Meningococcal Meningitis

By Audrey Oh

**Etiologic Agent**

*Neisseria meningitidis*

**Transmission**

*Neisseria meningitidis* is a bacterium that is often found in healthy, asymptomatic individuals [3]. Transmission between humans occurs via respiratory and throat secretions from infected individuals or through droplets in the air [8]. College students living in dormitories and family members of infected individuals are especially at risk of contracting the disease [4].

**Reservoirs**

Humans are the only natural reservoir of *Neisseria meningitidis* [3]. The bacteria tend to take up residence in the mucosal membrane of the posterior nasopharynx [14].

**General Characteristics of Microorganism**

*Neisseria meningitidis*, also called meningococcus, is a Gram-negative diplococcal bacterium. There exist at least 12 distinct serogroups classified by the structure of the antiphagocytic polysaccharide capsule surrounding the outer membrane of the bacteria. Most invasive strains belong to one of five serogroups: A, B, C, Y, and W-135 [8]. They may be further classified by the type of outer membrane proteins, which are designated from class 1 through class 5 [14].

Although normally a commensal organism, carriers may spread the pathogen to those who are not immune to the disease, where they can cross the mucosal membrane and enter the bloodstream to reach other organs. In 50% of these cases, the bacteria may cross the blood-brain barrier and invade the meninges and cerebrospinal fluid surrounding the brain and spinal cord, causing inflammation [8].

The pathogen is the leading cause of bacterial meningitis in children and teens, and the second leading cause of the disease in adults [9]. Like the closely related species *Neisseria gonorrhoeae*, the bacteria are often found within the cytoplasm of neutrophils that are attracted to sites of inflammation. The infection is therefore pyogenic [14].

**Identification**

Cerebrospinal fluid (CSF) is the best specimen for isolating and identifying the etiological agent of a suspected case of meningitis. CSF can be collected through a lumbar puncture and inoculated onto a supplemented chocolate agar plate and a blood agar plate. A blood specimen should be collected if a lumbar puncture cannot be performed [10]. Colonies grown on blood agar are round, convex, smooth, moist, and gray in color. On chocolate agar, the bacteria form colorless or gray opaque colonies [11].
Kovac’s oxidase test determines whether the specimen contains cytochrome oxidase, which can confirm the presence of *Neisseria meningitidis*. A positive result for glucose and maltose oxidation, but not lactose and sucrose, in a carbohydrate utilization test also indicates presence of a bacterial species belonging to genus *Neisseria*. The serogroup may be determined via agglutination reactions with specific antisera [10].

Imaging studies such as a CT scan or an MRI may be necessary to visualize meningeal lesions, cerebral edema, or cerebral ischemia if a patient exhibits an altered state of consciousness or seizure activity [12].

**Historical Information**

Gaspard Vieusseux, a Swiss physician, first identified the disease in 1805 during an outbreak in Geneva. Two pathologists in Italy, Marchiafava and Celli, described the presence of intracellular, oval-shaped micrococci in a sample of CSF in 1884. Anton Weichselbaum first identified the bacterium as the causative agent of meningococcal meningitis in 1887, when he found the pathogen in the CSF of six of his eight patients with the disease [13].

Prior to the 1920’s, the disease had a 70% mortality rate. At the beginning of the century, treatment with serum from immunized horses was introduced in Germany by Jochmann, and in the United States by Flexner [13]. The first case of successful treatment using intravenous and intrathecal administration of penicillin was in 1944 [12].

Historically, serogroup A has been the leading cause of meningococcal meningitis epidemics worldwide, and remains the most prevalent cause of the disease in Africa and Asia. Since the end of World War II, serogroups B and C are the most common causes of the disease in the United States, as well as in Europe [12,13].

**Signs and Symptoms**

The incubation period of meningococcal meningitis is typically 3 to 4 days but may range from 2 to 10 days [10]. Common symptoms include fever, chills, nausea and vomiting, stiff neck, photophobia, and rash [1,4]. A change in mental status may be present, especially in older patients [12]. Approximately one third of patients exhibit neurologic signs such as convulsions or coma [14].

In 40% of infected children, many of the classic signs and symptoms may be absent, and instead manifest in seizures and fever. About 10-20% of children develop Waterhouse-Friderichsen syndrome, which entails large petechial hemorrhages, septic shock, fever, and disseminated intravascular coagulation (DIC) [12]. Hypothermia is also commonly seen in newborns [14].

**Virulence Factors**

The primary endotoxin of *Neisseria meningitidis* is lipooligosaccharide (LOS), which is released when the bacteria undergoes autolysis during growth. The toxin suppresses synthesis of leukotriene B4, a strong chemokinetic and chemotactic factor of human
leukocytes [14]. Another important virulence factor is an immunoglobulin A (IgA) protease, which can cleave the Fab and Fc portions of the IgA antibody commonly found in mucosa [18].

The polysaccharide capsule surrounding the bacteria provides antiphagocytic protection from granulocytes, particularly during initial infection [18]. An important mechanism of virulence is the organism’s ability to exchange genetic material for capsule production, which enables capsular switching between serogroups [13]. Attachment to epithelial cells of the nasopharynx is accomplished by fimbriae [14].

Control/Treatment
Antibiotic treatment should be started immediately after diagnosis, and antimicrobial treatment immediately after lumbar puncture. Initial therapy before the etiologic agent is confirmed should consist of dexamethasone, a third-generation cephalosporin such as ceftriaxone or cefotaxime, vancomycin, acyclovir, and doxycycline. Following diagnosis, ceftriaxone is used as the drug of choice for meningococcal meningitis therapy. Alternatives include penicillin, ampicillin, chloramphenicol, fluoroquinolone, and aztreonam. Dexamethasone may also be used in children [12].

Despite antibiotic treatment, 10-15% of affected individuals die due to meningococcal meningitis. Survivors may experience permanent brain damage, hearing loss, kidney failure, and loss of limbs [4].

Prevention
Currently, two types of vaccines are available that can prevent meningitis caused by Neisseria meningitidis. The meningococcal conjugate vaccine (Menactra, Menveo, MenHibrix) is administered to children aged 9 months to ten years, and recommended as a booster for the ages 11 to 18. Adults can receive either MCV4 or the meningococcal polysaccharide vaccine (Menomune) [5,6]. Both vaccines protect against four types of meningococcal meningitis, caused by serogroups A, C, Y, and W-135. The FDA approved the first U.S. vaccine against serogroup B, Trumenba, in October 2014. The vaccine is given in a 3-part series for people 10 to 25 years of age [16].

For people in high-risk environments for contracting the disease, an antibiotic such as rifampin, ciprofloxacin, or ceftriaxone should be considered as a preventative measure [4]. However, antimicrobial intervention is not effective during the course of an outbreak due to the risk of multiple, prolonged sources of exposure [12].

Local and Global Outbreaks
Meningococcal disease caused by Neisseria meningitidis is distinctive from other types of bacterial meningitis due to its potential to cause large-scale epidemics. The region of sub-Saharan Africa encompassing Ethiopia in the east to Gambia in the west is known as the “Meningitis Belt” due to its high endemic and periodic large epidemic rates, primarily caused by serogroup A and serogroup C to a lesser extent [10].
Between January and May of 2013, there were 9,249 suspected cases of meningitis and 857 deaths, reported from 18 out of 19 African countries under watch for outbreaks. These numbers were the lowest ever recorded for the epidemic season in the last decade, presumably due to continued introduction of a newly developed meningococcal serogroup A conjugate vaccine since 2010, allowing for immunization of over 100 million people in the Meningitis Belt [7].

In March 2014, 121 cases and five deaths were reported in the West Nile Sub-region of Uganda, 26 of the cases in South Sudan refugees. Out of 84 samples, 32 were positive for serogroup W-135 [15].

In the U.S., incidence of meningococcal meningitis has remained relatively stable since 1960, at about 0.9 to 1.5 cases per 100,000 people yearly. However, the number of localized outbreaks has become more frequent since 1991 [12]. Princeton University recently experienced an outbreak of serogroup B meningococcal meningitis, with a total of eight cases and one associated case in a Drexel University student reported from March 2013 to March 2014. A serogroup B vaccine, Bexsero, which has been licensed in Europe, Canada, and Australia, was administered to students since December 2013, allowed for use by the FDA under an Investigational New Drug application [17].

References


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