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The Roles of the Host and the Pathogens in Urinary Tract Infections

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Abstract

The severity of urinary tract infections (UTIs) varies depending on the balance between the virulence of the infecting bacterial strain and the antibacterial host defense. Bacterial virulence is determined by a complex of factors in which bacterial adherence to the uroepithelium is the most important virulence factor, in addition to the production of toxins and the formation of biofilm. In immunocompromised patients and in patients with severely dysfunctional urinary tracts, however, the importance of bacterial virulence factors to cause symptomatic infection is decreased or nullified. The antibacterial host defense in the urinary tract depends mainly on native immunity and inflammation. Specific immunity, with antigen presentation and antibody production, does not play an important role in acute UTI. Recent research has provided a deeper understanding of the inflammation process in UTI and demonstrated that the individual variation of UTI susceptibility and renal damage not only depends on urinary tract dysfunctions but is also influenced by genetic polymorphisms in innate immune receptors and signaling proteins, crucial for the innate antibacterial defenses. The identification of these molecular mechanisms in UTI pathogenesis is an important focus for future research aimed at the development of novel nonantibiotic therapies.

Patient summary: The severity of urinary tract infections (UTIs) varies depending on the balance between the infecting bacterial strain and the antibacterial host defense. Bacterial virulence is determined by different virulence factors that enhance bacterial persistence and tissue damage. The susceptibility to an UTI is influenced by dysfunctions of the urinary tract and by genetic mechanisms that control the innate immune response to infections.

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1. Introduction

Urinary tract infections (UTIs) are among the most frequent infections encountered in the community and also one of the leading causes of hospital-acquired infections with significant consequences of morbidity and cost. UTIs may be acute symptomatic infections of varying severity and localization, but they may also result in the establishment of an asymptomatic carrier state, asymptomatic bacteriuria (ABU) (Fig. 1). The severity of the infection varies depending on the balance between the infecting bacterial strain and the antibacterial host defenses.

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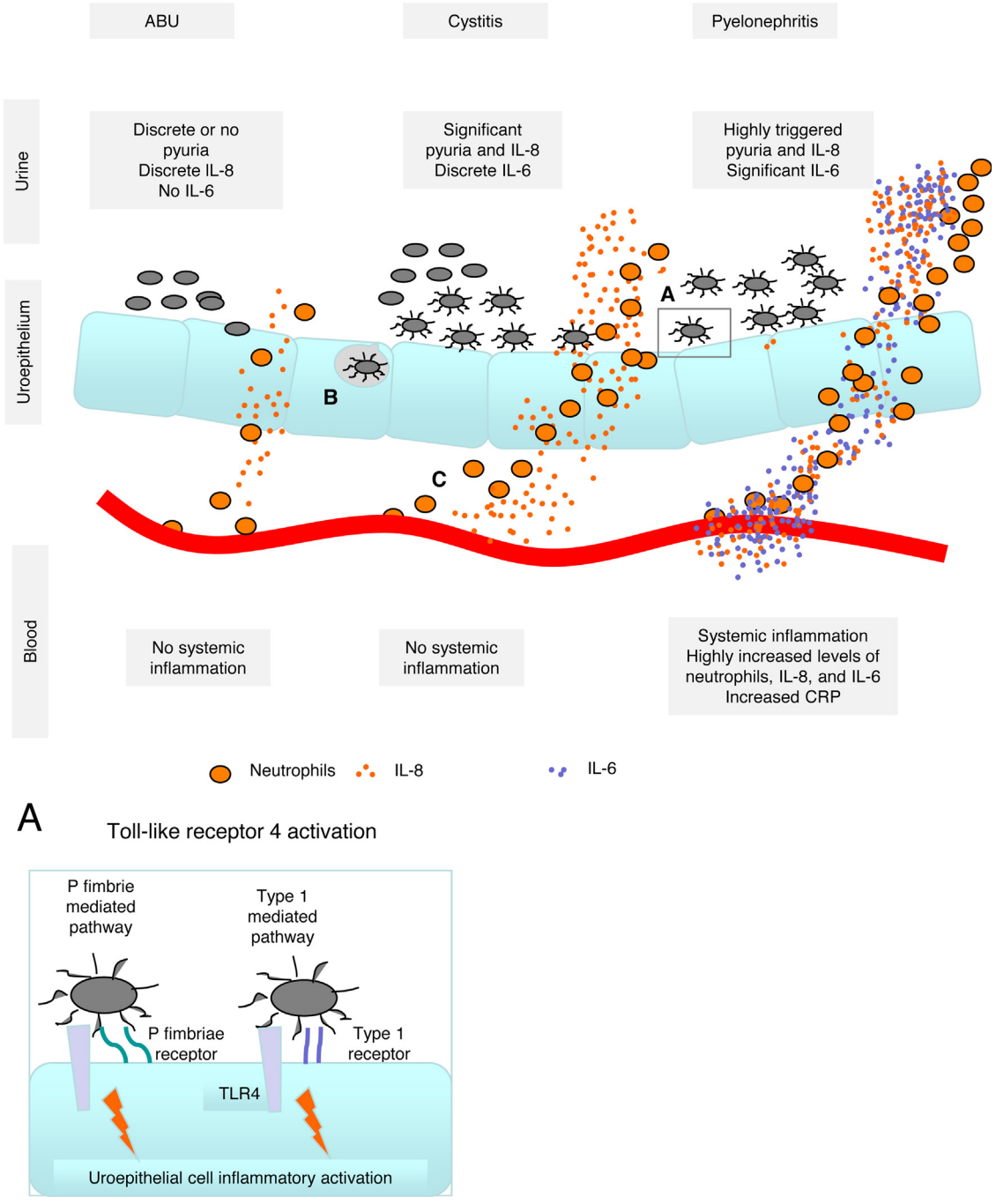

Fig. 1 – Schematic figure outlining bacterial challenge and activation of the host response in urinary tract infections. (A) In asymptomatic bacteriuria, there is no or only inefficient activation of the uroepithelium. In symptomatic urinary tract infection, bacterial contact with the uroepithelium is mediated by P or type 1 fimbriae and its receptors on the uroepithelium. Toll-like receptor 4 recognizes the gram-negative uropathogens, the uroepithelial cell is activated, and inflammatory mediators (interleukin [IL] 6 and IL-8) are produced [17]. (B) In recurrent cystitis, intracellular bacterial fabrics have been suggested [22]. (C) Neutrophils from the circulation transmigrate, guided by expressed IL-8 receptors (CXCR), by following the concentration gradient of IL-8 to the place of infection to combat the bacteria by phagocytosis [2].
ABU = asymptomatic bacteriuria; CRP = C-reactive protein; IL = interleukin; TLR4 = toll-like receptor 4; UTI = urinary tract infection.

Most UTIs are caused by *Escherichia coli*. The molecular determinants of bacterial virulence have been studied extensively, and the pathogenesis of infection is known to proceed from initial tissue contact and adherence through many intricate steps, ending either in resolution through bacterial clearance by the host defense or in persistence and chronicity [1–5]. Other identified *E coli* virulence factors include lipopolysaccharide (LPS) antigens, flagellation, and the production of toxins, siderophores, and hemolysin.

Although the focus on the bacterial factor has provided much insight into understanding UTI pathogenesis, it has long been obvious that host factors play a significant role. This is clearly demonstrated by patients with urinary tract dysfunctions who are susceptible for UTI caused by