Lower Urinary Tract Infections

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Purpose

The purpose of this course is to outline the pathophysiology and causative agents of lower urinary tract infections, differentiating between complicated and uncomplicated, and describing age and gender related differences and treatment options.

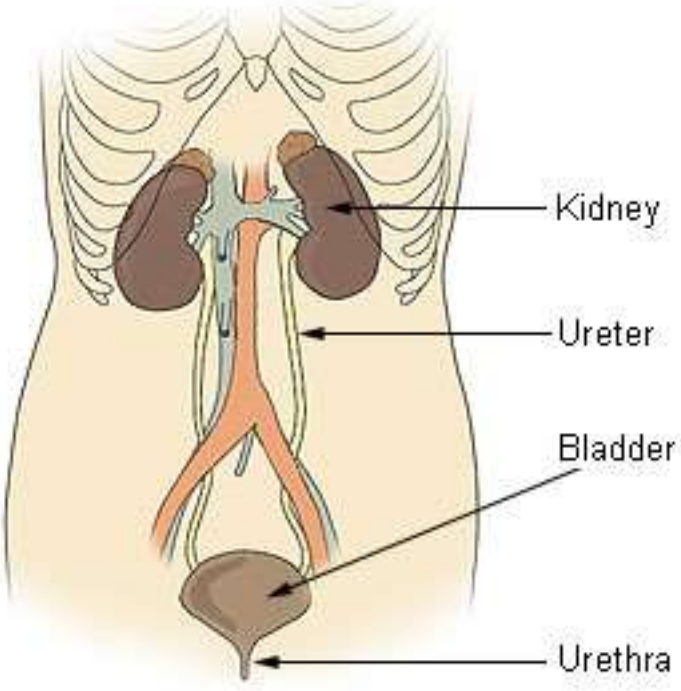
Goals

Upon completion of this course, the healthcare provider should be able to:

- Discuss complicated and uncomplicated lower urinary tract infections (UTIs), including at least 4 pathogenic agents.
- Describe a biofilm and its implications for UTIs.
- Describe 4 ways in which the bladder fights urinary infections.
- Discuss the effects of age and gender on UTIs
- Discuss at least 4 CDC recommendations for catheter use.
- Describe at least 5 common signs of uncomplicated lower UTIs.
- Describe the continuum from bacteriuria to MODS.
- Describe symptoms of lower UTIs in older adults.
- Describe 2 types of dipstick tests.
- Discuss urinalysis changes associated with UTI.
- Describe at least 3 common treatments for uncomplicated UTI and 3 for complicated UTI.

Introduction

Components of the Urinary System

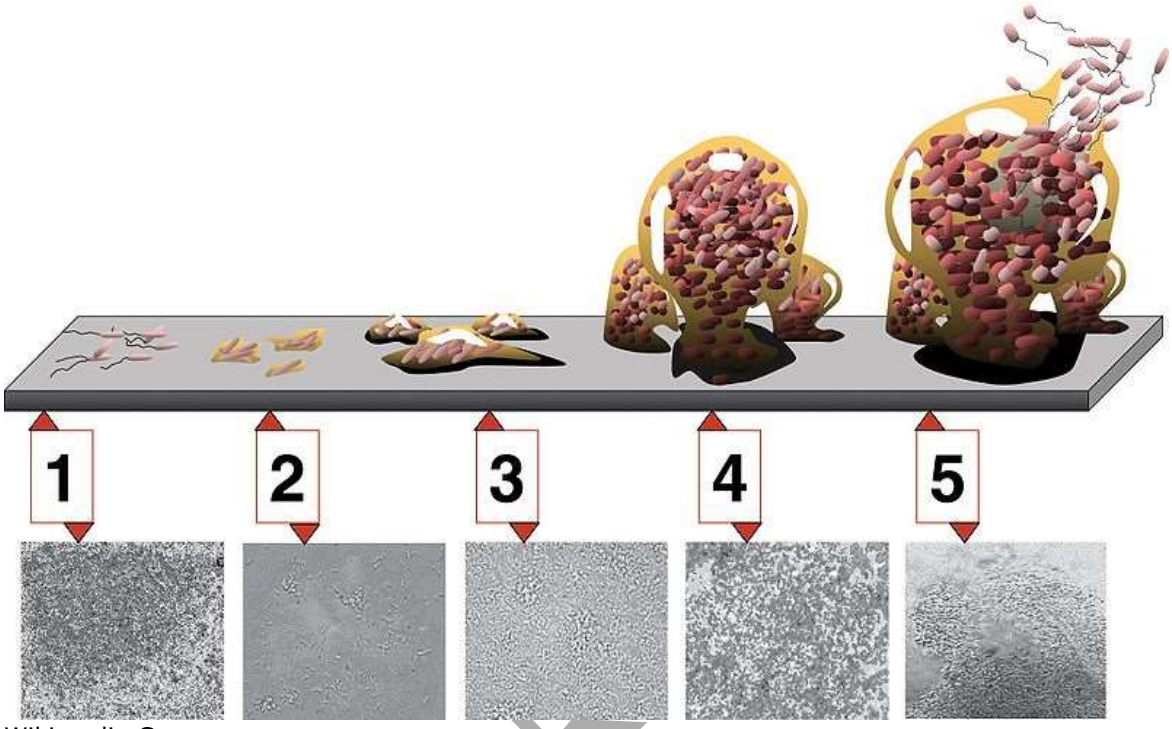


The urinary tract comprises the kidneys, ureters, bladder, and urethra. Urinary tract infections (UTIs), caused by pathogenic microorganisms invading the urinary tract are classified as lower UTIs if they affect the bladder (cystitis) or urethra (urethritis) while upper urinary tract infections affect the kidney (acute and chronic pyelonephritis, renal abscess, interstitial nephritis, and perirenal abscess).

UTIs account for about 6 million healthcare visits each year in the United States. **Community-acquired urinary tract infection** (CA-UTI) is usually uncomplicated and is common in young women. The most common pathologic agent is *Escherichia coli* while *Staphylococcus aureus* is responsible for 5 to 10% of infections.

Healthcare-acquire urinary infection (HA-UTI), HA-UTIs are nosocomial infections often caused by catheterization. These infections usually develop from different organisms and tend to be complicated and may result in chronic recurrent infection because of the growth of biofilms, which are resistant to treatment. Common pathological agents include enterobacteriaceae, *Pseudomonas aeruginosa* and *Acinetobacter* spp. Resistant strains are frequently encountered. Other agents include MRSA, *Enterococcus* spp. (including VRE), and *Candida spp*. Infections may be polymicrobial, especially if chronic urinary catheter or stents are present.

What is a biofilm?



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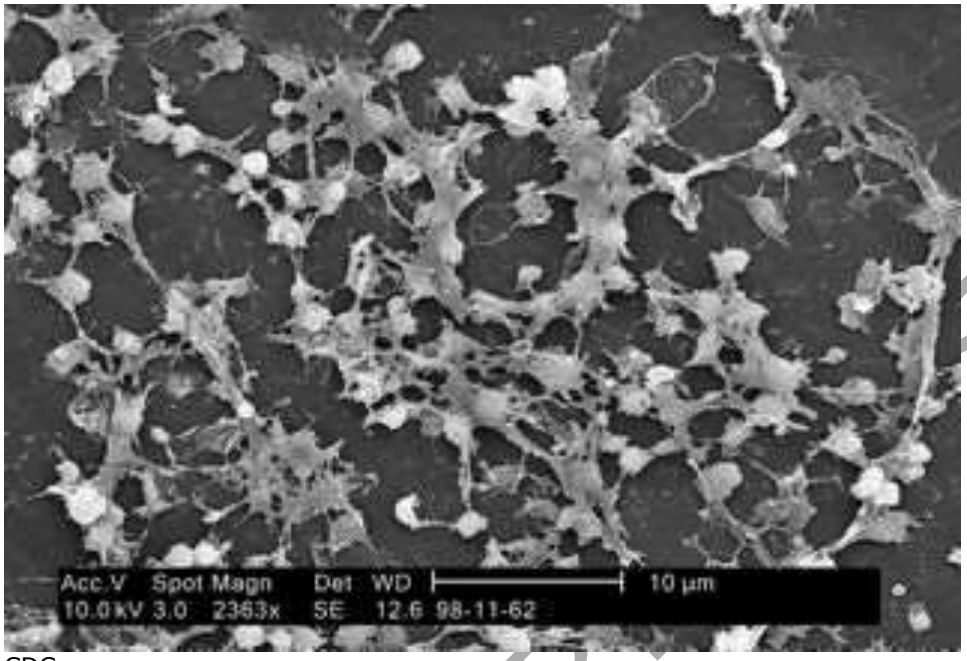
A **biofilm** comprises a variety of different bacteria and other pathogens that essentially band together to form a structure held together by polysaccharide "glue" or film. The biofilm protects the bacteria it encloses, providing increased resistance to antibiotics. Because the biofilm lacks adequate nutrients, the organisms have slower growth than free-roaming bacteria. Unfortunately, antibiotics often target cells with fast growth, so these organisms with their slow growth are more resistant. The stress related to life in the biofilm causes bacteria to release acids and proteins that counteract antibiotics and confuse the host's immune system.

Free-roaming bacteria emerge from the biofilm and circulate through the system, sometimes causing distant infections. These bacteria begin to grow faster and become more sensitive to antibiotics, but once medications are stopped, new free-forming bacteria again emerge from the biofilm and the cycle begins again. Once a biofilm is established in the body, it is very difficult to treat. Many chronic infections are caused by the formation of biofilms, especially with gum disease, urinary and bone infections. Invasive medical devices, such

as central venous catheters, urinary catheters, and prostheses, are common sites for biofilms.

Biofilm on the surface of a urinary catheter



CDC

Lower urinary tract infections

Normal urine is sterile. The first barrier to infection is the urethra, which separates the bladder from the external orifice. Urine flow normally flushes bacteria from the urethra. However, the urethra in adult females is only one factor in UTI incidence, which is higher in females.

Cystitis and Urethritis

For bladder infection, cystitis, to occur, bacteria must migrate into the urethra and bladder and attach to the epithelial cells of the mucous lining before they can be washed out by the flow of urine or destroyed by host-defense mechanisms. Urethritis often precedes cystitis. The most common infective agent in community-acquired UTI is *Escherichia coli* from the intestinal tract.

The urinary system has a number of safeguards to fight against infection:

- The rate of shedding of epithelial cells increases with bacterial invasion, so that the bacteria can be flushed out of the bladder before they can establish colonies.

- Glycosaminoglycan (GAG) molecule is a hydrophilic (water loving) protein that attracts water molecules and forms a water barrier between the bladder lining and the urine. Unfortunately, some commonly-used agents impair GAG: cyclamate, saccharin, aspartame, and tryptophan.
- Immunoglobulin A (IgA) in the urethra provides an immune barrier.
- Normal bacterial flora in the bladder interferes with the ability of *E.coli* to adhere to the bladder lining.

The lining of the bladder and urethra is continuous, and the female urethra commonly becomes contaminated with bacteria because of the close proximity of the urethral meatus to the anus, resulting in sexually-active females having the highest incidence of UTIs because bacteria is introduced into the urethra during sexual intercourse.

Usually organisms that invade the urethra are flushed out. In some cases, urethrovesical reflux occurs. For example, when a person sneezes coughs, or strains, the pressure in the bladder increases, and when the pressure suddenly releases, the bladder acts as a suction device, pulling urine back into the bladder from the urethra (and often bringing bacteria along with the urine). Urethrovesical reflux is common in young children. Other causes of urethrovesical reflux include dysfunction of the bladder neck or urethra and physical changes related to menopause, resulting in increased incidence of UTIs in post-menopausal women.

In addition to transurethral bacterial migration, infection can spread to the urinary tract through the bloodstream from infections at other primary sites, and by direct extension from a fistula from the intestines. However, the transurethral route is the most common. Lower UTIs can spread via the ureters to the kidneys, especially if treatment is delayed, resulting in pyelonephritis, an upper UTI.

Age and Gender Incidence of UTIs increases with age because of structural abnormalities and dysfunctional (neurogenic) bladder, sometimes secondary to stroke or diabetic neuropathy as well as to reduced immune response and frequent use of antibiotics, which results in resistance and increased infection. High levels of urinary glucose that may occur with diabetes increase risk of infection.

There are a number of other factors that contribute to increased risk of infection in older adults, including chronic illness, infected pressure

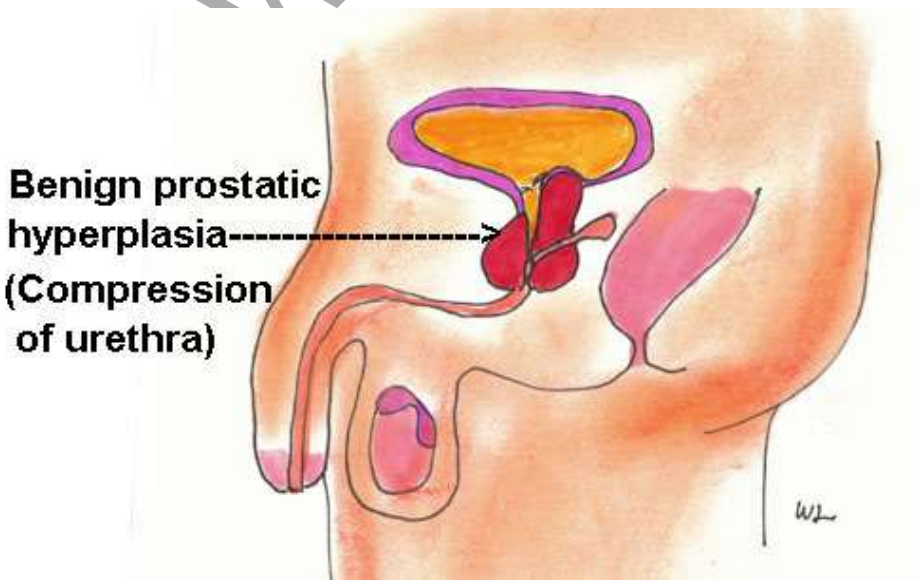
ulcers, immunocompromised condition, confusion, immobility, incomplete bladder emptying, and the use of a bedpan.

Older females may have incomplete emptying of the bladder, resulting in stasis. The decrease in estrogen causes increased susceptibility to bacterial colonization and allows increased bacterial adherence to the vagina and urethra. In general practice, about 20% of women >65 exhibit bacteriuria, but this number increases to 50% for those in long-term care.

Cystitis is much less common in males than females because the anus and the urethra are not in close proximity. However, males may develop cystitis from sexual intercourse with a woman with a vaginal *E.coli* infection or from insertion of a urinary catheter.

In younger males, prostatic secretions have an antibacterial effect that reduces incidence of infection, but secretions decrease with age. Young males who develop UTIs should be examined for structural abnormalities. Urethritis is more common in males than cystitis and may cause dysuria, the most common symptom of cystitis.

UTIs in males are often related to reproductive tract infections, such as epididymitis, prostatitis, or orchitis. Additionally, benign prostatic hypertrophy or prostatic cancer can compress the urethra and result in stasis from inability to empty the bladder. The use of catheters or condom catheters in older males increases risk of infection although less than indwelling catheters. Because of these changes with aging, by age 50, the incidence of UTI in males approaches that of females.



Catheterization In healthcare-acquired UTIs, risk factors include the length of stay in a facility and days of device (cystoscopies and urinary catheters) utilization. Urinary catheters should be avoided or should be left in for the shortest possible period of time because the longer the catheter remains in place or the more frequently the person is catheterized, the more likely the person is to develop a UTI. In fact, UTIs are the most common nosocomial infection. Research shows that most patients develop a UTI within 30 days or insertion of a catheter. Drainage bags provide a reservoir for pathogenic microorganisms, which can be transmitted to the hands of the healthcare worker.

UTIs are very common in those with spinal cord injuries that result in the need for intermittent or continuous catheterization or the use of condom catheters. Intermittent catheterization, if done properly, is less likely to result in infection than continuous catheterization. In the hospital, intermittent catheterization is usually done with aseptic technique while clean technique is acceptable in the home. Indwelling catheters must be removed within 2 days to significantly reduce risk.

CDC Guidelines Because of increased incidence of UTIs, the CDC (2009) has issued guidelines regarding the prevention of catheter-associated urinary tract infections. Recommendations include using catheters only for appropriate indications:

- Acute urinary retention or bladder outlet obstruction.
- Accurate urinary measurement in critically-ill patients
- Perioperative for selected surgical procedures (urinary tract, long duration, large-volume infusions or diuretics), or need for perioperative monitoring of urinary output
- To avoid urinary contamination of sacral or perineal wounds (incontinent patients)
- Need for prolonged immobilization (unstable thoracic or lumbar spine multiple injuries, such as pelvic fractures.

If catheterization cannot be avoided, the smallest size possible should be used to prevent trauma to the bladder neck and urethra, and catheters should be inserted with aseptic technique and standard precautions. The catheter should be secured to prevent movement and traction on the urethra. A closed system should be maintained. If a break in aseptic technique occurs, the catheter and collecting materials should be replaced. If UTI rates do not reduce, then healthcare

personnel should consider using antimicrobial-/antiseptic-impregnated catheters.

Studies indicate that hydrophilic catheters may have lower infection rates than standard catheters for intermittent catheterization. Silicone catheters are more resistant to encrustation than standard catheters in those with indwelling catheters that frequently obstruct.

Catheters should NOT be used in place of nursing care for patient with incontinence, to obtain urine specimens if the patient is able to urinate voluntarily, or for prolonged postoperative duration. Guidelines recommend substituting intermittent catheterization for continuous and the use of external catheters instead of indwelling for males.

Healthcare personnel should AVOID:

- Routinely changing the catheter.
- Routinely irrigating the catheter.
- Giving prophylactic antibiotics.
- Instilling antiseptic or antimicrobial solutions into urinary drainage bag.
- Cleaning the periurethral area with an antiseptic rather than soap and water.

Other Preventive methods

Adequate fluid intake and frequent and complete emptying of the bladder are the best preventive methods. Bacterial growth is inhibited in a pH of ≤5.5 or with high levels of urea. Dietary organic acids, derived from fruits and protein, acidify the urine and thus inhibit bacterial growth. Cranberry juice is believed to contain active compounds that help prevent *E.* coli from adhering to each other and forming biofilms. The amount of cranberry juice that is effective is not clear, but it seems to have a preventive effect for young women but not older adults. Cranberry juice should be avoided in those taking warfarin as it may increase risk of bleeding.

Symptoms

Uncomplicated UTI

Symptoms may vary widely. About 50% of those with bacteriuria have no symptoms. Typical symptoms of uncomplicated (community-acquired) lower urinary tract infection include:

- Dysuria (most common)

- Burning on urination.
- Frequency.
- Nocturia.
- Incontinence.
- Suprapubic, pelvic, or lower back pain.
- Fever.
- Headache.
- Hematuria

Complicated UTI Symptoms of complicated (healthcare-associated) UTI can also vary widely. Some people will remain asymptomatic with bacteriuria only evident on laboratory testing. Others may develop severe Gram-negative sepsis with symptoms of shock. UTIs are the most common cause of bacterial sepsis in those >65, with a mortality rate of about 50% for Gram-negative sepsis.

Bacteriuria occurs first and then may be followed by **bacteremia**, as the bacteria invade the blood system but have not yet caused a systemic infection. This may advance to **septicemia**, a systemic infection with associated symptoms, such as fever, malaise, and elevated white count.

As the infection spreads, **systemic inflammatory response syndrome** (SIRS) may occur. This generalized inflammatory response can affect many organ systems. SIRS includes two of the following symptoms:

- Elevated (>38°C) or subnormal rectal temperature (<36°C)
- Tachypnea or $PaCO_2$ <32 mm Hg.
- Tachycardia.
- Leukocytosis (>12,000) or leukopenia (<4000).

If the infection continues to worsen, sepsis may occur. **Sepsis** includes all symptoms related to SIRS as well as at least one of the following symptoms:

- Changes in mental status.
- Hypoxemia (<72 mm Hg) without pulmonary disease.
- Elevation in plasma lactate.
- Decreased urinary output <5 mL/kg for ≥1 hour.

Severe sepsis occurs with indications of increasing organ dysfunction with inadequate perfusion and/or hypotension. Symptoms of lactic acidosis may also occur.

Most deaths related to sepsis occur because of **multi-organ dysfunction syndrome** (MODS). Cardiac function is impaired, acute respiratory distress syndrome (ARDS) may develop, and acute tubular necrosis or cortical necrosis may lead to renal failure. Almost a third of patients develop thrombocytopenia, which can lead to disseminated intravascular coagulation (DIC). Liver damage and bowel necrosis may also occur.

Older adults

Older adults may not exhibit symptoms typical of complicated or uncomplicated UTIs. They may have frequency, urgency, and dysuria, but other symptoms are less specific and may lead to misdiagnosis. Symptoms seen in older adults can include:

- Fatigue (most common symptom).
- Cognitive impairment, especially with existing dementia.
- Altered sensorium.
- Lethargy.
- Poor appetite.
- New onset or increase in incontinence.
- Hyperventilation
- Low-grade fever.

Urine tests

Dipstick tests

Urine dipstick tests are available to quickly check for purulent material or bacteria in the urine, but the tests are most effective if high levels of bacteria are present. False positives are rare, but false negative readings may occur, so a dipstick urine examination should be confirmed with urinalysis, which can detect lower levels of bacteria. Dipsticks test for leukocyte esterase and/or nitrates. The nitrate dipstick test is more accurate than the leukocyte esterase test, but dipsticks that check for both are most accurate. With the nitrate dipstick, false negatives may result if diuresis has decreased urinary nitrate level, if there is inadequate intake of dietary nitrates, or if infections are caused by *enterococci* or *acinetobacter* because these bacteria do not produce nitrates. Usually, a high nitrate level indicates infection, but with some bacteria, this is not the case, so a false negative may occur.

Urinalysis	
Color	Pale yellow/ amber and darkens when urine is concentrated or other substances (such as blood or bile) or present.

Appearance	Clear but may be slightly cloudy.
Odor	Slight. Bacteria may give urine a foul smell, depending upon the organism. Some foods, such as asparagus, change odor.
Specific gravity	1.015 to 1.025. Determines kidney's ability to concentrate urinary solutes. SpGr compares the weight of urine (in particles) in comparison to distilled water. High fluid intake lowers the SpGr and low intake raises it. In kidney disease, SpGr often does not vary. SpGr may increase if protein levels increase or if there is fever, vomiting, or dehydration.
pH	Usually ranges 4.5 to 8 with average of 5 to 6. Medications, such as Mandelamine, some foods, such as cranberries, and Vitamin C may make urine acid (<7 pH). Alkaline urine (>7) occurs with bacteriuria, urinary tract infections, as well as kidney and respiratory diseases.
Sediment	Red cell casts from acute infections, broad casts from kidney disorders, and white cell casts from pyelonephritis. Leukocytes > 10 per ml^3 are present with urinary tract infections. Crystals should not be present. Frank blood may be caused by some parasites and diseases but also by drugs, smoking, excessive exercise, and menstrual fluids.
Glucose, ketones, protein, blood, bilirubin, and nitrate	Negative. Urine glucose may increase with infection (with normal blood glucose). Frank blood may be caused by some parasites and diseases but also by drugs, smoking, excessive exercise, and menstrual fluids. Increased red blood cells may result from lower urinary tract infections.
Urobilinogen	0.1-1.0 units.

Urine culture and sensitivities Culture and sensitivities are done to identify infective agents and determine which antibiotics they are
sensitive to. Results should show <10,000 organisms/ml of urine. Results of >10,000 are considered evidence of infection. However, care must be taken when obtaining a urine sample because bacteria found in the urine sample may result from pathogenic microorganisms or contamination from skin or improper handling. Considerations include:

- Urine may become easily contaminated if people practice poor hygiene and if clean catch procedures are not followed correctly.
- If urine is too dilute (as from diuresis or excess fluid intake), the sample may be inadequate for accurate culture.
- If urine is left too long at room temperature, organisms may begin to grow, skewing the results.
- If urine is refrigerated from >2 hours before testing, results may be inaccurate.

Urinary cultures are positive for urine infection if the organism is found on Gram stain and if two urine cultures isolate the same organism with >102 colonies/ml of urine in catheterized specimens or <105 colonies/ml of urine with patients receiving appropriate antibiotics.

Treatment Options

Treatment varies depending on whether the UTI is uncomplicated (*E. Coli)* or complicated *(Staphylococcus).*

Uncomplicated UTI

If people have had symptoms for <48 hours, usually adequate hydration and oral antibiotics are sufficient for treatment.

Antibiotics are usually provided for 3 days and for 10 to 14 days with pyelonephritis:

- Ciprofloxacin 200 to 500 mg BID.
- 160 mg TMP/800 mg SMZ (Bactrim®, Septra®) q 12 hours.
- Nitrofurantoin (Macrodantin®) 50 to 100 mg q 6 hr.
- Amoxicillin/clavulanate (Augmentin®) 500 mg q 12 hr or 250 mg q 8 hr.

For severe pain and/or dysuria, phenazopyridine (Pyridium®) for 1-2 days is indicated to relieve discomfort.

Women who are pregnant are usually treated with a 14-day course of antibiotics:

- Cephalosporin.
- Nitrofurantoin (Macrodantin®)

Young women who are otherwise healthy but develop an acute UTI with dysuria and other symptoms may be treated in the ED with a regimen referred to as treatment with the "Rule of Twos":

- 2 L IV fluids.
- 2 Tylenol #3.
- 2G ceftriaxone IV.

If the patient's temperature falls by 2° F and she can drink 2 glasses of water, she may be discharged but must take 2 co-trimoxazole BID for 14 days or ciprofloxacin 500 mg BID for 7 to 14 days.

While there is some controversy regarding treatment of asymptomatic bacteriuria, it is usually not treated except in pregnant women or those who are immunocompromised or otherwise at risk because of the danger of increasing antibiotic resistance.

Complicated UTI Complicated UTI is more difficult to treat and the choice of antibiotic depends on the infective agent and the spread of the infection. Treatment usually continues for 10 to 14 days. Commonly used agents include:

- Ceftriaxone (Rocephin®) 1-2 g IV daily or divided doses BID.
- Tobramycin (Nebcin®) with dosage varying, beginning with 3 mg/kg IV or IM q 8 hours.
- Cephalexin (Keflex®) 250 to 1000 mg q 6 hrs. for 10 to 14 days.
- Ertapenem (Ivanz®) 1 g qd for 14 days IV or 7 days IM.

Note: UTIs in males are usually considered complicated because incidence of pyelonephritis is high, so longer treatment is indicated.

Summary

Urinary tract infections (UTIs) comprise both lower UTIs (cystitis and urethritis) and upper urinary tract infections (acute and chronic pyelonephritis, renal abscess, interstitial nephritis, and perirenal abscess). UTI infection may be community-acquired (primarily *E. coli)* or healthcare acquired (commonly enterobacteriaceae, *Pseudomonas aeruginosa* and *Acinetobacter* spp). Healthcare-acquired UTIs are associated with the development of antibiotic resistant biofilms. UTIs are most common in young women but incidence increases in both males and females with age. Complicated UTIs may result in sepsis and MODS. Treatment for uncomplicated UTI is usually 3 days of antibiotics while complicated UTIs usually require 10-14 days.

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