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A Review of Uncomplicated Urinary Tract Infections

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1. Introduction

Urinary tract infections (UTIs) can be classified as either uncomplicated or complicated. Uncomplicated UTIs occur mostly in young women who are sexually active and who have normal genitourinary anatomy. These patients usually have had no previous risk factors otherwise, and no previous surgeries or manipulation of the genital tract. This chapter will discuss the epidemiology, pathogenesis, infecting organisms, clinical manifestations, diagnosis, treatment, and prevention of uncomplicated UTIs.

2. Epidemiology

UTIs are one of the most common infections caused by bacteria. UTIs account for more than 8 million doctor’s visits each year in the U.S. These infections generate more than 3 million prescriptions, and costs an estimated $3.5 billion dollars annually to treat (University of Michigan Health System, 2010). UTIs occur more frequently in women than in men, and will occur in roughly half of women during their lifetime. In men, decreased urinary flow from enlarged prostates increase the risk of infection. (University of Michigan Health System, 2010)

3. Pathogenesis

The urinary system includes the kidneys, ureters, bladder, and the urethra (Figure 1). This system removes body waste; specifically, urea, from the blood. Urea is carried in the bloodstream to the kidneys. The kidneys extract urea from the blood through filtering units called nephrons. Urea, along with other waste products and water, forms the urine. Urine then passes through the kidneys, to the ureters. From the ureters, urine flows into the bladder. The bladder collects urine and, intermittently, it passes out of the bladder into the urethra, which is a tube that excretes urine from the body. Many different problems can occur within the urinary tract. Aging can decrease the action of muscles within the urinary system and decrease excretion of urine; therefore, urine may
back up and an infection can develop. Injuries from trauma or surgery can also cause infection. In addition, other illnesses and medical conditions can predispose decreased emptying of urine, which can then predispose to infection. These illnesses include prostatic enlargement in elderly men, diabetes mellitus, nephrolithiasis (kidney stones), and other neurologic conditions that can also cause a neurogenic bladder. Manipulation and instrumentation such as insertion of urinary catheters can cause UTIs.

Fig. 1. Urinary System.

Usually, the urinary tract is able to eliminate harmful bacteria. High urine osmolarity and acidity inhibit the growth of most pathogens in the urine. However, these same characteristics can also decrease white blood cells’ effectiveness in clearing infection. As such, these urinary characteristics, despite being a noxious environment for bacteria to thrive, can also lower resistance to infections by rendering white blood cells less effective. (Alonto, 2007)

Bacteria can enter the urinary tract through two main routes: ascending route and hematogenous route. The most common way to develop UTI is via the ascending route. Bacteria can enter the urinary tract through the urethra. From the urethra, bacteria can then ascend into the bladder, ureters, and kidneys. Infection of the kidneys is called pyelonephritis. (Alonto, 2007)

Hematogenous route of infection can occur in patients who have bacteremia from other foci of infection such as endocarditis. The pathogenic bacteria that enter the bloodstream can then infect the renal parenchyma, causing pyelonephritis, and even renal abscesses.

UTIs are most commonly caused by bacteria that enter the bladder through the urethra. The genitourinary anatomy of women predisposes them to UTIs. Their urethras are shorter, and closer to the anus, providing easier access for fecal bacteria to enter the urethra. This is the major reason women experience infections significantly more frequently than men. Many other conditions can increase the chances of developing UTIs. These conditions include menopause, diabetes, advanced age, kidney stones, pregnancy, and urinary tract instrumentation. In men, prostatic hypertrophy blocks the flow of urine and, because of this, there is also increased chance of developing UTIs in men with this condition. Table 1 explains the most common terms used for urinary tract infections.
A Review of Uncomplicated Urinary Tract Infections

5

Urinary tract infection

Microbial (bacterial, viral, fungal, etc.) infection that affects any part of the urinary tract

Lower urinary tract infection

Infection of either the bladder or the urethra.

Upper urinary tract infection

Although the upper urinary tract is composed of the kidneys and ureters, upper urinary tract infection generally affects the kidneys.

Pyelonephritis

Infection affecting the kidneys

Cystitis

Infection affecting the bladder

Urethritis

Infection affecting the urethra. Common pathogens causing urethritis include *Chlamydia trachomatis* and *Neisseria gonorrhoeae*

Cervicitis

Infection affecting the cervix. Mostly due to pathogens causing sexually transmitted diseases such as *Chlamydia trachomatis* and *Neisseria gonorrhoeae*

Prostatitis

Infection of the prostate

Renal abscess

Infection of the renal parenchyma which forms purulent collection within or around the renal parenchyma

Bacteruria

Presence of bacteria in the urine. Does not necessarily indicate presence of infection. Does not need to be treated in most instances, if patient is asymptomatic.

Pyuria

Presence of white blood cells in the urine. Indicates inflammation, not necessarily from infection.

<table>
<thead>
<tr>
<th>Urinary tract infection</th>
<th>Microbial (bacterial, viral, fungal, etc.) infection that affects any part of the urinary tract</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lower urinary tract infection</td>
<td>Infection of either the bladder or the urethra.</td>
</tr>
<tr>
<td>Upper urinary tract infection</td>
<td>Although the upper urinary tract is composed of the kidneys and ureters, upper urinary tract infection generally affects the kidneys.</td>
</tr>
<tr>
<td>Pyelonephritis</td>
<td>Infection affecting the kidneys</td>
</tr>
<tr>
<td>Cystitis</td>
<td>Infection affecting the bladder</td>
</tr>
<tr>
<td>Urethritis</td>
<td>Infection affecting the urethra. Common pathogens causing urethritis include <em>Chlamydia trachomatis</em> and <em>Neisseria gonorrhoeae</em></td>
</tr>
<tr>
<td>Cervicitis</td>
<td>Infection affecting the cervix. Mostly due to pathogens causing sexually transmitted diseases such as <em>Chlamydia trachomatis</em> and <em>Neisseria gonorrhoeae</em></td>
</tr>
<tr>
<td>Prostatitis</td>
<td>Infection of the prostate</td>
</tr>
<tr>
<td>Renal abscess</td>
<td>Infection of the renal parenchyma which forms purulent collection within or around the renal parenchyma</td>
</tr>
<tr>
<td>Bacteruria</td>
<td>Presence of bacteria in the urine. Does not necessarily indicate presence of infection. Does not need to be treated in most instances, if patient is asymptomatic.</td>
</tr>
<tr>
<td>Pyuria</td>
<td>Presence of white blood cells in the urine. Indicates inflammation, not necessarily from infection.</td>
</tr>
</tbody>
</table>

Table 1. Terms Used for Specific Urinary Tract Infections.

4. Infecting organisms

Uropathogens have characteristics that enable them to be successful in causing infections of the urinary tract. Adhesins enable the attachment to host membranes. Capsular polysaccharides, hemolysins, cytotoxic necrotizing factor (CNF) protein, and aerobactins are other factors that enable uropathogens to invade the urinary tract. Table 2 lists common virulence factors associated with pathogens causing UTIs. (Brusch, 2010)

<table>
<thead>
<tr>
<th>Virulence Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adherence</td>
</tr>
<tr>
<td>Calculi formation</td>
</tr>
<tr>
<td>Toxin production</td>
</tr>
<tr>
<td>Lipopolysaccharides</td>
</tr>
<tr>
<td>Capsular polysaccharide</td>
</tr>
<tr>
<td>Hemolysins</td>
</tr>
<tr>
<td>Biofilm</td>
</tr>
<tr>
<td>Aerobactins</td>
</tr>
</tbody>
</table>

Table 2. Virulence Factors in Uropathogens.

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The most common pathogen causing UTIs is *Escherichia coli* (*E. coli*), causing 70-95% of urinary tract infections. Other organisms that can be responsible for UTIs include Gram-positive cocci, such as *Staphylococcus saprophyticus* and *Enterococcus faecalis*. Other Gram-negative organisms responsible for causing UTIs include *Klebsiella* species and *Proteus* species. Hospitalized patients can develop complicated UTIs, and more common organisms isolated in these infections include Gram-negative organisms such as *Pseudomonas aeruginosa*, *Enterobacter* species, and *Acinetobacter* species; Gram-positive organisms including *Staphylococcus aureus*; and even yeast. Table 3 lists organisms that can be seen in urinary tract infections. (Brusch, 2010)

<table>
<thead>
<tr>
<th></th>
<th>Pyelonephritis</th>
<th>Cystitis</th>
<th>Urethritis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gram-positive Bacteria</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td><em>Staphylococcus aureus</em></td>
<td></td>
<td><em>Chlamydia trachomatis</em></td>
</tr>
<tr>
<td></td>
<td><em>Staphylococcus saprophyticus</em></td>
<td></td>
<td><em>Neisseria gonorrhoeae</em></td>
</tr>
<tr>
<td><strong>Gram-negative Bacteria</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>Escherichia coli</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>Klebsiella species</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>Proteus species</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>Pseudomonas aeruginosa</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>Enterobacter species</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Gram-positive Bacteria</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>Staphylococcus saprophyticus</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>Enterococcus species</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>Staphylococcus aureus</em></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 3. Organisms Associated with Urinary Tract Infections.

### 5. Clinical manifestations

The clinical manifestations of UTIs can vary significantly, especially in the extremes of age. UTIs in children can present with different symptoms. Symptoms in children younger than 2 years of age tend to be nonspecific, and can include fever, vomiting, and failure to thrive. In contrast, the elderly patient who has a UTI may be asymptomatic. When symptoms are present, they can include abdominal pain or mental status changes. However, the classic symptoms of acute uncomplicated cystitis include dysuria, change in urinary frequency, urinary urgency, hematuria, and suprapubic pain. Fever is usually absent in those with lower UTIs. In general, acute uncomplicated pyelonephritis classically presents with flank pain, abdominal pain, nausea, vomiting, fever, and costovertebral angle tenderness. Symptoms of cystitis may or may not be present in those with pyelonephritis. When present, these signs can occur 24-48 hours prior to appearance of symptoms of pyelonephritis. Some patients with acute pyelonephritis can present with sepsis.
6. Diagnosis

There are many different etiologies, both infectious and non-infectious, that can present with acute dysuria. The differential diagnosis of acute dysuria may include pyelonephritis, cystitis, urethritis, infectious vaginitis, atrophic vaginitis, and interstitial cystitis. A good history and physical examination usually gives the clinician enough information to make a correct diagnosis in most situations.

<table>
<thead>
<tr>
<th>Acute cystitis</th>
<th>Acute pyelonephritis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urethritis</td>
<td></td>
</tr>
</tbody>
</table>

Chlamydia trachomatis  
Neisseria gonorrhoeae  
Trichomonas vaginalis  
Candida albicans  
Herpes simplex virus  
Irritant urethritis

<table>
<thead>
<tr>
<th>Vaginitis</th>
</tr>
</thead>
</table>
| Candida albicans  
Trichomonas vaginalis  
Bacterial vaginosis  
Atrophic vaginitis |

| Interstitial cystitis |

Table 4. Differential Diagnoses of Acute Cystitis.

The most valuable diagnostic test for UTI is a urine analysis. The preferred definition of pyuria is at least 10 leukocytes/mm³ of midstream urine by counting changer. Using this definition, the majority of patients with bacteruria will have pyuria as well. Pyuria is present in almost all patients with acute cystitis. If pyuria is not seen, an alternative cause for the patient’s symptoms will need to be considered. (Brusch, 2010)

Urinary dipstick is a rapid screening test for detecting pyuria, as it can detect the presence of leukocyte esterase. The urine dipstick also detects nitrite, which signifies the presence of Enterobacteriaceae, bacteria which convert nitrite to nitrate. Although the nitrite test is a sensitive test for detecting Enterobacteriaceae, it may not detect other pathogens. (Brusch, 2010)

Urine in the bladder is sterile. However, because the urethra is usually contaminated with bacteria, collected urine specimens are frequently not sterile. A midstream, clean-voided urine, can separate contamination from urinary tract infection. Urine specimens from most patients with UTIs should have at least 10⁵ bacteria/mL. Patients without infection should have less than 10⁴ bacteria/mL. However, there are some patients with urinary infections that have fewer than 10⁵ bacteria/mL in urine. (Sobel & Kaye, 2005)

The Infectious Diseases Society of America consensus definition of cystitis for use in antibiotic treatment studies is 10³ bacteria/mL or more of an uropathogen, and for pyelonephritis 10⁴ bacteria/mL.

Acceptable methods for urine collection include midstream clean catch, catheterization, and suprapubic aspiration. (Sobel & Kaye, 2005)
7. Treatment

Because overuse and abuse of antimicrobial agents has led to rapidly evolving resistance of pathogens to this precious class of medications, appropriate administration of antibiotics to treat UTIs cannot be overemphasized. Appropriate use of antibiotics include correct indications, correct choice of antibiotic(s) (according to local resistance data or culture data), and timely administration of the agent(s) with appropriate dosage and treatment duration.

7.1 Asymptomatic bacteriuria (Alcaide & Lichtstein, 2004)

This condition is defined by the presence of more than 10^5 bacteria/mL in the urine of a patient without urinary tract and/or constitutional symptoms. Antibiotic treatment for asymptomatic bacteriuria is not indicated unless the woman is pregnant or the patient is about to undergo a urologic procedure, e.g. cystoscopy. Prescribing antibiotics in patients with asymptomatic bacteriuria exposes them to potential adverse drug reactions, such as development of C. difficile infection and increased selective pressure leading to the development of antimicrobial resistance. Unfortunately, despite data not supporting the prescription of antibiotics to patients with asymptomatic bacteriuria, many clinicians administer antibiotics to this group of patients based on individual habit or convention rather than clinical evidence or guidelines.

7.2 Acute uncomplicated cystitis (AUC)

As described in the section “Infecting Organisms”, the most common etiologic agent of AUC is E. coli. Other common pathogens are S. saprophyticus, E. faecalis, Klebsiella species and Proteus species. The selection of antibiotics should target the above common pathogens. The following is a detailed description of commonly used antibiotics recommended for treating AUC (Mascaretti, 2003a; Dielubanza & Schaeffer, 2011; Gupta et al., 2011).

7.2.1 Nitrofurantoin monohydrate/macrocysts

Nitrofurantoin is reduced by bacterial flavoproteins to highly reactive intermediates which are active in damaging the DNA of susceptible bacteria. Most stains of E. coli, S. saprophyticus and Enterococcus species are sensitive to nitrofurantoin. However, most species of Proteus and Klebsiella are less susceptible to this drug. Nitrofurantoin is indicated for the treatment of AUC only. Because it is eliminated without achieving antibacterial concentration in plasma or tissues, nitrofurantoin is not indicated for treating pyelonephritis. Because the rate of excretion of nitrofurantoin is linearly related to creatinine clearance, impaired renal function may decrease its efficacy and increase systemic toxicity of the drug (Petri, 2006).

Common side effects of nitrofurantoin are nausea, vomiting and diarrhea. However, the macrocrystal form appears to have lower gastrointestinal adverse reactions. Insidious irreversible interstitial pulmonary fibrosis can develop in elderly taking nitrofurantoin chronically. Therefore, patients who are taking this drug long term should undergo pulmonary function tests and chest radiography periodically. Gupta et al. demonstrated that a 5-day course of nitrofurantoin is equivalent, clinically and microbiologically, to a 3-day course of trimethoprim-sulfamethoxazole (Gupta et al., 2007). The 2011 updated IDSA guidelines for uncomplicated urinary tract infection also recommended using nitrofurantoin monohydrate/macrocysts 100 mg by mouth twice daily for 5 to 7 days (Gupta et al., 2011).
7.2.2 Trimethoprim/sulfamethoxazole (TMP/SMX)
TMP/SMX inhibits bacterial DNA, RNA and protein synthesis by interfering with folic acid synthesis. TMP/SMX’s spectrum will cover *E. coli* and *S. saprophyticus*, the two most uropathogens in causing AUC. TMP/SMX has excellent tissue penetration, so it can be used to treat upper urinary tract infection, including uncomplicated pyelonephritis. Skin rash and gastrointestinal adverse reactions; including nausea, vomiting, and anorexia are the common side effects of TMP/SMX. The dose should be reduced in patients with renal impairment.

TMP/SMX 160/800mg (double strength tablets) by mouth twice daily for 3 days is the recommended regimen for empirical treatment of AUC, provided the local community resistance prevalence of common uropathogens to TMP/SMX is less than 20%.

7.2.3 Fosfomycin trometamol
Fosfomycin inhibits bacterial cell wall synthesis by irreversibly inactivating the enzyme pyruvoyl transferase, an enzyme crucial in the synthesis of cell walls by bacteria. Fosfomycin exhibits a broad spectrum of activity against Gram positive and gram negative bacteria including *E. coli* and *P. mirabilis* (Mascaretti, 2003b). Fosfomycin is well tolerated. Common side effects are headache, diarrhea and nausea.

In a multicenter clinical trial comparing single-dose fosfomycin with a 7-day course of nitrofurantoin for the treatment of AUC in female patients, Stein showed that bacteriologic and clinical cure rates of a single 3-g dose of fosfomycin and 7-day course of nitrofurantoin were comparable (Stein, 1999). Minassian et al. from The United Kingdom also demonstrated that a single dose of 3g of fosfomycin trometamol had a comparable microbiological cure rate and was similar to a 5-day course of trimethoprim (Minassian et al., 1998). Fosfomycin is approved as a single dose of 3g powder mixed with water to treat AUC.

7.2.4 Fluoroquinolones
The fluoroquinolones inhibit relaxation of supercoiled DNA and cause breakage of DNA strands by inhibiting DNA gyrase and topoisomerase IV in susceptible bacteria. The fluoroquinolones that are commonly used to treat AUC are ciprofloxacin and levofloxacin. Both offer excellent coverage for Gram positive and Gram negative bacteria including *Enterobacteriaceae*. Common side effects of ciprofloxacin and levofloxacin are headache, nausea, diarrhea, abdominal pain and constipation. A rare complication may be Achilles tendon rupture in elderly patients.

Arredonodo-Garcia et al. conducted a randomized, multicenter, open-label, prospective study to compare the bacteriologic and clinical efficacy of oral ciprofloxacin 250mg twice daily for 3 days vs oral trimethoprim/sulfamethoxazole 160/800mg twice daily for 7 days vs oral norfloxacin 400mg twice daily for 7 days for treatment of AUC. The authors were able to show that a 3-day regimen of oral ciprofloxacin was clinically and bacteriologically at least as effective as a 7-day course of TMP-SMX and norfloxacin (Arredondo-Garcia et al., 2004). The empirical regimen of oral ciprofloxacin and oral levofloxacin for treating AUC is 250 mg twice daily for 3 days and 250 mg once a day for 3 days, respectively.

7.2.5 β-lactam agents
β-lactam agents that can be used to treat AUC include amoxicillin-clavulanate and oral second and third generation cephalosporins. Only amoxicillin-clavulanate will be described.
in this chapter. Amoxicillin inhibits bacterial cell wall synthesis by binding to the penicillin-binding proteins. Clavulanate inhibits β-lactamases that inactivate amoxicillin.

Amoxicillin-clavulanate has a broad spectrum which covers Gram positive bacteria, including *S. saprophyticus*; and Gram negative bacteria, including *E. coli* and *P. mirabilis*. Most common side effects of amoxicillin-clavulanate are diarrhea, nausea, vomiting and skin rash. Serious side effects include *C. difficile* colitis and Stevens-Johnson syndrome.

In a randomized, single-blind treatment trial of 370 women with AUC with either a 3-day regimen of amoxicillin-clavulanate vs a 3-day regimen of oral ciprofloxacin, Hooton et al. demonstrated that the former was not as effective as the latter for the treatment of AUC (Hooton et al., 2005). Therefore, the recommended empirical regimen for treating AUC with amoxicillin-clavulanate is 500/125 mg by mouth three times a day for a range of 3 to 5 days.

### 7.3 Infectious Disease Society of America (IDSA) guidelines for treatment of uncomplicated urinary tract infections

The 2010 updated International Clinical Practice Guidelines for the treatment of acute uncomplicated cystitis (AUC) and pyelonephritis in women was published in the March 1, 2011 issue of Clinical Infectious Disease (Gupta et al., 2011). These guidelines were also endorsed by the European Society for Microbiology and Infectious Diseases. Table 5 summarizes the treatment guidelines for acute uncomplicated cystitis. Table 6 indicates the retail price of antibiotics used in treating AUC.

<table>
<thead>
<tr>
<th>AGENT</th>
<th>DOSE</th>
<th>DURATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nitrofurantoin monohydrate</td>
<td>100 mg BID</td>
<td>5 – 7 days</td>
</tr>
<tr>
<td>Nitrofurantoin macrocrystal</td>
<td>100 mg BID</td>
<td>5 – 7 days</td>
</tr>
<tr>
<td>Trimethoprim-sulfamethoxazole</td>
<td>160/800 mg BID</td>
<td>3 days</td>
</tr>
<tr>
<td>Fosfomycin trometamol</td>
<td>3 g</td>
<td>Single dose sachet</td>
</tr>
<tr>
<td>Fluoroquinolones</td>
<td>Dose varies by agent</td>
<td>3-day regimen</td>
</tr>
<tr>
<td>B-lactams</td>
<td>Dose varies by agent</td>
<td>3-5 day regimen</td>
</tr>
</tbody>
</table>

Table 5. Treatment guidelines for urinary tract infections published in 2010 by The Infectious Disease Society of America.

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Retail Price</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nitrofurantoin monohydrate (100 mg twice daily)</td>
<td>$13.50 (3 days)</td>
</tr>
<tr>
<td></td>
<td>$18.90 (7 days)</td>
</tr>
<tr>
<td>Nitrofurantoin macrocrystal (100 mg twice daily)</td>
<td>$19.00 (3 days)</td>
</tr>
<tr>
<td></td>
<td>$26.13 (7 days)</td>
</tr>
<tr>
<td>Trimethoprim-sulfamethoxazole (160/800 mg twice daily)</td>
<td>$4.00 (3 days)</td>
</tr>
<tr>
<td>Fosfomycin trometamol (3 g single-dose sachet)</td>
<td>$50.86 (1 day)</td>
</tr>
<tr>
<td>Ciprofloxacin (250 mg twice daily)</td>
<td>$17.70 (3 days)</td>
</tr>
<tr>
<td>Levofloxacin (25 mg once daily)</td>
<td>$36.00 (3 days)</td>
</tr>
<tr>
<td>Amoxicillin-clavulanate</td>
<td>$13.80 (3 days)</td>
</tr>
<tr>
<td></td>
<td>$23.00 (5 days)</td>
</tr>
</tbody>
</table>

Prices derived from www.drugstore.com

Table 6. Retail price in the United States for commonly used antibiotics to treat AUC.
7.4 Treatment of uncomplicated pyelonephritis
The IDSA guidelines also recommend the following for management of acute uncomplicated pyelonephritis (Gupta et al., 2011).

- A urine culture and susceptibility test should always be performed, and initial empirical therapy should be tailored to the infecting uropathogen.
- Oral ciprofloxacin (500 mg twice daily) for 7 days, with or without an initial 400 mg dose of intravenous ciprofloxacin, is appropriate in patients not requiring hospitalization where the prevalence of resistance of community uropathogens to fluoroquinolones does not exceed 10%. If the prevalence of fluoroquinolone resistance is thought to exceed 10%, an initial 1-time intravenous dose of a long-acting parenteral antimicrobial, such as 1 g of ceftriaxone or a consolidated 24-h dose of an aminoglycoside is recommended.
- A once-daily oral fluoroquinolone, including ciprofloxacin (1000 mg extended release for 7 days) or levofloxacin (750mg for 5 days), is an appropriate choice for therapy in patients not requiring hospitalization where the prevalence of resistance of community uropathogens is not known to exceed 10%.
- Oral trimethoprim-sulfamethoxazole (TMP/SMX) (160/800 mg twice-daily for 14 days) is appropriate if the uropathogen is known to be susceptible. If TMP/SMX is used when the susceptibility is not known, an initial intravenous dose of a long-acting parenteral antimicrobial, such as 1 g of ceftriaxone or a consolidated 24-hour dose of an aminoglycoside is recommended.
- Oral β-lactam agents are less effective than other agents. If an oral β-lactam agent is used, an initial intravenous dose of a long-acting parenteral antimicrobial, such as 1g of ceftriaxone or a consolidated 24-hour dose of an aminoglycoside is recommended.
- Cases requiring hospitalization should initially be treated with an intravenous antimicrobial regimen; such as a fluoroquinolone, an aminoglycoside with or without ampicillin, an extended-spectrum cephalosporin, or extended-spectrum penicillin with or without an aminoglycoside, or a carbapenem. The choice among these agents should be based on local resistance data, and the regimen should be tailored on the basis of susceptibility results.

8. Prevention
The prevention of UTIs can be classified into two categories, non-antimicrobial and antimicrobial strategies.

8.1 Non antimicrobial strategy
A large population-based case-control study conducted by Fihn, et al. demonstrated that use of condoms coated with the spermicide nonoxynol-9 during intercourse was associated with a higher incidence of urinary tract infection caused by E. coli in young women (Fihn et al., 1996). Hooton et al. also demonstrated in a prospective study that recent use of a diaphragm with spermicide was one of the independent risk factors for symptomatic UTI (Hooton et al., 1996). Thus, sexually active women should be advised to avoid spermicide use during intercourse. Postcoital voiding has been advocated as a positive behavioral modification to prevent UTI (Stamm, 2010). However, a population-based, prospective cohort study did not showed that postcoital voiding was associated with decreased incidents of acute cystitis after multivariable analysis (Jackson et al., 2004)
Other non-antimicrobial strategies to prevent acute UTI have been investigated. Cranberries and other berries containing proanthocyanidins was proven, in vitro, to prevent uropathogens such as *E. coli* from adhering to urinary epithelium (Zafriri et al., 1989). Kontiokari et al. conducted an open, randomized controlled 12-month follow-up trial which showed that cranberry-lingonberry was more effective in reducing recurrence of UTI compared to lactobacillus GG drink or no intervention (Kontiokari et al., 2001). However, a recent double-blind, placebo-controlled study of the effects of cranberry on risk of recurring UTI study demonstrated that, among healthy college women with acute UTI, those drinking 8 oz of 27% cranberry juice twice daily, did not experience a decrease in the 6-month incidence of a second UTI, compared with those drinking a placebo (Barbosa-Cesnik et al., 2011).

Use of lactobacillus-containing probiotics has been proposed for the prevention of UTI. However, a review article by Barrons et al concluded that use of lactobacillus for the prevention of UTI remain inconclusive and controversial (Barrons et al., 2008). Although a randomized double-blind, placebo-controlled trial of a topically applied intravaginal estriol cream revealed that estriol was more effective in preventing recurrent UTI in postmenopausal women (Raz & Stam, 1993), the use of low dose oral estrogen did not reduce frequency of UTI (Brown et al., 2001; Cardozo et al., 1998).

In recent years, there has been great enthusiasm for the development of a vaccine to prevent UTIs because of the increasing resistance of uropathogens against antimicrobials and concerns for adverse reactions from antimicrobials. A double-blind study involved 75 patients randomly assigned to either placebo or vaginal mucosal suppository vaccines. The vaccine suppositories contained 10 strains of heat-killed uropathogenic bacteria. The study demonstrated that vaginal suppository vaccines were effective in reducing recurrence of *E. coli* UTI compared to placebo (Hopkins, 2007). So far there is no licensed vaccine for prevention of UTIs available in the USA.

8.2 Antimicrobial strategies (Dielubanza & Schaeffer, 2011; Foster, 2008)

Antimicrobial prophylaxis is a more effective way to prevent recurrence of UTI. However, this strategy carries the potential of promoting resistance and development of adverse reactions.

Low-dose continuous antimicrobial prophylaxis nitrofurantoin (100 mg daily), cephalexin (250 mg daily), and TMP-SMX (daily or 3 times a week) have been used successfully as low-dose antimicrobial prophylaxis for women with frequent UTIs.

Other strategies that were found to be effective in preventing recurrent UTI are postcoital prophylaxis and self-start therapy. Postcoital prophylaxis is appropriate for women who tend to develop UTI after intercourse. A single dose of antibiotic is used following intercourse. Self-start therapy is for women who are unwilling to take antibiotic continuously for prevention of recurrent UTI. By this method, the patient diagnoses UTI herself with a urine dipstick or by recognizing incipient UTI symptoms and starts a 3-day course of antibiotics immediately.

9. References


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A Review of Uncomplicated Urinary Tract Infections


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Urinary tract infections (UTIs) are among the most common bacterial infections worldwide, and they are also the leading cause of hospital-acquired infections. Therefore, the appropriate management of UTIs is a major medical and financial issue. This book covers different clinical manifestations of UTI, with special emphasis on some hard-to-treat diseases, and special conditions in respect of treatment; antibiotic resistance and the available alternative strategies for the prevention and treatment of UTIs and it deals with urinary tract infections in children. The aim of this book is to give a summary about the different aspects of the diagnosis, management and prevention of urinary tract infections for all medical disciplines.

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