

Treatment of Urinary Tract Infections in Nonpregnant Women

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This Practice Bulletin was developed by the ACOG Committee on Practice Bulletins—Gynecology with the assistance of Jeanne Sheffield, MD. The information is designed to aid practitioners in making decisions about appropriate obstetric and gynecologic care. These guidelines should not be construed as dictating an exclusive course of treatment or procedure. Variations in practice may be warranted based on the needs of the individual patient, resources, and limitations unique to the institution or type of practice.

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ABSTRACT: An estimated 11% of U.S. women report at least one physician-diagnosed urinary tract infection (UTI) per year, and the lifetime probability that a woman will have a UTI is 60% **1** **2** . Despite the frequency of UTIs, there is confusion about diagnostic strategies, and changes in antimicrobial resistance among uropathogens require alterations in traditional treatment regimens. The purpose of this bulletin is to address the diagnosis, treatment, and prevention of uncomplicated acute bacterial cystitis and acute bacterial pyelonephritis in nonpregnant women. Complicated UTIs (eg, in patients with diabetes mellitus, abnormal anatomy, prior urologic surgery, a history of renal stones, an indwelling catheter, spinal cord injury, immunocompromise, or in pregnant patients) are a heterogeneous group of conditions beyond the scope of this bulletin.

Background

Definitions

Urinary tract infections are among the most common bacterial infections in adults and may involve the lower or upper urinary tract or both. *Asymptomatic bacteriuria* refers to considerable bacteriuria in a woman with no symptoms. When the infection is limited to the lower urinary tract and occurs with symptoms of dysuria and frequent and urgent urination and, occasionally, suprapubic tenderness, it is termed *cystitis*. *Acute pyelonephritis* is defined as infection of the renal parenchyma and pelvicaliceal system accompanied by significant bacteriuria, usually occurring with fever and flank pain. Recurrent UTI with the same organism after adequate therapy is termed a *relapse*. *Reinfection* is a recurrent UTI caused by bacteria previously isolated after treatment and a negative intervening urine culture result or a recurrent UTI caused by a second isolate.

Prevalence and Epidemiology

The burden from UTIs on both the clinical and financial aspects of health care in the United State is immense. Approximately 62.7 million adults aged 20 years and older have reported at least one episode of a UTI or cystitis ³, 50.8 million (81%) of whom were women. In 2000, there were an estimated 11 million office and out-patient hospital visits by patients aged 20 years and older with a UTI (approximately 9 million visits by women). The cost to the health care system in 2000 was estimated to be 3.5 billion dollars for evaluation and treatment ² ³. More than one half of women will have at least one UTI during their lifetime ¹, and 3–5% of all women will have multiple recurrences ⁴. The prevalence of asymptomatic bacteriuria also is higher in women than men; 5–6 % in young, sexually active, non-pregnant women, compared with less than 0.1% in young men. The prevalence increases to 20% in women older than 65 years ⁵.

Pathophysiology and Microbiology

Urinary tract infections result from interactions between host biologic and behavioral factors and microorganism virulence. Most cases are caused by ascending infection from the urethra into the bladder. The female urethra is short, and the external one third is often colonized by pathogens from normal vaginal and enteric flora. Bacteria travel up the urethra during urethral massage, sexual intercourse, or mechanical instrumentation. Once in the bladder, bacterial factors play a major role in colonization and infection. Although UTIs are caused by many species of microorganisms, most (80–90%) are caused by uropathogenic *Escherichia coli* (predominantly O, K, and H antigen serotypes) ^{1 4 5 6}. These *E coli* serogroups have a number of virulence factors that facilitate colonization and invasion of the vagina and urinary tract. Specific virulence factors, such as Type 1 fimbria, P-fimbria, and S-fimbria, enhance binding to vaginal and uroepithelial cells. Virulence factors also increase resistance to serum bactericidal activity and resistance to host phagocytic activity. Certain *E coli* subgroups also are associated with ascending infection into the renal parenchyma, causing pyelonephritis (predominantly P-fimbriated *E coli*).

The remaining 10–20% of UTIs are caused by other microorganisms, occasionally colonizing the vagina and periurethral area ^{1 4 5 6}. *Staphylococcus saprophyticus* frequently causes lower UTIs and has been isolated in 3% of nonpregnant, sexually active, reproductive-aged women with pyelonephritis ⁷. *Proteus*, *Pseudomonas*, *Klebsiella*, and *Enterobacter* species all have been isolated in women with cystitis or pyelonephritis, and these frequently are associated with structural abnormalities of the urinary tract, indwelling catheters, and renal calculi ^{5 6}. *Enterococcus* species also have been isolated in women with structural abnormalities. Gram-positive isolates, including group B streptococci, are increasingly isolated along with fungal infections in women with indwelling catheters ⁶. Anaerobic organisms and mycoplasmas are uncommonly isolated from UTIs and probably have a minor role in urinary tract pathogenesis.

Although ascending infection is the predominant route of infection in the urinary tract, occasionally infection may arise from hematogenous or lymphatic spread. Bloodborne pathogens may seed the renal parenchyma during episodes of bacteremia. Renal abscesses may arise from bacterial endocarditis bacteremia from *Staphylococcus aureus*. Rare cases of pyelonephritis, caused by fungemia from *Candida* species in hospitalized patients, have been reported. Although lymphatic connections are present along the ureters and kidneys and reverse lymphatic flow into the kidneys has been reported, lymphatic spread of microorganisms leading to UTI is rare ⁸.

Risk Factors

Risk factors for UTI in women vary among the different age groups. In school-aged girls, common risk factors include congenital abnormalities and new onset of sexual activity. Risk factors for premenopausal and post-menopausal women are listed in the box. With advancing age, the rate of UTI increases, likely because of the hypoestrogenic state and vaginal epithelium atrophy, impaired voiding, and changes in hygiene **7** **9** . A life-time history of UTIs also is an important predictor of UTIs in postmenopausal women **10** .

Diagnosis

Clinical History and Examination

Acute bacterial cystitis usually presents clinically as dysuria, with symptoms of frequent and urgent urination, secondary to irritation of the urethral and bladder mucosa. Women also may experience suprapubic pain or pressure and rarely have hematuria. Fever is uncommon in women with uncomplicated lower UTI. Acute urethritis secondary to infection from *Neisseria gonorrhoeae* and *Chlamydia trachomatis* or pain secondary to genital herpes simplex virus type 1 and herpes simplex virus type 2 may occur with similar clinical symptoms and should be ruled out.

In contrast, upper UTI or acute pyelonephritis frequently occurs with a combination of fever and chills, flank pain, and varying degrees of dysuria, urgency, and frequency. Severe flank pain radiating to the groin is more indicative of renal calculi. Occasionally, renal pain may radiate to other abdominal areas, necessitating evaluation for cholelithiasis, cholecystitis, pelvic inflammatory disease, gastric ulcers, and appendicitis. Older women with UTI may be asymptomatic, present moribund from septic shock (urosepsis), have symptoms only of urinary incontinence, or have any combination of these symptoms.

Risk Factors For Urinary Tract Infection in Premenopausal and Postmenopausal Women

Premenopausal Women

- History of urinary tract infection
- Frequent or recent sexual activity

- Diaphragm contraception use
- Use of spermicidal agents
- Increasing parity
- Diabetes mellitus
- Obesity
- Sickle cell trait
- Anatomic congenital abnormalities
- Urinary tract calculi
- Neurologic disorders or medical conditions requiring indwelling or repetitive bladder catheterization

Postmenopausal Women

- Vaginal atrophy
- Incomplete bladder emptying
- Poor perineal hygiene
- Rectocele, cystocele, urethrocele, or uterovaginal prolapse
- Lifetime history of urinary tract infection
- Type 1 diabetes mellitus

Laboratory Evaluation

Bacteriuria is diagnosed using a clean-voided midstream urine sample. Traditionally, 100,000 single isolate bacteria per milliliter has been used to define significant bacteriuria, with excellent specificity, but a sensitivity of 50% ¹. To diagnose bacteriuria, decreasing the colony count to 1,000–10,000 bacteria per milliliter in symptomatic patients will improve the sensitivity without significantly compromising specificity. Urine dipstick testing for leukocyte esterase or nitrite is a rapid and inexpensive method with a sensitivity of 75% and specificity of 82% ^{1 11}. It is a good screening test, but women with negative test results and symptoms should still have a urine culture or urinalysis or both performed because false-negative results are common. A standard urinalysis will detect pyuria, defined as 10 leukocytes per milliliter, but pyuria alone is not a reliable predictor of infection. However, pyuria and bacteriuria together on microscopic examination results markedly increases the probability of UTI. The use of a postvoid residual volume measure, urodynamic testing, cystourethroscopy, or radiologic imaging is not cost-effective in women unless they have evidence of a complicated infection or renal calculi. These are rarely

necessary to diagnose acute uncomplicated cystitis and pyelonephritis.

Antimicrobial Resistance

A major consequence of indiscriminate prescribing practices of common antibiotics is the emergence of antimicrobial resistance. Data from areas reporting antimicrobial susceptibility profiles have shown an alarming increase in the prevalence of resistance to amoxicillin and trimethoprim–sulfamethoxazole, as high as 30% in some populations ^{12 13}. Particularly for acute pyelonephritis, urine culture and susceptibility testing can help tailor antimicrobial choices. If available, local community or hospital surveillance data should be reviewed to guide empirical therapy for UTIs. These data should be periodically updated as susceptibility patterns change over time. Resistance rates higher than 15–20% necessitate a change in antibiotic class.

General Principles of Treatment

Uncomplicated Acute Bacterial Cystitis

In the past, uncomplicated acute cystitis has been treated with 7–10 days of antimicrobial therapy. However, recent data have shown that 3 days of therapy is equivalent in efficacy to longer duration of therapy, with eradication rates exceeding 90%. Recommended agents for the 3-day therapy are detailed in the next section and in **Table 1**. Of note, β -lactams, such as first-generation cephalosporins and amoxicillin, are less effective in the treatment of uncomplicated acute cystitis than those antimicrobials listed in **Table 1**. This is because of increasing resistance among the common uropathogens, rapid excretion from the urinary tract, and the inability to completely clear gram-negative rods from the vagina, increasing the risk for recurrence ^{5 14}.

Table 1. Treatment Regimens for Uncomplicated Acute Bacterial Cystitis

Antimicrobial Agent	Dose	Adverse Events
Trimethoprim–sulfamethoxazole	One tablet (160 mg trimethoprim–800 mg sulfamethoxazole), twice daily for 3 days	Fever, rash, photosensitivity, neutropenia, thrombocytopenia, anorexia, nausea and vomiting, pruritus, headache, urticaria, Stevens–Johnson syndrome, and toxic epidermal necrosis
Trimethoprim	100 mg, twice daily for 3 days	Rash, pruritus, photosensitivity, exfoliative dermatitis, Stevens–Johnson syndrome, toxic epidermal necrosis, and aseptic meningitis
Ciprofloxacin	250 mg, twice daily for 3 days	Rash, confusion, seizures, restlessness, headache, severe hypersensitivity, hypoglycemia, hyperglycemia, and Achilles tendon rupture (in patients older than 60 years)
Levofloxacin	250 mg, once daily for 3 days	Same as for ciprofloxacin
Norfloxacin	400 mg, twice daily for 3 days	Same as for ciprofloxacin
Gatifloxacin	200 mg, once daily for 3 days	Same as for ciprofloxacin
Nitrofurantoin macrocrystals	50–100 mg, four times daily for 7 days	Anorexia, nausea, vomiting, hypersensitivity, peripheral neuropathy, hepatitis, hemolytic anemia, and pulmonary reactions
Nitrofurantoin monohydrate macrocrystals	100 mg, twice daily for 7 days	Same as for nitrofurantoin macrocrystals
Fosfomycin tromethamine	3 g dose (powder) single dose	Diarrhea, nausea, vomiting, rash, and hypersensitivity

Acute Pyelonephritis

Acute pyelonephritis traditionally has been treated with hospitalization and parenteral antibiotics. However, there has been a recent shift to outpatient management, when possible, with an emphasis on cost-savings although this management scheme is based on results from few large treatment trials **14**. In otherwise healthy women who are clinically stable and able to tolerate oral antimicrobial agents and fluids, outpatient management is acceptable and has similar efficacy **14**. The reliability of the patient and the social situation also should be taken into account when determining inpatient versus outpatient management. A urine culture is performed and empiric antibiotic therapy initiated as detailed in the next section. As in acute cystitis, β -lactams are not first-line therapy in most cases. There is a high rate of ampicillin resistance in organisms causing pyelonephritis and a high rate of recurrence in those women treated with β -lactams. The exception to this is if a gram-positive organism is the causative agent. Amoxicillin or amoxicillin combined with clavulanic acid may then be used. Regardless of management scheme, 14 days of oral or parenteral antibiotics or both is now standard, with cure rates approaching 100%. Outcomes after a 2-week course are equivalent to the traditional 6-week parenteral course, with no differences in recurrence rates. A substantial clinical response should be evident by 48–72 hours after initiating therapy. A urine culture test of cure usually is performed when the 2-week course of antibiotics is completed.

Recurrent Urinary Tract Infection

Recurrent UTIs are common in women, occurring in up to 25–50% within 1 year of initial infection. Of all women, 3–5% will have multiple recurrences over many years ^{1 4}. Management of recurrent UTIs should start with a search for known risk factors associated with recurrence. These include frequent intercourse, long-term spermicide use, diaphragm use, a new sexual partner, young age at first UTI, and a maternal history of UTI ^{15 16}. Behavioral changes, such as using a different form of contraception instead of spermicide, should be advised. Antimicrobial treatment of recurrent UTIs is based on patient desire and frequency of recurrences. A 3-day course of one of the antimicrobial regimens listed in **Table 1** is started to clear the infection. A urine culture test of cure 1–2 weeks later to confirm clearance is suggested.

For women with frequent recurrences, continuous prophylaxis with once-daily treatment with nitrofurantoin, norfloxacin, ciprofloxacin, trimethoprim, trimethoprim–sulfamethoxazole, or another agent listed in **Table 1** has been shown to decrease the risk of recurrence by 95% ⁴. This can be continued for 6–12 months and then reassessed. Women with recurrences associated with sexual activity may benefit from postcoital prophylaxis—a single dose of one of the agents listed in **Table 1**, taken after sexual intercourse, is effective in decreasing recurrences ^{1 17 18}.

Urinary Tract Infections in Postmenopausal Women

Antimicrobial therapy for UTIs in postmenopausal women is influenced by a number of factors. The organisms causing UTIs in this population differ from the causative agents in younger women. *Staphylococcus saprophyticus* rarely is isolated; however, gram-negative bacteria and enterococci are common (*E coli* remains the most common causative organism). Pharmacokinetic and pharmacodynamic changes also influence medication choices to limit drug toxicity and interactions ^{19 20}. Despite these differences, few studies have adequately evaluated treatment options in these women. In a meta-analysis that evaluated 13 trials, including a total of 1,435 older women with UTIs, it was concluded that 3–6 days of antibiotic treatment was equivalent to longer courses of treatment (7–14 days), with fewer adverse events ²⁰. Single-dose therapy was not as effective as longer treatment regimens and should not be used. Another randomized, controlled trial assessing the optimal duration of antibiotic therapy for uncomplicated UTIs in women aged 65 years or older concluded that the 3-day regimen was equally effective but better tolerated than a 7-day course ²¹.

Patient-Initiated Therapy

Many women with recurrent UTIs are aware of symptom onset. As the cost of office and hospital emergency room visits continues to increase, patient-initiated therapy has become a viable option for treatment. Women are given a prescription for one of the 3-day dosage regimens listed in **Table 1** and should be instructed to start therapy when symptoms develop. Some clinicians also will give the women urine dipsticks and use pyuria as well as symptoms as an indication to initiate treatment. If symptoms do not improve in 48 hours, clinical evaluation should be performed. Patient-initiated therapy has been found to be safe, effective, and economical **22 23 24** .

Clinical Considerations and Recommendations

Is empiric treatment of urinary tract infection without performing urinalysis appropriate?

It is a common practice among primary care physicians to empirically treat women with symptoms of a lower UTI without performing laboratory analyses. It has been considered a cost-effective strategy, decreasing the number of diagnostic tests and office visits **25 26** . However, many women, especially postmenopausal women, without a laboratory-proven UTI have symptoms of intermittent dysuria or urgent or frequent urination. Empiric treatment of these women leads to unnecessary antibiotic use and the development of antimicrobial resistance. Testing for pyuria, by urinalysis or by urinary dipstick testing, improves the likelihood of identifying infection by 25% or more **1 27 28 29** . Thus, in women without a history of a laboratory-confirmed UTI, an office visit for urinalysis or dipstick testing is appropriate. Women with frequent recurrences and prior confirmation by diagnostic tests who are aware of their symptoms may be empirically treated without recurrent testing for pyuria.

When is urine culture necessary?

The initial treatment of a symptomatic lower UTI with pyuria or bacteriuria does not require a urine culture. However, if clinical improvement does not occur within 48 hours or in the case of recurrence, a urine culture is useful to help tailor treatment. A urine culture should be performed in all cases of upper UTIs.

In what situations do patients require further evaluation?

Imaging of the urinary tract rarely is required in women— it is not cost-effective nor does it provide useful information in the setting of uncomplicated lower or upper UTIs. Women with infections that do not respond to appropriate antimicrobial therapy or in whom the clinical status worsens require further evaluation. Renal ultrasonography is the best non-invasive method to evaluate renal collecting system obstruction. An intravenous pyelography also may be useful in this situation. Contrast-enhanced computed tomography or magnetic resonance imaging is useful to obtain an image of the renal parenchyma in order to rule out a perinephric abscess or phlegmon.

How should uncomplicated acute bacterial cystitis in women be treated?

A 3-day antimicrobial regimen is now the recommended treatment for uncomplicated acute bacterial cystitis in women, with bacterial eradication rates consistently higher than 90%. **Table 1** lists the current recommended regimens for treatment, both 3-day and 7-day courses. Use of trimethoprim–sulfamethoxazole for 3 days is considered the preferred therapy, with a 94% bacterial eradication rate. However, in areas where resistance to this antimicrobial agent exceeds 15–20%, another one of the listed regimens should be chosen. The other medications that have shown equivalency include trimethoprim alone, ciprofloxacin, levofloxacin, norfloxacin, and gatifloxacin. The fluoroquinolones, although highly effective, should not be used as a first-line agent in areas where resistance prevalence to trimethoprim–sulfamethoxazole is low—currently resistance to the fluoroquinolones is uncommon, and overuse will likely hinder the ability to effectively use this class of antimicrobials in patients with complicated UTIs and those patients with respiratory and other non–urinary tract infections. Most experts now agree that use of sulfonamides, ampicillin, and amoxicillin is less effective than use of trimethoprim–sulfamethoxazole and the fluoroquinolones (see previous section) and should not be used as first-line therapy.

Use of nitrofurantoin, a drug frequently used in the pregnant population, is not well studied in nonpregnant women with acute cystitis. It is not recommended for use in a 3-day regimen but has been found to be effective in a 7-day antimicrobial regimen and is listed in **Table 1**. Resistance to nitrofurantoin remains low (less than 5%) **1**. The low prevalence of resistance and its ability to concentrate in urine continue to make nitrofurantoin a useful medication in the treatment of uncomplicated cystitis, particularly in areas where resistance rates to the first-line medications are high. It is ineffective against *Proteus mirabilis*. Of note, nitrofurantoin can rarely induce hemolytic anemia in patients with glucose-6-phosphate dehydrogenase deficiency, and use should be avoided in these patients **30**. Compared with the nitrofurantoin macrocrystal formulation, which requires frequent dosing

(four times per day) and has a high likelihood of gastrointestinal side effects, monohydrate macrocrystal formulation is given twice daily, so side effects occur less frequently.

How should uncomplicated acute pyelonephritis be treated?

Women who present with acute pyelonephritis should have an initial urine culture and susceptibility testing before the initiation of antimicrobial therapy. Intravenous hydration should be started while the clinical assessment is being performed. Women who are severely ill, have complications, are unable to tolerate oral medications or fluids, or who the clinician suspects will be noncompliant with outpatient therapy should be hospitalized and receive empiric broad-spectrum parenteral antibiotics. Knowledge of specific antimicrobial resistance in the community should influence the choice of initial antimicrobial agent. Once the urine and susceptibility culture results are available, therapy is altered as needed. Most women can be treated on an outpatient basis initially or given intravenous fluids and one parenteral dose of an antibiotic before being discharged and given a regimen of oral therapy.

The initial antimicrobial regimen is empiric. If a grampositive organism is identified on a Gram stain, amoxicillin or ampicillin are acceptable treatment choices. Grampositive organisms in clusters (probable Staphylococci) maybe treated initially with cephalosporin. In all other cases, β -lactam agents no longer are recommended **14** . First-line therapy now is use of a fluoroquinolone for 14 days. In areas where resistance rates are low, trimethoprim–sulfamethoxazole use is an acceptable alternative **31** . For women with severe illness or urosepsis who require hospitalization, the broad-spectrum parenteral antibiotics available include aminoglycosides plus ampicillin, piperacillin or first-generation cephalosporins, aztreonam, third-generation cephalosporins, piperacillin tazobactam, or parenteral fluoroquinolones used alone or in combination, depending on the individual case. In all cases of acute pyelonephritis, whether the patient is treated on an inpatient or outpatient basis, 14 days of total antimicrobial therapy should be completed. Treatment of severe complications associated with pyelonephritis, such as septic shock, acute respiratory distress syndrome, and multiorgan failure, is beyond the scope of this bulletin.

A notable clinical response should be evident by 48–72 hours. If no improvement is noted or if the patient's status worsens, it may be necessary to change therapy based on results of available susceptibility testing of the initial isolate. Routine imaging studies are not recommended in women with uncomplicated acute pyelonephritis.

Is single-dose therapy as effective as therapy of longer duration for uncomplicated acute bacterial cystitis?

Antimicrobials recommended for single-dose therapy produce inhibitory concentrations of antibiotics for 12–24 hours. The benefits of a single-dose course include cost, directly observed therapy so compliance is not an issue, fewer side effects, and a potentially decreased chance of resistance. If used, single-dose therapy should be reserved for young, sexually active women with a normal urinary tract who have had symptoms for no more than 1 week. However, single-dose therapy generally is considered less effective than the same antimicrobials used in a 3-day course of treatment with regards to bacterial eradication and clinical cure rates **14 20 32 33**. In a few recent trials that evaluated the use of single-dose gatifloxacin, fosfomycin tromethamine, rifloxacin, and pefloxacin, early promise has been shown, using clinical cure rates as the outcome measure, but questions of adverse side effects and higher recurrence rates necessitate further study **14 34 35**.

How effective are interventions to prevent recurrence of cystitis?

The first-line intervention for the prevention of the recurrence of cystitis is prophylactic or intermittent antimicrobial therapy, as discussed previously. Recurrences are prevented in 95% of cases **4**. However, multiple other nonmedical and medical interventions have been suggested. There is little evidence that aggressive hydration to prevent recurrences has any major effect, and this practice can theoretically worsen urinary retention issues, decrease urinary pH affecting the antibacterial activity of urine itself, and dilute antimicrobial concentrations in the urinary tract. It currently is not recommended for prevention of UTI recurrence. Likewise, postcoital voiding has not been proved effective **1 36**, nor have douching or wiping techniques **1**. The benefit of vaginal lactobacilli application also remains unproven **37**.

Drinking cranberry juice has been shown to decrease symptomatic UTIs. This is because of the proanthocyanidin-inhibiting attachment of urinary pathogens to the urinary tract epithelial cells **38 39**. In a recent meta-analysis addressing the effectiveness of drinking cranberry juice and taking other formulations, it was reported that taking cranberry formulations was more effective compared with taking placebo **40**. In one of the studies in the meta-analysis, it was reported that both drinking cranberry juice and taking cranberry tablets significantly decreased the number of women with at least one symptomatic UTI per year to 18% and 20%, respectively, compared with 32% for those taking placebo **41**. However, there are insufficient data to determine the length of therapy and the concentration required to prevent recurrence long term.

Methenamine salts (methenamine hippurate and methenamine mandelate) have long been used for the prevention of UTI. They produce formaldehyde, which acts as a bacteriostatic agent **42**. In a meta-analysis reviewing 11 trials using methenamine hippurate, it was found that, although well tolerated, there

analysis reviewing 11 trials using methenamine hippurate, it was found that, although well tolerated, there was not enough evidence to conclusively support this use for urinary prophylaxis **43**.

Recurrence rates are high among postmenopausal women. The hypoestrogenic state with associated genitourinary atrophy likely contributes to the increased prevalence. Oral and vaginal exogenous estrogens have been studied with varying results. Estrogen-releasing pessaries and rings have had some success in decreasing UTI recurrences **44** **45**, as have topical estrogen creams **46**. Although in one study a benefit from oral estrogen therapy was found **47**, in other larger studies no reduction in UTI frequency in postmenopausal women receiving oral estrogen was shown **48** **49**. Large, randomized trials are required before exogenous estrogen therapy can be conclusively recommended for UTI recurrence prevention.

Vaginal mucosal vaccines have been proposed to improve long-term resistance to recurrent UTIs. Vaccine targets include the Type I and Type II pili. One study has shown some promise **50**, but currently no vaccines are available for clinical use.

When should asymptomatic bacteriuria be treated?

Screening for and treatment of asymptomatic bacteriuria is not recommended in nonpregnant, premenopausal women. Asymptomatic bacteriuria has not been shown to be harmful in this population, nor does treatment of asymptomatic bacteriuria decrease the frequency of symptomatic infections **51**. The current Infectious Diseases Society of America guidelines for the diagnosis and treatment of asymptomatic bacteriuria in adults, released in 2005, list specific groups in whom treatment of asymptomatic bacteriuria is recommended. These include all pregnant women, women undergoing a urologic procedure in which mucosal bleeding is anticipated, and women in whom catheter-acquired bacteriuria persists 48 hours after catheter removal. They do not recommend treatment of asymptomatic bacteriuria in women with diabetes mellitus, older institutionalized patients, older patients living in a community setting, patients with spinal cord injuries, or patients with indwelling catheters **51**.

Summary of Recommendations and Conclusions

The following recommendations and conclusions are based on good and consistent scientific evidence (Level A):

- Screening for and treatment of asymptomatic bacteriuria is not recommended in non-pregnant, premenopausal women.

- Resistance rates higher than 15–20% necessitate a change in antibiotic class.
- In all cases of acute pyelonephritis, whether treatment is on an inpatient or outpatient basis, 14 days of total antimicrobial therapy should be completed.
- A 3-day antimicrobial regimen is the preferred treatment duration for uncomplicated acute bacterial cystitis in women, including women aged 65 years and older.

The following conclusion is based on limited or inconsistent evidence (Level B):

- The initial treatment of a symptomatic lower UTI with pyuria or bacteriuria or both does not require a urine culture.

The following conclusions are based primarily on consensus and expert opinion (Level C):

- Beta-lactams, such as first-generation cephalosporins and amoxicillin, are less effective in the treatment of acute uncomplicated cystitis than those antimicrobials listed in **Table 1**.
- To diagnose bacteriuria, decreasing the colony count to 1,000–10,000 bacteria per milliliter in symptomatic patients will improve the sensitivity without significantly compromising specificity.

Proposed Performance Measure

The percentage of women in whom acute pyelonephritis is diagnosed who are treated with 14 days of antimicrobial therapy

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The MEDLINE database, the Cochrane Library, and ACOG's own internal resources and documents were used to conduct a literature search to locate relevant articles published between January 1985 and April 2007. The search was restricted to articles published in the English language. Priority was given to articles reporting results of original research, although review articles and commentaries also were consulted. Abstracts of research presented at symposia and scientific conferences were not considered adequate for inclusion in this document. Guidelines published by organizations or institutions such as the National Institutes of Health and the American College of Obstetricians and Gynecologists were reviewed, and additional studies were located by reviewing bibliographies of identified articles. When reliable research was not available, expert opinions from obstetrician-gynecologists were used.

Studies were reviewed and evaluated for quality according to the method outlined by the U.S. Preventive Services Task Force:

- I Evidence obtained from at least one properly designed randomized controlled trial.
- II-1 Evidence obtained from well-designed controlled trials without randomization.
- II-2 Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one center or research group.
- II-3 Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments also could be regarded as this type of evidence.
- III Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

Based on the highest level of evidence found in the data, recommendations are provided and graded according to the following categories:

- Level A—Recommendations are based on good and consistent scientific evidence.
- Level B—Recommendations are based on limited or inconsistent scientific evidence.
- Level C—Recommendations are based primarily on consensus and expert opinion.

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