The most common etiologic agent in patients with uncomplicated UTI is *Escherichia coli* (90% of cases), followed by *Staphylococcus saprophyticus*. Other agents include *Klebsiella* spp, *Enterococcus faecalis, Enterococcus faecium, Proteus* spp, *Providencia stuartii*, and *Morganella morganii*. In patients with complicated UTI, *E. coli* is still the most frequent uropathogen, but at a lower rate than in uncomplicated UTI. Other causative organisms are *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, *Enterobacter* spp, *Serratia marcescens, Stenotrophomonas maltophilia, Enterococcus* spp, and *Candida* spp.

Anaerobic agents are infrequent causes of UTI; when present, they represent fistulae between the digestive tract and the urinary tract. *Staphylococcus aureus* UTI most often represents bacteremia with bacteriuria resulting from clearance of bloodstream bacteria by the kidney. Whereas 1% of individuals with a UTI get pyelonephritis, 20% to 40% of pregnant women with a UTI develop pyelonephritis, and 30% of patients with pyelonephritis have bacteremia. In diabetic and transplanted patients with UTI, the incidence of bacteremia is higher.

PATHOGENESIS

There are at least three routes by which bacteria can enter the bladder or kidney: ascending, hematogenous, and lymphatic. Lymphatic spread is the least common route. The hematogenous route is important for gram-positive organisms such as *S. aureus* or *Candida* spp but unimportant for gram-negative bacilli. The ascending route is the most important for enteric bacteria, and this mechanism is supported by higher frequency of UTI in women, given the shorter length of the female urethra, and in individuals with an indwelling Foley catheter.

Before reaching the urinary bladder or kidney, the microorganism must colonize the external part of the urinary tract. Probably the most important aspect in the establishment of UTI is the interaction between host factors (e.g., secretor phenotype, P1 blood group, uroplakin I and II) and bacterial virulence factors (the adhesins, P fimbriae, and type I fimbriae [pili]). The urinary bladder is normally covered by a glycosaminoglycan surface that prevents binding of bacteria that transiently enter the bladder. P-fimbriated uropathogenic *E. coli* bind to alpha 1-4 linked, galactose-galactose disaccharide moieties found on uroepithelial cells, and these gal-gal glycolipids are also expressed on the P1 blood group. People with P1 blood group are overrepresented among individuals with either recurrent UTI and pyelonephritis. Also, people who lack P1 blood group are less prone to complicated UTI.

Studies have shown that P-fimbriated *E. coli* is present in 60% to 100% of isolates from patients with UTI. Ascending UTI infection can be inhibited experimentally by epithelial cell surface receptor analogues. Type I fimbriae bind to glycoprotein uroplakin I and II. *E. coli* expressing type I fimbriae are responsible for most cases of cystitis.

Once *E. coli* is attached to uroepithelial cells, both mechanical and biochemical factors facilitate the development of full-blown UTI. The local trauma and mechanical massage of the urethra during sexual intercourse help deliver bacteria into the bladder and, if vesicoureteral reflux or another ureteral anatomic defect is present, into the kidney. Foley catheter placement also helps to propel bacteria into the bladder, and all patients with a long-term indwelling catheter in place will eventually develop UTI. All uropathogenic organisms have the ability to multiply in the urine.

From the standpoint of the host, other factors associated with the development of UTI are a new sex partner (within 1 year), use of diaphragms and spermicides, family history of UTI in a first-degree relative, and lower expression of CXCR1, an

TABLE 98-1 THERAPY FOR UNCOMPLICATED URINARY TRACT INFECTIONS

	CYSTITIS			*PYELONEPHRITIS*		
ANTIMICROBIAL AGENT	**USEFUL THERAPEUTICALLY**	**DOSE AND DURATION**	**COMMENTS**	**USEFUL THERAPEUTICALLY**	**DOSE AND DURATION**	**COMMENTS**
Nitrofurantoin monohydrate macrocrystals	*Yes, first line	100 mg bid for 5 days	Cheap, well tolerated SE: N, H Low impact on microbiome	No	NA	Reduced renal tissue penetration
Trimethoprim-sulfamethoxazole	*Yes, first line	160/800 mg bid for 3 days	If resistance is known to be <20% SE: rash, urticaria, N, V	Yes	160/800 mg bid for 14 days	*If organism susceptibility is known †If not, give an initial LA IV agent
Fosfomycin trometamol	*Yes, first line	3 g single-dose sachet	May be less efficient SE: N, D, H	No	NA	Active against MRSA ESBL, VRE
Fluoroquinolones (ciprofloxacin levofloxacin)	†Yes, second line	3-day regimen 250 mg bid 250 mg qd	High collateral damage SE: N, V, D, H, tendinitis	*Yes, first line	Dose varies; 7-14 days	If resistance is known to be <10%
β-Lactams	‡Yes, second line	Dose varies by agent; 5-7 days	Less effective, increased side effects SE: N, V, D, rash, urticaria	‡Yes Use cautiously Less efficient	Dose varies; 10-14 day regimen	‡Give an initial LA IV agent

Data from Gupta K, Hooton TM, Naber KG, et al: International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: a 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases—executive summary, Clin Infect Dis 52:561–564, 2011.

D, Diarrhea; ESBL, extended-spectrum β-lactamase; H, headache; IV, intravenous; LA, long acting; N, nausea; NA, not applicable; MSRA, methicillin-resistant *Staphylococcus aureus*; SE, side effects; V, vomiting; VRE, vancomycin-resistant enterococci.

*AI level of evidence from current guidelines.

†AIII level of evidence from current guidelines.

‡BI level of evidence from current guidelines.