Urinary Tract Infection Pathogenesis: Host Factors

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KEYWORDS

• Modifiable host factors • Nonmodifiable host factors • Sexual intercourse
• Estrogen status • Urogenital microbiota • Female gender

KEY POINTS

- Host factors in urinary tract infection include both modifiable aspects that patients and physicians may be able to influence and thus reduce risk, and nonmodifiable factors with future potential for therapeutics or risk profiling.
- Examples of modifiable host factors include sexual intercourse, choice of contraceptives, exposure to antimicrobials, estrogen status, and influences on the urogenital microbiota.
- Examples of nonmodifiable host factors include female gender and genetic influences.
- To assist patients in reducing the risk of UTI, currently clinicians should consider reviewing modifiable host factors and helping patients decide if relevant interventions are appropriate.
- In the future, genetically based, nonmodifiable host factors in the pathogenesis of UTI may be clinically relevant to risk profiling in certain populations, such as children.

INTRODUCTION

Epidemiology

Urinary tract infections (UTIs) are among the most common infections throughout the life span in both genders, in both ambulatory and hospitalized patients. Although the Centers for Disease Control and Prevention (CDC) do not designate UTI as a reportable disease, ambulatory visits for UTI are captured in the CDC annual National Ambulatory Medical Care Survey (NHAMCS).[1] According to most recent available data from the NHAMCS, in 2007 there were 8.6 million ambulatory visits for UTI in both men and

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women in the United States.[1] As described in greater detail herein, girls and women are disproportionately affected by UTI.[2]

Disease Description

Several specific syndromes of UTI are known, such as acute uncomplicated cystitis (AUC), or bladder infection, and acute uncomplicated pyelonephritis (AUP). AUC is defined as a compatible clinical syndrome, including symptoms such as dysuria, urinary frequency, or urgency occurring in an otherwise healthy, nonpregnant woman.[3] If laboratory studies are obtained, diagnostic findings include the presence of pyuria in voided urine and a urine culture positive for a uropathogen in amounts of at least 10^3 cfu/mL.[3] Clinically, AUP is characterized by fever, costovertebral angle tenderness, and/or flank pain, and other systemic symptoms, also in a nonpregnant, otherwise healthy woman, and the syndrome may also include lower urinary tract signs and symptoms.[4] Laboratory criteria are the same as for AUC.[4]

UTI involving the bladder and/or kidneys is generally classified as complicated or uncomplicated. Complicated UTI is defined as an infection occurring in a patient with comorbid medical conditions and/or anatomic abnormalities of the urinary tract that may increase the difficulty of diagnosing UTI as well as the likelihood of various adverse outcomes, such as a resistant causative bacteria, delayed or inadequate response to antimicrobial therapy, a need for prolonged therapy or hospitalization, and significant morbidity.[5] Commonly encountered complicating factors for UTI include pregnancy, functional bladder abnormalities such as neurogenic bladder, renal transplant, urinary stones, structural abnormalities of the urinary tract, diabetes, male gender, urinary catheterization or instrumentation, recent hospitalization or antibiotic exposure, and advanced age. Most complicating factors are also important host factors in the pathogenesis of UTI.

PATHOPHYSIOLOGY

Overview of UTI Pathogenesis: Bacterial Uropathogenesis and Interplay with Host Factors

Although this article focuses on host factors in the pathogenesis of UTI, a brief review of bacterial factors in UTI is relevant, given the interplay of host susceptibility and bacterial virulence that occurs in most infections. UTI has served as an excellent model of bacterial pathogenesis throughout years of study in multiple laboratories, with most studies focusing on virulence traits of *Escherichia coli*, the most common cause of UTI in all age groups and clinical settings.[6] Although the busy clinician is appropriately currently focused on diagnosis, treatment, and prevention of UTI, some of the genetic susceptibility issues discussed here relate to specific host responses to bacterial traits. At least for children, there is a possibility in the near future of using genetic testing to detect specific genetically determined susceptibility to pyelonephritis.[6] In addition, some newer preventive measures, discussed in the article by Geerlings and colleagues elsewhere in this issue, are based on specific findings learned through detailed study of bacterial pathogenesis in UTI.

As noted, *E coli* causes 80% to 90% of AUC or AUP in young, healthy, sexually active women,[7] as well as most complicated UTIs.[8] *E coli* are generally divided into intestinal pathogens and extraintestinal *E coli* (ExPEC), based on the disease syndromes linked to the organisms epidemiologically. Numerous laboratory-based and clinical-epidemiologic studies have demonstrated a subset of ExPEC specifically associated with UTI, the uropathogenic *E coli* (UPEC), organisms expressing traits rendering them specially adapted to express virulence and fitness in the urinary tract