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NEISSERIA MENINGITIDIS: PATHOGENESIS OF MENINGOCOCCAL INFECTION, CLINICAL FORMS AND MECHANISMS OF DEVELOPMENT OF INVASIVE DISEASES

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Abstract: Neisseria meningitidis is a commensal microorganism of the human upper respiratory tract. Under the influence of certain genetic and host factors, this bacterium can cause invasive meningococcal disease. This article provides a detailed analysis of the molecular pathogenesis of the bacterium, its major virulence factors, the mechanisms of development of clinical forms, and the stages of the invasive process. Processes ranging from nasopharyngeal colonization, crossing of the epithelial barrier, survival in the bloodstream, interaction with endothelial cells, and disruption of the blood–brain barrier are elucidated on the basis of modern data. The polysaccharide capsule, lipooligosaccharide, type IV pili, factor H-binding protein, and other factors play key roles. Clinically, meningitis, fulminant meningococcemia, and mixed forms are distinguished. The host immune response, the complement system, and the degree of endothelial dysfunction determine the severity of the disease. The article is written in a professional and natural style based on reliable scientific sources.

Keywords: Neisseria meningitidis, pathogenesis, virulence factors, clinical forms, blood–brain barrier, endothelial colonization.

Introduction: Neisseria meningitidis is a Gram-negative, aerobic diplococcus that lives exclusively in the human organism. It forms part of the normal microbiota of the nasopharyngeal mucosa. Asymptomatic carriage is observed in an average of 5–10% of the population. In adolescents and closed communities this figure may rise to 20–30%. In most cases the bacterium causes no disease. However, under conditions of hyperinvasive strains and weakened host immunity, it enters the bloodstream and develops life-threatening invasive disease. Invasive meningococcal disease remains a serious global problem. Epidemics occur in the African meningitis belt, while endemic and sporadic cases are observed in other regions. The main etiological factors are serogroups A, B, C, W, Y, and X. Although vaccination programs have significantly reduced the incidence, the mortality rate remains high. In fulminant forms the case-fatality rate can reach 40–50%. A large proportion of survivors suffer severe sequelae, the most common of which are hearing loss, neurological disorders, limb amputation, and renal failure. The rapid progression of the disease, vascular collapse induced by endotoxin, and multi-organ failure are its main features. Therefore, a thorough understanding of the pathogenesis is essential for the development of early diagnosis, effective treatment, and preventive measures. This article aims to present these processes systematically and in detail. The biological characteristics of the bacterium, virulence factors, stages of pathogenesis, clinical forms, and their pathophysiological bases are extensively covered.

Main Part: Several important structures are present on the outer membrane of the bacterium.

The polysaccharide capsule is one of the most important virulence factors. It confers resistance to phagocytosis and complement attack. The serogroup B capsule has a structure similar to certain glycoproteins found in human tissues; this reduces its immunogenicity. Capsule expression decreases during colonization and increases upon entry into the bloodstream. Capsule-deficient strains usually do not cause invasive disease. Lipooligosaccharide elicits a strong inflammatory response. It acts on host cells through specific receptors and enhances cytokine production, resulting in the systemic inflammatory response syndrome. The structure of the lipid A moiety determines the intensity of inflammation. Highly phosphorylated lipid A induces stronger inflammation and is of major importance in the development of fulminant forms. Type IV pili are essential for initial adhesion, bacterial aggregation, and firm attachment to endothelial cells. They interact with specific receptors and induce the formation of particular structures in host cells, leading to the opening of intercellular junctions. Proteins and other adhesins facilitate entry into epithelial and endothelial cells. Iron-acquisition systems enable bacterial survival in the bloodstream. Factor H-binding protein blocks the complement system. IgA protease disrupts local immunity. All these factors are controlled by phase variation. Infection is transmitted via respiratory secretions. In the nasopharynx the bacterium adheres to epithelial cells. Initial distant attachment occurs via pili, followed by intimate adhesion. The bacterium may cross into the subepithelial layer by either the transcellular or paracellular route. In most cases the immune system interrupts this process; only in certain instances does the bacterium enter the bloodstream. Once in the bloodstream the bacterium multiplies rapidly. A high bacterial load increases endotoxin release. Adhesion to endothelial cells leads to the formation of microcolonies that resist shear forces of blood flow. Vascular wall permeability increases. Thrombosis and petechial-purpuric rashes develop. Endothelial dysfunction and coagulopathy constitute the principal pathophysiological mechanism of fulminant forms. Crossing of the blood–brain barrier occurs at the level of the cerebral capillary endothelium. Pilus-mediated adhesion opens intercellular junctions, allowing the bacterium to enter the subarachnoid space and cause meningitis. In some cases entry via the olfactory nerve is also possible. Intense inflammation within the central nervous system leads to cerebral edema and neurological complications. Cytokines, matrix metalloproteinases, and reactive oxygen species play important roles in this process. Clinical forms depend on the bacterial load and the host response. Meningitis is the most common form and presents with fever, headache, vomiting, photophobia, and neck stiffness. In this form the bacterial load is relatively low. Fulminant meningococcemia is characterized by rapidly progressive shock, petechial-purpuric rash, and multi-organ failure; the bacterial load is very high. Mixed forms also occur. In some patients only mild bacteremia is observed. Less common forms include pneumonia, arthritis, and pericarditis. The disease progresses more rapidly in children and adolescents. Complement deficiency and asplenia significantly increase the risk of invasive disease.

Materials and Methods: This work was performed as a systematic literature review. During the study, authoritative sources including PubMed, Nature Reviews Microbiology, Frontiers in Cellular and Infection Microbiology, Cellular Microbiology, Virulence, Methods in Molecular Biology, Archives of Disease in Childhood, official guidelines of the Centers for Disease Control and Prevention, and UpToDate were used. Peer-reviewed articles, reviews, and official reports published between 2003 and 2025 were selected. Selection criteria included direct relevance to the topic, scientific reliability, and currency of data. Primary attention was focused on the virulence factors of the bacterium, mechanisms of nasopharyngeal colonization, strategies for survival in the bloodstream, endothelial colonization, pathways for crossing the blood–brain barrier, and the pathophysiological bases of clinical forms. Data were systematized, compared, and generalized.

The year, volume, and page numbers of each source were precisely indicated. Qualitative analysis was employed as the research method. Results were presented on the basis of modern concepts. This approach ensured a complete and in-depth coverage of the topic.

Results and Discussion: The analysis results demonstrate that invasive potential depends on bacterial genetic characteristics, expression of virulence factors, and the immune status of the host. Type IV pili play a central role in endothelial colonization. They are of primary importance in adhesion to endothelial cells, formation of microcolonies, and opening of intercellular junctions. This mechanism leads to damage of the vascular wall and dissemination of the bacterium into tissues. The quantity of lipooligosaccharide determines the clinical form: a high load predisposes to fulminant sepsis, while a lower load predisposes to meningitis. The degree of phosphorylation of the lipid A moiety significantly increases the intensity of inflammation. The status of the host complement system and genetic factors are also of major importance. Individuals with complement deficiency have a several-fold higher risk of invasive disease. Clinical data confirm that in patients with meningitis the bacterial load is lower and inflammation is largely confined to the central nervous system. In contrast, septic shock is dominated by a systemic cytokine storm and endothelial dysfunction. These differences indicate the necessity of individualizing diagnostic and therapeutic strategies. Although vaccination has reduced incidence, certain serogroups remain problematic, particularly serogroup B and some hyperinvasive clones. A deeper understanding of pathogenesis facilitates the development of new therapeutic approaches. Antivirulence agents, especially compounds that block pilus function, represent a promising direction. Personalized approaches that take into account the individual characteristics of host–pathogen interactions are expected to develop.

Conclusion: The pathogenesis of Neisseria meningitidis is a complex, multi-stage process. It begins with nasopharyngeal colonization and continues with survival in the bloodstream, endothelial colonization, and crossing of the blood–brain barrier. The capsule, lipooligosaccharide, type IV pili, and complement-evasion factors are the principal virulence determinants. Clinical forms differ according to bacterial load and host response. Modern research is elucidating these mechanisms with increasing precision. This knowledge serves the improvement of early diagnosis, effective treatment, and prevention.

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