Introduction
Before 1905 (the year treatment with antimenningococcal serum started) the case fatality rate (CFR) of invasive meningococcal disease (IMD) was 70 to 90% [1]. Patients with severe sepsis or septic shock died rapidly, usually within 24 hours. Patients with meningitis and other clinical manifestations could live as long as 6 to 8 weeks before succumbing [1]. Since *Neisseria meningitidis* did not produce any recognizable exotoxin it was hypothesized that endotoxin, a yet undefined chemical component of Gram-negative bacteria, played an important role in the pathogenesis of this disease. Research conducted during the last 30 years has confirmed the crucial role of lipopolysaccharide (LPS, endotoxin) in meningococcal disease and also documented the role of non-LPS components as proinflammatory molecules [2].

Transmission, adaptation, and penetration to the circulation
*N. meningitidis* (Figure 3.1) is transmitted by droplets or exchange of saliva. Infection starts within 10 days, usually 2 to 4 days after a non-immune person has been exposed to an asymptomatic carrier or an untreated patient. Before the symptoms develop, the transmitted virulent meningococci adapt locally on specific nonciliated epithelial cells
in the nasopharynx and tonsils (Figure 3.2) [2,3]. Bacteria evade the immune system partly via phase and antigenic variation, altering LPS and certain outer membrane proteins and down-regulating pili, before passing through the mucosal barrier and penetrating into the submucosal layer [3–5]. Subsequently they enter the circulation, most likely in the upper respiratory tract. When reaching the circulation it is assumed that they once more undergo phase variation of surface structures, thereby decreasing immune recognition through molecular mimicry [4–6]. This is accomplished by:

- up-regulating type IV pili;
- altering the terminal part of the LPS side chain to express the L3, 7, 9 epitopes; and
- adding sialic acid to LPS.

These changes result in an increased resistance to antibodies and complement. The capsule polysaccharides consist of long sugar filaments that protect meningococci from the antibacterial effect of human blood, mainly by down-regulating phagocytosis. Survival and growth in the blood are required for meningococci to develop into a systemic infection. *N. meningitidis* has the propensity to invade the meninges.