TABLE 162-1 TREATMENT STRATEGIES FOR ACUTE UNCOMPLICATED CYSTITIS

Drug and Dose	Estimated Clinical Efficacy, %	Estimated Bacterial Efficacy,[a] %	Common Side Effects
Nitrofurantoin, 100 mg bid × 5–7 d	84–95	86–92	Nausea, headache
TMP-SMX, 1 DS tablet bid × 3 d	90–100	91–100	Rash, urticaria, nausea, vomiting, hematologic abnormalities
Fosfomycin, 3-g single-dose sachet	70–91	78–83	Diarrhea, nausea, headache
Pivmecillinam, 400 mg bid × 3–7 d	55–82	74–84	Nausea, vomiting, diarrhea
Fluoroquinolones, dose varies by agent; 3-d regimen	85–95	81–98	Nausea, vomiting, diarrhea, headache, drowsiness, insomnia
β-Lactams, dose varies by agent; 5- to 7-d regimen	79–98	74–98	Diarrhea, nausea, vomiting, rash, urticaria

[a]Microbial response as measured by reduction of bacterial counts in the urine.

Note: Efficacy rates are averages or ranges calculated from the data and studies included in the 2010 Infectious Diseases Society of America/European Society of Clinical Microbiology and Infectious Diseases Guideline for Treatment of Uncomplicated UTI. TMP-SMX, trimethoprim-sulfamethoxazole; DS, double-strength.

Resistance to nitrofurantoin remains low despite >60 years of use. Since this drug affects bacterial metabolism in multiple pathways, several mutational steps are required for the development of resistance. Nitrofurantoin remains highly active against *E. coli* and most non–*E. coli* isolates. *Proteus, Pseudomonas, Serratia, Enterobacter*, and yeasts are all intrinsically resistant to this drug. Although nitrofurantoin has traditionally been prescribed as a 7-day regimen, similar microbiologic and clinical efficacies are noted with a 5-day course of nitrofurantoin or a 3-day course of TMP-SMX for treatment of women with acute cystitis; 3-day courses of nitrofurantoin are not recommended for acute cystitis. Nitrofurantoin does not reach significant levels in tissue and cannot be used to treat pyelonephritis.

Most fluoroquinolones are highly effective as short-course therapy for cystitis; the exception is moxifloxacin, which may not reach adequate urinary levels. The fluoroquinolones commonly used for UTI include ofloxacin, ciprofloxacin, and levofloxacin. The main concern about fluoroquinolone use for acute cystitis is the propagation of fluoroquinolone resistance, not only among uropathogens but also among other organisms causing more serious and difficult-to-treat infections at other sites. Fluoroquinolone use is also a factor driving the emergence of *C. difficile* outbreaks in hospital settings. Most experts now call for restricting fluoroquinolones to specific instances of uncomplicated cystitis in which other antimicrobial agents are not suitable. Quinolone use in certain populations, including adults >60 years of age, has been associated with an increased risk of Achilles tendon rupture.

Except for pivmecillinam, β-lactam agents generally have not performed as well as TMP-SMX or fluoroquinolones in acute cystitis. Rates of pathogen eradication are lower and relapse rates are higher with β-lactam drugs. The generally accepted explanation is that β-lactams fail to eradicate uropathogens from the vaginal reservoir. A proposed role for intracellular biofilm communities is intriguing. Many strains of *E. coli* that are resistant to TMP-SMX are also resistant to amoxicillin and cephalexin; thus, these drugs should be used only for patients infected with susceptible strains.

Urinary analgesics are appropriate in certain situations to speed resolution of bladder discomfort. The urinary tract analgesic phenazopyridine is widely used but can cause significant nausea. Combination analgesics containing urinary antiseptics (methenamine, methylene blue), a urine-acidifying agent (sodium phosphate), and an antispasmodic agent (hyoscyamine) also are available.

PYELONEPHRITIS

Since patients with pyelonephritis have tissue-invasive disease, the treatment regimen chosen should have a very high likelihood of eradicating the causative organism and should reach therapeutic blood levels quickly. High rates of TMP-SMX-resistant *E. coli* in patients with pyelonephritis have made fluoroquinolones the first-line therapy for acute uncomplicated pyelonephritis. Whether the fluoroquinolones are given orally or parenterally depends on the patient's tolerance for oral intake. A randomized clinical trial demonstrated that a 7-day course of therapy with oral ciprofloxacin (500 mg twice daily, with or without an initial IV 400-mg dose) was highly effective for the initial management of pyelonephritis in the outpatient setting. Oral TMP-SMX (one double-strength tablet twice daily for 14 days) also is effective for treatment of acute uncomplicated pyelonephritis if the uropathogen is known to be susceptible. If the pathogen's susceptibility is not known and TMP-SMX is used, an initial IV 1-g dose of ceftriaxone is recommended. Oral β-lactam agents are less effective than the fluoroquinolones and should be used with caution and close follow-up. Options for parenteral therapy for uncomplicated pyelonephritis include fluoroquinolones, an extended-spectrum cephalosporin with or without an aminoglycoside, or a carbapenem. Combinations of a β-lactam and a β-lactamase inhibitor (e.g., ampicillin-sulbactam, ticarcillin-clavulanate, piperacillin-tazobactam) or imipenem-cilastatin can be used in patients with more complicated histories, previous episodes of pyelonephritis, or recent urinary tract manipulations; in general, the treatment of such patients should be guided by urine culture results. Once the patient has responded clinically, oral therapy should be substituted for parenteral therapy.

UTI IN PREGNANT WOMEN

Nitrofurantoin, ampicillin, and the cephalosporins are considered relatively safe in early pregnancy. One retrospective case-control study suggesting an association between nitrofurantoin and birth defects has not been confirmed. Sulfonamides should clearly be avoided both in the first trimester (because of possible teratogenic effects) and near term (because of a possible role in the development of kernicterus). Fluoroquinolones are avoided because of possible adverse effects on fetal cartilage development. Ampicillin and the cephalosporins have been used extensively in pregnancy and are the drugs of choice for the treatment of asymptomatic or symptomatic UTI in this group of patients. For pregnant women with overt pyelonephritis, parenteral β-lactam therapy with or without aminoglycosides is the standard of care.

UTI IN MEN

Since the prostate is involved in the majority of cases of febrile UTI in men, the goal in these patients is to eradicate the prostatic infection as well as the bladder infection. A 7- to 14-day course of a fluoroquinolone or TMP-SMX is recommended if the uropathogen is susceptible. If acute bacterial prostatitis is suspected, antimicrobial therapy should be initiated after urine and blood are obtained for cultures. Therapy can be tailored to urine culture results and should be continued for 2–4 weeks. For documented chronic bacterial prostatitis, a 4- to 6-week course of antibiotics is often necessary. Recurrences, which are not uncommon in chronic prostatitis, often warrant a 12-week course of treatment.

COMPLICATED UTI

Complicated UTI (other than that discussed above) occurs in a heterogeneous group of patients with a wide variety of structural and functional abnormalities of the urinary tract and kidneys. The range of species and their susceptibility to antimicrobial agents are likewise heterogeneous. As a consequence, therapy for complicated UTI must be individualized and guided by urine culture results. Frequently, a patient with complicated UTI will have prior urine culture data that can be used to guide empirical therapy while current culture results are awaited. Xanthogranulomatous pyelonephritis is treated with nephrectomy. Percutaneous drainage can be used