S.) each year.[1] As a result, approximately $3 billion dollars are expended in the diagnosis and treatment of UTIs in the U.S. alone.[2] The likelihood of developing a UTI varies with age and gender. UTIs are more prevalent in females due to their anatomic and physiologic differences from males.[2] Females are 30 times more likely to develop a UTI than males and an estimation of about 25% to 40% of women will experience a UTI at some point in their life.[2] In comparison to females, male neonates are at a greater risk primarily due to structural abnormalities and noncircumcision.[3] About 3% to 7% of females between ages 1 through 6 years develop a UTI compared to 1% to 2% in males.[3] The incidence continually increases 1% to 2% for each decade of life until 10% to 20% of women are bacteriuric after 70 years.[2] Adult males have a very low percentage of UTIs up until the age of 65 when the percentage of UTIs become relatively equal to females.[3] The percent increase in the elderly can be attributed to the population's frequency in hospitalizations and residing in nursing homes.

Risk Factors

Risk factors that are associated with UTIs that are seen in both males and females include insertion of a urinary catheter or instrument, renal disease, neurologic dysfunction, and urinary tract obstruction.[2,4,5] Insertion of a catheter, duration of catheterization, and susceptibility of the patient are directly correlated to infection.[2,6,7] Although catheter technique has improved drastically, the contamination of catheter junctions and urine collection bags pave a pathway for bacteria to invade the bladder.[2] In the U.S., catheter associated UTIs contribute to 70-80% of complicated cases.[8] The urine's natural ability to flush and remove bacteria becomes disrupted when blockage forms in the urinary tract. Also, bacteria may flow back into the kidney via vesicoureteral reflux, causing kidney dysfunction.[3] Examples of urinary tract obstruction are kidney stones, tumors, and structural abnormalities.

Male UTI risk factors are those who are uncircumcised or older men with prostatic hyperplasia.[2,4,9,10] The chances of prostatic hyperplasia increase as men age, which leads to obstruction in urine flow and susceptibility of a UTI. Risk factors that pertain only to females are sexual activity, previous UTI, use of cervical diaphragm, use of spermicidal jellies, pregnancy, diabetes, and menopause.[2,4,9,10] During pregnancy, urine pH and osmolality become advantageous for bacteria growth. Menopausal women undergo hormonal changes such as the reduction of estrogen. Estrogen deficiency causes the loss of vaginal lactobacilli, which creates a favorable environment for pathogenic bacteria.[2,3]

Etiology

UTIs are classified based on its location as either upper or lower urinary tract infections. Upper UTIs involve the kidneys and are referred to as pyelonephritis.[2,3,4] Lower UTIs normally involve the bladder and are referred to as cystitis. Additionally, UTIs are categorized as either complicated or uncomplicated.[2,3,4] There are various characteristics that label a patient as having complicated or uncomplicated UTIs (Table 1).[2,3,4,6,7] The most common UTIs are acute uncomplicated cystitis.

Table 1

Characteristics of Uncomplicated and Complicated UTIs[2,3,4,6,7]	
Uncomplicated	**Complicated**
Acute cystitis in women Community-acquired UTI Acute pyelonephritis in young healthy women	Men Children Pregnant Immunocompromised Diabetic Recurrent UTI (>3 episodes per year) Hospital-acquired UTI Abnormalities of urinary tract Instrumentation/catheterization Unusual pathogens (yeast, *Mycoplasma*) Renal failure

Uncomplicated UTIs are mainly community-acquired and involve a single pathogen. In contrast, complicated UTIs are largely hospital-acquired and involve multiple organisms. Organisms that cause uncomplicated UTIs are typically gram negative with 80-90% of incidences caused by *Escherichia coli* (*E. coli*).[3] Similarly, *E. coli* accounts for the majority of complicated UTIs at 20% to 30%.[2] Other causative organisms of UTIs are *Staphylococcus saprophyticus*, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Pseudomonas aeruginosa*, and *Enterococcus faecalis*.[2,3]

Pathophysiology

There are three potential ways for bacteria to invade the urinary tract and cause infection: the ascending, hematogenous, and lymphatic pathways.[2-5,9] The most common route of infection is through the ascending pathway. Due to the close proximity of the female urethra and perirectal area, colonization of bacteria is believed to originate from fecal flora.[3] Other explanations for the colonization of bacteria in the urethra are use of spermicidal agents and sexual activity/intercourse.[2,3,5] Following the colonization of the urethra, the pathogens quickly multiply and ascend the ureters to the kidneys.[3] This pathway may explain why UTIs occur more often in women than men. More unusual routes of entry are the hematogenous and lymphatic pathways. Infection from the hematogenous pathway occurs when the blood supply carries pathogens to the urinary tract. Although there is a connection between the bladder and kidney via the lymphatic system, there is lack of evidence showing the lymphatic pathway as a significant mechanism for the development of infection.[2,3,9]

There are three factors that determine the development of infection: size of inoculum, virulence of the microorganism, and competency of the natural host defense mechanism.[3] A primary factor for the colonization of bacteria in the urinary tract is the failure of the host defense mechanisms.[3] Host defense mechanisms refer to the urinary tract's ability to counteract with virulence factors of bacteria. A few mechanisms include the components of urine, urinary tract mucosa, urinary inhibitors of bacterial adherence, and inflammatory response.[5] Urine is composed of antibacterial substances like organic acids and urea, which contribute to low pH and high osmolality, respectively.[2,3] Low pH and high osmolality make up a poor environment for bacteria to thrive. Thus, urination plays an important role in inhibiting growth and rapidly eliminating pathogens.[3] Adhesive properties of bacteria determine its capability to colonize and cause infection. For example, *E. coli* utilizes its rigid, hair-like appendages called fimbriae as an adhesion mechanism.[2] Fimbriae binds to mannose residues present in glycolipid components on epithelial cells.[2] The bladder mucosa itself resists adhesion by being coated with a urinary mucus called glycosaminoglycan.[3] In addition, Tamm-Horsfall proteins that are secreted into the urine contain mannose residues that prevent adherence of bacteria to uroendothelial cells.[3,5] However, these protective mechanisms may only work against small inocula of bacteria.[5] Large inocula or bacteria with mannose resistant fimbriae tend to overcome the barriers.[3,5] Consequently, the bacteria is able to ascend to the kidneys and cause pyelonephritis. At the time of bacterial spread and colonization, the body stimulates an inflammatory response by releasing polymorphonuclear leukocytes (PMNs).[3] Once PMNs are deployed, the phagocytic white blood cells mobilize to the site of infection and ingest

any foreign particles to control the spread of infection.[3]

Clinical Presentation

The clinical presentation of a patient may often aid the diagnosis of a UTI; however, signs and/or symptoms alone are not solely diagnostic. Clinical manifestations of UTIs may be asymptomatic or symptomatic and thus differing treatment approaches are utilized based on this subjective data. Patients with symptoms may also vary based on the presence of catheter(s), which is a predisposing risk factor for the development of a UTI.[3,4] Symptoms associated with urinary tract infections may also vary with age of affected patients, as well as, the location of infection.[3,4] Typically symptoms are associated with the location of the infection: upper urinary tract symptoms (pyelonephritis) and lower urinary tract symptoms (cystitis). In contrast to these subjective findings in a physical exam, urine culture remains the "gold standard" in the diagnosis of UTIs.

Hallmark characteristics associated with lower UTIs are established as localized symptoms including urgency and dysuria, with some reports of suprapubic pain/heaviness.[3,4] In comparison to upper UTIs, local symptoms may still be present and may precede additional symptoms.[3] Symptoms of pyelonephritis may include fever with or without chills, flank pain, headache, nausea, and vomiting.[3,4] It should be emphasized that not all symptoms may present at once and typically symptoms vary greatly by patient.[3,4] In the geriatric population, local symptoms, such as urgency, frequency, dysuria, and hesitancy, may be present at baseline due to other comorbidities.[3] Older patients may also be asymptomatic in regards to localized symptoms that would be suspected.[3] Symptoms differing from these localized symptoms may include altered mental status and abdominal pain.[3]

Diagnosis

Symptoms alone are not diagnostic of a UTI and neither should symptoms alone be used as justification for pharmacotherapy.[2] Patients with suspected UTI should have urine collection ordered for urinalysis, as well as microscopic evaluation of urine sample.[2,3] In addition to all of the previously mentioned methods of determining a diagnosis of a UTI, urine culture still remains the most reliable and accurate method of UTI diagnoses.[2,3] Preliminary results of urine cultures are often not available for at least 48 hours, which is often when prescribers deviate from recommended practice, especially in the primary care/non-emergent settings. Urinalysis, while not solely diagnostic on its own, often provides beneficial information that aids practitioners in evaluation of possible UTIs.

When evaluating objective parameters in the determination of a urinary tract infection, the urine collection process should be the first step. While mid-stream urine collection techniques seem to be recommended by numerous sources, a study conducted by Lifshitz E, et al found that mid-stream collection technique did not reduce the rate/incidence of urine contaminants in the outpatient setting.[11] Their sample included young women with suspected cystitis; therefore, the authors concluded that the mid-stream collection (clean-catch) technique may still be valuable for other populations.[11] This being understood, it should be recognized that methods to reduce contamination of the sample should still be taken. When mid-stream collection is not ideal, alternative measures of urine collection may be used. Alternative urine collection techniques include suprapubic bladder aspiration and catheterization.[3] Urine dip sticks are frequently utilized in the aid of suspected UTI diagnoses. Urine dipstick analysis provides measurements of specific gravity, pH, glucose, protein, ketone, blood, leukocyte esterase, nitrites, and white blood cells (WBCs).[2] Of these measurements, presence of leukocyte esterase, hematuria, nitrites, and pyuria seem to be the most helpful in urine sample evaluation.[12,13] Leukocyte esterase test is an indirect measure of the presence of bacteria.[14] A positive leukocyte esterase test may be beneficial in evaluation of possible UTI; however, it is limited in the instances of low bacterial counts and should be reviewed alongside nitrite test results for most specificity in regards to UTIs.[14] Hematuria defined as >3 RBCs per high-power field (HPF) in at least two separate urine samples, may also be an indicator of UTI; however, due to its low specificity to

UTIs, it should not be used alone in urinalysis evaluation.[12] Nitrite tests yield simple positive or negative results. A positive nitrite test may indicate the presence of bacteria present that are able to reduce nitrates to nitrites.[13] A positive result is very sensitive for UTIs; however, a negative result does not rule out infection, as some bacteria do not reduce nitrates to nitrites.[12,13] Presence of pyuria defined as >10 WBC/mm^3 is a relatively non-specific test for detection of UTI and should not be used alone to confirm diagnosis of UTI.[3,13]

Followed by urinalysis is urine culture. While urine cultures differ in convenience (rapid test result turnaround), it remains the gold-standard of true UTI diagnoses. Significant bacteriuria is defined as $>10^5$ colony forming units (cfu) per milliliter of urine.[3,13] Symptomatic women may not meet the criteria for cfu/mL, as those with true UTIs are often found to have lower quantitative counts. A review by Stamm WE, et al states that it is reasonable for symptomatic women to have colony counts of $>10^2$ cfu/mL to indicate infection.[15] In contrast, Infectious Diseases Society of America (IDSA) Guidelines for the Diagnosis and Treatment of Asymptomatic Bacteriuria indicate the following criteria for diagnosis of asymptomatic bacteriuria in Table 2.[16]

Table 2

Quantitative UTI Diagnostic Criteria[16]		
Gender	Number of urine specimens	Quantitative Counts
Women	2	$\geq 10^5$ cfu/mL
Men	1	$\geq 10^5$ cfu/mL

While evaluation of urine culture is ideal, it may not always be a possible, especially in the ambulatory patient. Due to slow turnaround of urine cultures, practitioners are not always able to evaluate this gold standard for diagnosis.

Urinary Tract Infection Screening Recommendations

Screening involves urinalysis evaluation and urine culture gathering to determine the clinical presence of a UTI.[16] A review conducted by Nicholle LE, et al concluded that screening for UTIs in asymptomatic pregnant women is the only circumstance that may provide beneficial outcomes.[16] UTIs may pose a significant risk to the developing fetus, which warrants screening in these patients.[16] Their review also found that screening the following asymptomatic patients does not result in beneficial outcomes (reduction of symptomatic episodes): premenopausal (non-pregnant) women, diabetic women, older persons living in the community, institutionalized elderly patients, patients with spinal cord injury, and currently catheterized patients.[16]

Diagnosis of Urinary Tract Infections in Catheterized Patients

Patients that present with signs/symptoms of UTI with indwelling urethral, indwelling suprapubic, or intermittent catheterization and urine specimen of ≥1 bacterial species and $\geq 10^3$ cfu/mL should be considered to have a true urinary tract infection.[17] In contrast, screening recommendations parallel that of previous recommendations, emphasizing that routine screening should not be performed in asymptomatic patients.[16,17] Definition of asymptomatic bacteriuria in patients with indwelling urethral, indwelling suprapubic, or intermittent catheterization is urine specimen of ≥1 bacterial species with counts of $\geq 10^5$ cfu/mL.[17] Catheterized patients are at a greater risk of developing UTIs, which often correlates to perhaps unwarranted treatment in some instances. It is important for providers to evaluate signs and symptoms of UTI in these patients as treating patients who remain asymptomatic is not recommended.

Treatment of Urinary Tract Infections

For the treatment of acute uncomplicated cystitis, preferred therapy includes nitrofurantoin, trimethoprim-sulfamethoxazole (TMP/SMZ), and fosfomycin trometamol.[18] Alternative therapies are beta-lactams and fluoroquinolones.[18] For the

treatment of pyelonephritis, fluoroquinolones and TMP/SMZ are considered first line agents while beta-lactams are alternative agents.[18]

Nitrofurantoin can be used to treat uncomplicated cystitis for 5-7 days. Nitrofurantoin was originally studied by the manufacturer to provide a duration of treatment of 7 days.[19] However, nitrofurantoin may be given for 5 days according to IDSA guidelines after reviewing multiple studies demonstrating similar efficacy between 5 day regimen versus 7 day regimen.[18,20-23] Flavoproteins reduce nitrofurantoin to reactive intermediates. The reactive intermediates inhibit many of the bacterial functions, aerobic energy metabolism and the synthesis of bacterial deoxyribonucleic acid (DNA), ribonucleic acid (RNA), cell wall, and protein, by inactivating or altering bacterial macromolecules.[20,24] Nitrofurantoin is administered with meals to improve absorption and decrease adverse effects; suspension may be mixed with water, milk, or fruit juice.[24] Macrodantin®/Furadantin's® dosing is 50 to 100 mg four times a day while Macrobid® is 100 mg twice a day. Common adverse effects are nausea, vomiting, and headache. Severe adverse events include: hemolytic anemia, peripheral neuropathy, and pulmonary reactions.[19,24] Nitrofurantoin is contraindicated in anuria or patients with CrCl less than 60 mL/min.

TMP/SMZ 160/800 mg (1 double-strength tablet) twice-daily for 3 days is another first line agent utilized in the treatment of acute uncomplicated cystitis.[18,20] If local resistance rates of uropathogens exceed 20%, use a different medication. The 20% resistance rate threshold is an expert recommendation based off of four clinical trials and mathematical modeling studies.[18,21-23,25] For pyelonephritis, TMP/SMZ 160/800 mg twice-daily for 14 days is appropriate. If susceptibility of pyelonephritis infection is unknown, give 1 g of ceftriaxone IV or an aminoglycoside.[18] Trimethoprim inhibits dihydrofolic acid reduction to tetrahydrofolate resulting in inhibiting enzymes of the folic acid pathway.[20] Sulfamethoxazole interferes with bacterial folic acid synthesis and growth via inhibition of dihydrofolic acid formation from para-aminobenzoic acid (PABA).[19,20] TMP/SMZ should be taken with 8 oz glass of water to prevent crystalluria and kidney stones.[19,20] Common adverse events of TMP/SMZ are rash, urticaria, nausea, vomiting, and photosensitivity.[19,20] Severe side effects include *Clostridium difficile*-induced diarrhea, anaphylaxis, agranulocytosis, and hepatic necrosis.[19,20] Alternative medications are to be considered for patients that have sulfonamide allergy and patients that are pregnant (low folic acid may cause congenital malformations).[19,20]

Fosfomycin trometamol 3 g in a single dose can be used to treat acute uncomplicated cystitis.[18] It is an appropriate choice for therapy where it is available due to minimal resistance and decreased likelihood for collateral damage; however, the US Food and Drug Administration (FDA) states that fosfomycin has inferior efficacy compared with the standard short course regimens.[18] Fosfomycin is indicated for women $\geq$18 years old.[26] Fosfomycin is prepared by pouring the contents of envelope into 3 to 4 oz of cool water (not hot), stir until it's dissolved, and take immediately.[26] Some common adverse effects include: diarrhea, headache, vaginitis, nausea, rhinitis, back pain, dysmenorrhea, pharyngitis, dizziness, abdominal pain, dyspepsia.[26]

The fluoroquinolones (ofloxacin, ciprofloxacin, and levofloxacin) are highly efficacious in 3-day regimens and may be used as second line agents for acute cystitis.[18] However, they have high predisposition for collateral damage and should be conserved for instances in which their use is specifically warranted.[18] Topoisomerase II is an enzyme that is needed for DNA replication and transcription, DNA repair, recombination, and transposition.[19,20] Fluoroquinolones inhibit DNA gyrase (topoisomerase II) resulting in the antibiotic being bactericidal.[19,20] Fluoroquinolones are also utilized in the treatment of pyelonephritis, oral ciprofloxacin 500 mg twice daily for 7 days may be given with or without IV ciprofloxacin 400 mg.[18] Additional therapies to treat pyelonephritis are a once-daily oral ciprofloxacin 1000 mg extended release for 7 days or levofloxacin 750 mg for 5 days.[27,28] If there is 10% resistance to fluoroquinolones, a one-time dose of 1 g ceftriaxone or 24 hour dose

of aminoglycoside is recommended.[18] Equivalent cure rates have been shown between large studies comparing 500 mg extended release once daily ciprofloxacin and 250 mg twice daily ciprofloxacin.[27,28] Therefore, a patient may be given oral fluoroquinolones once or twice daily according to Acute Uncomplicated Cystitis and Pyelonephritis in Women guidelines.[18] Fluoroquinolone's common side effects are diarrhea, nausea, vomiting, headache, and photosensitivity.[19,20,29] Severe side effects include tendon rupture unusual joint or tendon pain, muscle weakness, a "pins and needles" tingling or pricking sensation, numbness in the arms or legs, confusion, hallucinations.[29] If a patient experiences any severe side effects, the fluoroquinolone should be stopped immediately and switch to a different antibiotic for the remainder of the course. As of July 2016, the FDA is recommending that health care providers should not prescribe systemic fluoroquinolones to patients who have other treatment options for uncomplicated UTI.[20] Fluoroquinolones chelate with a metal rendering the antibiotic inactive, therefore counseling patients on avoiding multivitamins, antacids, and milk while taking a fluoroquinolone or separate the antibiotic at least 2 hours before or 4 hours after meals.[30]

When other agents cannot be used for acute uncomplicated cystitis, beta-lactams (amoxicillin-clavulanate, cefdinir, cefaclor, and cefpodoxime proxetil) can be used for a duration of 3 to 7 days.[18-20] Beta-lactams are generally not first line due to more resistance from bacteria, less efficacy, and more adverse events compared to the rest of the first line agents.[18] Ampicillin and amoxicillin should not be used especially for the reasons listed above. For pyelonephritis, beta-lactams are not first line but if used it is for 10-14 days with ceftriaxone 1 g IV or a consolidated 24 hour dose of an aminoglycoside based on patient specific dosing parameters.[18] Beta-lactams are bactericidal by binding to penicillin-binding proteins (PBPs) thus interfering with cell wall synthesis.[20,31-34] Common side effects are rash, diarrhea, headache, nausea, and vomiting.[32,33] Severe reactions are anaphylaxis, *Clostridium difficile*-induced diarrhea, and toxic epidermal necrolysis.[30-33]

Women requiring hospitalization for pyelonephritis are to be treated with either: an intravenous fluoroquinolone; an aminoglycoside with or without ampicillin; an extended-spectrum beta-lactam with or without an aminoglycoside; or a carbapenem.[18,29] The choice between which drug regimen depends on availability and susceptibility.

Special populations

In pregnant women who are asymptomatic, the U.S. Preventative Service Task Force and Sanford Guide recommend screening women in 1st trimester.[30,35] If the culture yields growth diagnostic of a UTI, treat with amoxicillin, nitrofurantoin, oral cephalosporin, TMP-SMX, or TMP alone.[30] Continue to screen monthly for reoccurrences. The importance of the initial screening is because during pregnancy, there is a urinary stasis and reduced defenses against reflux of bacteria to kidneys.[3] The lowered defenses is caused by decreased peristalsis, reduced bladder tone, and severe dilation of renal pelvis and ureters.[3] TMP-only dosing is 100 mg every 12 hours or 200 mg every 24 hours for 10 days.[30]

Catheter-Associated Urinary Tract Infection (CA-UTI) is a complicated UTI. Treatment duration for a prompt resolution of symptoms is seven days; while those with a delayed response, treatment is 10 to 14 days regardless of whether the patient remains catheterized.[17] A 5-day regimen of levofloxacin may be considered in patients with CA-UTI who are not severely ill. A 3-day antimicrobial regimen may be considered for women aged 65 years or older who develop CA-UTI without upper urinary tract symptoms after an indwelling catheter has been removed. First line options for complicated UTI/catheter are ampicillin + gentamicin (2 mg/kg load then 1.7 mg/kg Q8hr); piperacillin-tazobactam (3.375 g IV q 4-6hr; if pseudomonas 4.5 g Q6hr); Doripenem (500 mg IV Q8hr, 1-hour infusion); imipenem (0.5 g IV Q12hr); Meropenem (1 g IV Q8h) for up to 2-3 weeks.[29] Alternative line therapies include: Ciprofloxacin (400 mg IV Q12h); gatifloxacin (400 mg IV q12h); levofloxacin (750 mg IV q24h); ceftazidime (2g IV q8) for up to 2-3 weeks or ceftolozane-tazobactam (1.5 g IV q8h) for 7 days.[30] Whenever possible, switch to an

oral fluoroquinolone or TMP/SMZ.[30] Catheter associated prophylaxis using cranberry product, antibiotics, methenamine salts, or daily meatal cleansing with povidone-iodine solution, silver sulfadiazine, polyantibiotic ointment/cream, or green soap and water is not recommended for routine use.[17] Antibiotic prophylaxis has led to emergence of resistant strains of bacteria with only postponing the development of bacteriuria. Therefore, antibiotic prophylaxis is not recommended for short or long-term catheterization.[17]

Table 3

Summary of Acute Uncomplicated Cystitis Treatment[6,18,30-33,36]

First Line Agents
• Nitrofurantoin
  ○ Macrodantin®/Furadantin® ~ 50 to 100 mg four times daily for 5 to 7 days
  ○ Macrobid® ~ 100 mg twice daily for 5 to 7 days
• TMP-SMZ, 160/800 mg twice daily for 3 days
  ○ Don't use if patient has severe sulfonamide allergy
  ○ Not recommended if local uropathogen resistance is greater than 20%
• Fosfomycin trometamol, 3 gm sachet in a single dose

Second Line agents
• Fluoroquinolone (FQ)
  ○ Ciprofloxacin, 250 mg twice daily for 3 days
  ○ Levofloxacin, 250 mg or 500 mg once daily for 3 days
  ○ Not recommended with resistance to FQ >10%
• Beta-lactams
  ○ Amoxicillin-clavulanate, 500 mg/125 mg twice daily for 7 days
  ○ Cefpodoxime poxetil, 100-mg twice daily for 3 to 7 days
  ○ Cefaclor, 250 ORALLY every 8 hours for 5 to 9 days
  ○ Cefdinir, 300 mg twice per day for 3 to 10 days

Table 4

Summary of Treatment for Women with Pyelonephritis[18,30]

• Fluoroquinolones
  ○ Ciprofloxacin 500 mg BID for 7 days ± Intravenous antibiotic or an initial 400 mg dose of intravenous ciprofloxacin
  ○ Ciprofloxacin XR 1000 mg once daily for 7 days
  ○ Levofloxacin 750 mg once daily for 5 days
*If resistance to fluoroquinolones is greater than 10%, add an intravenous antibiotic†

• TMP/SMZ DS (160/800 mg) BID for 14 days plus IV antibiotic   ○ Only use if pathogen is susceptible

• Beta-lactams (amoxicillin-clavulanate, cefdinir, cefaclor, or cefpodoxime proxetil)
  ○ Use beta-lactams if fluoroquinolones or TMP/SMZ are contraindicated
  ○ Length of treatment: 10 to 14 days
  ○ Must be given with an intravenous antibiotic

†Intravenous antibiotics include ceftriaxone 1 gm and consolidated 24 hour dose of an aminoglycoside

Table 5

Summary of Treatment for Women Hospitalized with Pyelonephritis[18,30]
First Line Options • Ampicillin + gentamicin (2 mg/kg load then 1.7 mg/kg q8h) • Pipercillin-tazobactam (3.375 g IV q 4-6h; if pseudomonas 4.5 g q6h) • Meropenem (1 g IV q8h) • Ceftriaxone (1-2 g IV q24h • Ciprofloxacin (400 mg IV q12h) for up to 2-3 weeks • Gatifloxacin (400 mg IV q12h) for up to 2-3 weeks • Levofloxacin (750 mg IV q24h) for up to 2-3 weeks *Treat for 14 days
Alternative Options • Piperacillin-tazobactam (3.375 g IV q 4-6h; if pseudomonas 4.5 g q6h) • Doripenem (500 mg IV q8h, 1-hour infusion) • Ertapenem (1g IV q24h) • Ticarcillin/clavulanate (3.1g IV q6h) *Treat for 14 days **The choice between which drug regimen depends on availability and susceptibility

Table 6

Treatment for Complicated UTI and Catheter-Associated UTI[17,30]

No catheter-associated UTI prophylaxis is recommended utilizing the following agents/methods:
• Cranberry products
• Antibiotics
• Methenamine salts
• Daily meatal cleansing with:
  ○ Povidone-iodine solution
  ○ Silver sulfadiazine
  ○ Polyantibiotic ointment/cream
  ○ Green soap and water

First Line Agents: Use one of the following below treatments for up to 2 to 3 weeks • Ampicillin + gentamycin (2 mg/kg load then 1.7 mg/kg q8h) • Piperacillin-tazobactam (3.375 g IV q 4-6h; if pseudomonas 4.5 g q6h) • Doripenem (500 mg IV q8h, 1-hour infusion) • Imipenem (0.5 g IV q12h) • Meropenem (1 g IV q8h)
Alternative Agents* • Ciprofloxacin (400 mg IV q12h) for up to 2 to 3 weeks • Gatifloxacin (400 mg IV q12h) for up to 2 to 3 weeks • Levofloxacin (750 mg IV q24h) for up to 2 to 3 weeks • Ceftazidime (2 gm IV q8h) for up to 2 to 3 weeks • Ceftolozane-tazobactam (1.5 gm IV q8h) for 7 days *Switch to oral FQ or TMP/SMZ whenever possible
Abbreviations: milligram (mg); kilogram (kg); gram (gm); intravenous (IV); q (every); h(hour)

Conclusion

UTIs are common infections that affect significantly more females than males. Symptoms and treatment are driven by a UTIs location (upper or lower) and characterization (complicated or uncomplicated). Urine culture is the "gold standard" for diagnosis. Antibiotics such as nitrofurantoin, TMP/SMZ, and fosfomycin are recommended first line pharmacotherapy, while fluoroquinolones and beta-lactams are considered second line pharmacotherapy.

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