numbers of dysmorphic red blood cells, white blood cells, or crystals; in general, counts of bacteria are less accurate than are counts of red and white blood cells. The authors' clinical recommendation is that the patient's symptoms and presentation should outweigh an incongruent result on automated urinalysis.

The detection of bacteria in a urine culture is the diagnostic "gold standard" for UTI; unfortunately, however, culture results do not become available until 24 h after the patient's presentation. Identifying specific organism(s) can require an additional 24 h. Studies of women with symptoms of cystitis have found that a colony count threshold of $>10^2$ bacteria/mL is more sensitive (95%) and specific (85%) than a threshold of 10^5/mL for the diagnosis of acute cystitis in women. In men, the minimal level indicating infection appears to be 10^3/mL. Urine specimens frequently become contaminated with the normal microbial flora of the distal urethra, vagina, or skin. These contaminants can grow to high numbers if the collected urine is allowed to stand at room temperature. In most instances, a culture that yields mixed bacterial species is contaminated except in settings of long-term catheterization, chronic urinary retention, or the presence of a fistula between the urinary tract and the gastrointestinal or genital tract.

DIAGNOSIS

The approach to diagnosis is influenced by which of the clinical UTI syndromes is suspected (Fig. 162-4).

Uncomplicated Cystitis in Women Uncomplicated cystitis in women can be treated on the basis of history alone. However, if the symptoms are not specific or if a reliable history cannot be obtained, then a urine dipstick test should be performed. A positive nitrite or leukocyte esterase result in a woman with one symptom of UTI increases the probability of UTI from 50% to ~80%, and empirical treatment can be considered without further testing. In this setting, a negative dipstick result does not rule out UTI, and a urine culture, close clinical follow-up, and possibly a pelvic examination are recommended. These recommendations are made with the caveat that no factors associated with complicated UTI, such as pregnancy, are known to be present.

Cystitis in Men The signs and symptoms of cystitis in men are similar to those in women, but this disease differs in several important ways in the male population. Collection of urine for culture is strongly recommended when a man has symptoms of UTI, as the documentation of bacteriuria can differentiate the less common syndromes of acute and chronic bacterial prostatitis from the very common entity of chronic pelvic pain syndrome, which is not associated with bacteriuria and thus is not usually responsive to antibacterial therapy. If the diagnosis is unclear, localization cultures using the two- or four-glass Meares-Stamey test (urine collection after prostate massage) should be undertaken to differentiate between bacterial and nonbacterial prostatic syndromes, and the patient should be referred to a urologist. Men with febrile UTI often have an elevated serum level of prostate-specific antigen as well as an enlarged prostate and enlarged seminal vesicles on ultrasound—findings indicative of prostate involvement. In 85 men with febrile UTI, symptoms of urinary retention, early recurrence of UTI, hematuria at follow-up, and voiding difficulties were predictive of surgically correctable disorders. Men with none of these symptoms had normal upper and lower urinary tracts on urologic workup.

Asymptomatic Bacteriuria The diagnosis of ASB involves both microbiologic and clinical criteria. The microbiologic criterion is usually $\geq 10^5$ bacterial CFU/mL except in catheter-associated disease, in which $\geq 10^2$ CFU/mL is the cutoff. The clinical criterion is that the person has no signs or symptoms referable to UTI.

TREATMENT URINARY TRACT INFECTIONS

Antimicrobial therapy is warranted for any symptomatic UTI. The choice of antimicrobial agent and the dose and duration of therapy depend on the site of infection and the presence or absence of complicating conditions. Each category of UTI warrants a different approach based on the particular clinical syndrome.

Antimicrobial resistance among uropathogens varies from region to region and impacts the approach to empirical treatment of UTI. *E. coli* ST131 is the predominant multilocus sequence type found worldwide as the cause of multidrug-resistant UTI. Recommendations for treatment must be considered in the context of local resistance patterns and national differences in some agents' availability. For example, fosfomycin and pivmecillinam are not available in all countries but are considered first-line options where they are available because they retain activity against a majority of uropathogens that produce extended-spectrum β-lactamases. Thus, therapeutic choices should depend on local resistance, drug availability, and individual patient factors such as recent travel and antimicrobial use.

UNCOMPLICATED CYSTITIS IN WOMEN

Since the species and antimicrobial susceptibilities of the bacteria that cause acute uncomplicated cystitis are highly predictable, many episodes of uncomplicated cystitis can be managed over the telephone (Fig. 162-4). Most patients with other UTI syndromes require further diagnostic evaluation. Although the risk of serious complications with telephone management appears to be low, studies of telephone management algorithms generally have involved otherwise healthy white women who are at low risk for complications of UTI.

In 1999, TMP-SMX was recommended as the first-line agent for treatment of uncomplicated UTI in the published guidelines of the Infectious Diseases Society of America. Antibiotic resistance among uropathogens causing uncomplicated cystitis has since increased, appreciation of the importance of collateral damage (as defined below) has increased, and newer agents have been studied. Unfortunately, there is no longer a single best agent for acute uncomplicated cystitis.

Collateral damage refers to the adverse ecologic effects of antimicrobial therapy, including killing of the normal flora and selection of drug-resistant organisms. Outbreaks of *Clostridium difficile* infection offer an example of collateral damage in the hospital environment. The implication of collateral damage in this context is that a drug that is highly efficacious for the treatment of UTI is not necessarily the optimal first-line agent if it also has pronounced secondary effects on the normal flora or is likely to change resistance patterns. Drugs used for UTI that have a minimal effect on fecal flora include pivmecillinam, fosfomycin, and nitrofurantoin. In contrast, trimethoprim, TMP-SMX, quinolones, and ampicillin affect the fecal flora more significantly; these drugs are notably the agents for which rising resistance levels have been documented.

Several effective therapeutic regimens are available for acute uncomplicated cystitis in women **(Table 162-1)**. Well-studied first-line agents include TMP-SMX and nitrofurantoin. Second-line agents include fluoroquinolone and β-lactam compounds. Single-dose fosfomycin treatment for acute cystitis is widely used in Europe but has produced mixed results in randomized trials. There is increasing experience with the use of fosfomycin against UTIs (including complicated infections) caused by multidrug-resistant *E. coli*. Pivmecillinam is not currently available in the United States or Canada but is a popular agent in some European countries. The pros and cons of other therapies are discussed briefly below.

Traditionally, TMP-SMX has been recommended as first-line treatment for acute cystitis, and it remains appropriate to consider the use of this drug in regions with resistance rates not exceeding 20%. TMP-SMX resistance has clinical significance: in TMP-SMX-treated patients with resistant isolates, the time to symptom resolution is longer and rates of both clinical and microbiologic failure are higher. Individual host factors associated with an elevated risk of UTI caused by a strain of *E. coli* resistant to TMP-SMX include recent use of TMP-SMX or another antimicrobial agent and recent travel to an area with high rates of TMP-SMX resistance. The optimal setting for empirical use of TMP-SMX is uncomplicated UTI in a female patient who has an established relationship with the practitioner and who can thus seek further care if her symptoms do not respond promptly.