Many factors predisposing women to cystitis also increase the risk of pyelonephritis. Factors independently associated with pyelonephritis in young healthy women include frequent sexual intercourse, a new sexual partner, a UTI in the previous 12 months, a maternal history of UTI, diabetes, and incontinence. The common risk factors for cystitis and pyelonephritis are not surprising given that pyelonephritis typically arises through the ascent of bacteria from the bladder to the upper urinary tract. However, pyelonephritis can occur without clear antecedent cystitis.

About 20–30% of women who have had one episode of UTI will have recurrent episodes. Early recurrence (within 2 weeks) is usually regarded as relapse rather than reinfection and may indicate the need to evaluate the patient for a sequestered focus. Intracellular pods of infecting organisms within the bladder epithelium have been demonstrated in animal models of UTI, but the importance of this phenomenon in humans is not yet clear. The rate of recurrence ranges from 0.3 to 7.6 infections per patient per year, with an average of 2.6 infections per year. It is not uncommon for multiple recurrences to follow an initial infection, resulting in clustering of episodes. Clustering may be related temporally to the presence of a new risk factor or to the sloughing of the protective outer bladder epithelial layer in response to bacterial attachment during acute cystitis. The likelihood of a recurrence decreases with increasing time since the last infection. A case-control study of predominantly white premenopausal women with recurrent UTI identified frequent sexual intercourse, use of spermicide, a new sexual partner, a first UTI before 15 years of age, and a maternal history of UTI as independent risk factors for recurrent UTI. The only consistently documented behavioral risk factors for recurrent UTI include frequent sexual intercourse and spermicide use. In postmenopausal women, major risk factors for recurrent UTI include a history of premenopausal UTI and anatomic factors affecting bladder emptying, such as cystoceles, urinary incontinence, and residual urine.

In pregnant women, ASB has clinical consequences, and both screening for and treatment of this condition are indicated. Specifically, ASB during pregnancy is associated with preterm birth and perinatal death of the fetus and with pyelonephritis in the mother. A Cochrane meta-analysis found that treatment of ASB in pregnant women decreased the risk of pyelonephritis by 75%.

The majority of men with UTI have a functional or anatomic abnormality of the urinary tract, most commonly urinary obstruction secondary to prostatic hypertrophy. That said, not all men with UTI have detectable urinary abnormalities; this point is particularly relevant for men ≤45 years of age. Lack of circumcision is also associated with an increased risk of UTI because *Escherichia coli* is more likely to colonize the glans and prepuce and subsequently migrate into the urinary tract.

Women with diabetes have been found to have a two- to threefold higher rate of ASB and UTI than women without diabetes; there is insufficient evidence to make a corresponding statement about men. Increased duration of diabetes and the use of insulin rather than oral medication are also associated with a higher risk of UTI among women with diabetes. Poor bladder function, obstruction in urinary flow, and incomplete voiding are additional factors commonly found in patients with diabetes that increase the risk of UTI. Impaired cytokine secretion may contribute to ASB in diabetic women.

ETIOLOGY

The uropathogens causing UTI vary by clinical syndrome but are usually enteric gram-negative rods that have migrated to the urinary tract. The susceptibility patterns of these organisms vary by clinical syndrome and by geography. In acute uncomplicated cystitis in the United States, the etiologic agents are highly predictable: *E. coli* accounts for 75–90% of isolates; *Staphylococcus saprophyticus* for 5–15% (with particularly frequent isolation from younger women); and *Klebsiella, Proteus, Enterococcus*, and *Citrobacter* species, along with other organisms, for 5–10%. Similar etiologic agents are found in Europe and Brazil. The spectrum of agents causing uncomplicated pyelonephritis is similar, with *E. coli* predominating. In complicated UTI (e.g., CAUTI), *E. coli* remains the predominant organism, but other aerobic gram-negative rods, such as *Pseudomonas aeruginosa* and *Klebsiella, Proteus, Citrobacter, Acinetobacter*, and *Morganella* species, also are frequently isolated. Gram-positive bacteria (e.g., enterococci and *Staphylococcus aureus*) and yeasts are also important pathogens in complicated UTI. Data on etiology and resistance are generally obtained from laboratory surveys and should be understood in the context that organism identification is performed only in cases in which urine is sent for culture—i.e., typically, when complicated UTI or pyelonephritis is suspected. The available data demonstrate a worldwide increase in the resistance of *E. coli* to antibiotics commonly used to treat UTI. North American and European surveys from women with acute cystitis have documented resistance rates of >20% to trimethoprim-sulfamethoxazole (TMP-SMX) and to ciprofloxacin in some regions. In community-acquired infections, the increased prevalence of uropathogens producing extended-spectrum β-lactamases has left few oral options for therapy. Since resistance rates vary by local geographic region, with individual patient characteristics, and over time, it is important to use current and local data when choosing a treatment regimen.

PATHOGENESIS

The urinary tract can be viewed as an anatomic unit united by a continuous column of urine extending from the urethra to the kidneys. In the majority of UTIs, bacteria establish infection by ascending from the urethra to the bladder. Continuing ascent up the ureter to the kidney is the pathway for most renal parenchymal infections. However, introduction of bacteria into the bladder does not inevitably lead to sustained and symptomatic infection. The interplay of host, pathogen, and environmental factors determines whether tissue invasion and symptomatic infection will ensue (Fig. 162-1). For example, bacteria often enter the bladder after sexual intercourse, but normal voiding and innate host defense mechanisms in the bladder eliminate these organisms. Any foreign body in the urinary tract, such as a urinary catheter or stone, provides an inert surface for bacterial colonization. Abnormal micturition and/or significant residual urine volume promotes true infection. In the simplest of terms, anything that increases the likelihood of bacteria entering the bladder and staying there increases the risk of UTI.

Bacteria can also gain access to the urinary tract through the bloodstream. However, hematogenous spread accounts for <2% of documented UTIs and usually results from bacteremia caused by relatively virulent organisms, such as *Salmonella* and *S. aureus*. Indeed, the isolation of either of these pathogens from a patient without a catheter or other instrumentation warrants a search for a bloodstream source. Hematogenous infections may produce focal abscesses or areas of pyelonephritis within a kidney and result in positive urine cultures. The pathogenesis of candiduria is distinct in that the hematogenous route is common. The presence of *Candida* in the urine of a noninstrumented

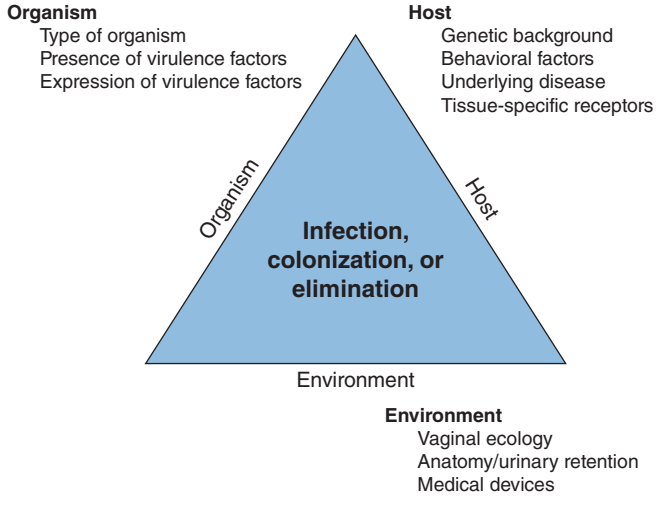

FIGURE 162-1 Pathogenesis of urinary tract infection. The relationship among specific host, pathogen, and environmental factors determines the clinical outcome.