Meningococcal Meningitis

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Etiologic Agent

The disease meningococcal meningitis, also known as meningococcus, is caused by the bacteria Neisseria meningitidis (1). Disease occurs when the bacteria passes through the blood-brain barrier, and infects the cerebral spinal fluid, CSF, of the meninges in the central nervous system (4).

Transmission

Meningococcal meningitis is spread by droplets from the upper respiratory system during close contact between individuals (2). These droplets come from the bacteria’s portal of entry and exit: the nose and mouth, and may be inhaled or ingested by a person due to coughing or kissing (3) (5). Once the infected droplets have been transmitted, they may penetrate the mucous membranes, entering the bloodstream and possibly the central nervous system causing disease (4).

Reservoirs

There are no other hosts of the disease except humans, and the reservoir is the human nasopharynx (6) (7) (9) (14). It is known that the bacterium attaches to respiratory cells of the mucous membrane in the nasopharynx, but the mechanism by which it enters the central nervous system is unknown (4) (8) (7). It is possible to be a carrier of N. meningitidis, and never develop disease, but it depends on several unknown factors (4) (7).

General characteristics of microorganism

N. meningitidis is an aerobic, Gram-negative diplococcal bacterium which appears to be kidney or coffee bean shaped (4) (9) (10). It has no structures for motility, but is encapsulated. It requires a complex nutrition supply provided by a blood (BAP) or chocolate agar plate (CAP) when cultured, and a specific environment for growth due to its fastidious nature: human body temperature and 5% CO₂ (10). The colonies that form when cultured on a BAP are “round, smooth, moist, convex, and gray”; while the colonies that form on CAP are “large, colorless-to-gray, opaque colonies” (10). There are 12 serogroups based on the various capsular polysaccharides: A, B, C, H, I, K, L, X, Y, Z, 29E, and W135; the most virulent of which are A, B, C, X, Y, and W135 (9) (7) (14).

Key tests for identification

If N. meningitidis is suspected, blood will be drawn, and a lumbar puncture will be performed to grow cultures, perform serum tests, and test the cerebral spinal fluid for presence of the
pathogen (3)(5) (11) (19). It is also possible that a nasopharyngeal swab will be performed to look for the presence of the bacterium in the mucous membrane (7). Cultures may be successfully grown on blood or chocolate agar plates (10). A sample may be used to perform a Gram stain to look for the presence of Gram-negative diplococci characteristic of *N. meningitidis* (10). After culturing, the Kovac’s oxidase test may be performed; if positive, then carbohydrate utilization tests will be completed in cystine trypticase agar (7) (10) (15). *N. meningitidis* will oxidize maltose and glucose, but not lactose or sucrose (7) (10) (15). Once completed, further testing for specific antigens/serogroups is done with slide agglutination tests. Depending on the facility, rapid diagnostic test strips coated in monoclonal antibodies might be available (10) (14). Additionally, polymerase chain reaction, PCR, may be used to identify the presence of *N. meningitidis* (14) (15) (16).

**Signs and symptoms of disease**

Major signs and symptoms are flu-like including fever, headache, vomiting, and stiff neck; confusion or altered mental status, photophobia, and rash are also likely. Signs and symptoms are somewhat different in infants and children including vomiting, irritability or distress, stiffness, lethargy, and decreased appetite (5) (7) (11) (12) (13). The onset of signs and symptoms may be rapid, and may not include all signs and symptoms depending on the location of the infection (blood and/or meninges) (5) (7) (11) (12). The incubation period of the disease is anywhere from 2 to 14 days, but the average is less than a week (9).

**Historical information**

The first likely case of meningococcal disease was documented during the 16th Century, and in 1805 the first outbreak was noted in Switzerland; however, it was almost 100 years later when *N. meningitidis* was discovered in cerebral spinal fluid of infected patients (15) (16). Upon discovery of the etiologic agent, it was almost another 100 years before a vaccine was established and licensed for a single serogroup in the United States (16). Now there are several vaccines covering serogroups A, B, C, W, and Y in the United States (16) (17).

**Virulence Factors**

An important factor that increases *N. meningitidis’* pathogenicity, or virulence, is the presence of a polysaccharide capsule which prevents engulfment by phagocytes (7). The bacterium is also able to produce IgA protease which is an enzyme that breaks down IgA antibodies produced by the body’s immune system. The purpose of these antibodies is to prevent the attachment of infecting microorganisms to mucosal surfaces (18). Furthermore, since *N. meningitidis* is a Gram-negative bacterium, it produces endotoxins which cause many of the symptoms associated with the disease (18). With the ability to avoid phagocytes, destroy specific antibodies, and produce endotoxins, the bacterium has a greater chance of causing disease in the body.

**Control and Treatment**
Since *N. meningitidis* is a bacterium, the best form of treatment is the use of antibiotics. A broad spectrum antibiotic may be used prior to confirmation of the presence of *N. meningitidis*; however, once verified, the use of penicillin is recommended (7) (14) (15) (16) (19). If allergies to penicillin are present, chloramphenicol or a third-generation cephalosporin may be substituted (7) (9). There are some strands with antibiotic resistance, but the occurrence of resistant strands is low in the United States (16). It is possible to use steroids for treatment as well to reduce the swelling caused by disease; however, this method of treatment is not used frequently (5). Furthermore, antibiotics may be given prophylactically in situations where an individual was in close contact with a person known to have the disease (3) (9) (11) (15).

**Prevention and Vaccine information**

The best form of prevention is vaccination; however, handwashing and avoiding those known to be ill are good preventative measures as well (3) (11) (13). Also, as previously described, antibiotics may be given prophylactically to prevent a secondary infection. Currently, there are three types of vaccines available in the US: a polysaccharide vaccine for A, C, W, and Y serogroups, several conjugate vaccines, and a recombinant vaccine for serogroup B (20). The polysaccharide vaccine, MPSV4, covers A, C, W, and Y serogroups, and contains “purified bacterial capsular polysaccharides” (16). One of the conjugate vaccines, MenACWY-D, contains polysaccharides of serotypes A, C, W, and Y conjugated with a diphtheria toxoid protein carrier (16). MenACWY-CRM is another conjugated vaccine that contains capsular polysaccharides of serogroups A, C, W, and Y as well, but in various amounts and in conjugation with CRM197 (16). The most recent conjugate vaccine is Hib-MenCY-TT. This vaccine contains capsular polysaccharides of serogroups C and Y of *N. meningitidis*, and serogroup B of *Haemophilus influenzae* conjugated to tetanus toxoid (16). The recombinant vaccines of serogroup B contain recombinant surface proteins of *N. meningitidis* produced in *Escherichia coli* (21) (22). Another vaccine specifically for serogroup A has been available in Africa since 2005, and has greatly reduced the incidence rate of the disease in the region (30). Different vaccines are recommended in different situations depending on age, location, and risk of being infected. Students living in dorms, those traveling to locations with high rates of occurrence, those without a functioning spleen, and those serving in the military (3) (5) (6) (13).

**New Trials**

As the vaccine Trumenba was recently approved in 2014 by the USFDA, there is a current clinical trial in Oakland evaluating the immunogenicity of the vaccine for *N. meningitidis* serogroup B (23). The trial is currently in phase 4 so its purpose is to ensure there are no adverse side-effects or additional information not noted during phases 1 through 3 (24). There is also another trial in the US evaluating children who received the MenACWY-CRM vaccine between the ages of 2 months and 23 months (25). Another trial that is currently taking place in India is comparing the efficacy of ampicillin to ceftriaxone as a prophylaxis in traumatic brain injury patients involving air in the cranium (26).
Local cases or outbreaks

According to the CDC in 2013, “rates of meningococcal meningitis continued to be at historic lows (0.18 per 100,000 population)” with serogroup B primarily causing disease in infants and serogroups C, Y, or W causing 73% of disease in people older than 11 years of age (27). This incidence rate is down from 0.61 in 2003; the number of deaths is also down from 123 in 2005 to 26 in 2011 (27). There were two outbreaks involving serogroup B at campuses in New Jersey and California resulting in 13 cases and 1 death (27). There were a reported 556 cases in the US in 2013 including all serogroups with the highest number of cases in February and lowest in September; 30 of those cases reported for the year were in Texas (27). The lowest rates were seen in the 15-24-year-old age range, and the highest in those younger than 1 year (27).

Global cases or outbreaks (with incidence figures)

The region known as the “Meningitis Belt” ranging from Gambia in Western Africa to Ethiopia in Eastern Africa is a hyper-endemic region for meningococcal meningitis with frequent epidemics (28). The majority of the cases were caused by serogroup A until formation of the vaccine MenAfriVac, and the rates of disease in this region are the highest in the world “reaching up to 1,000 cases per 100,000 (compared to the 0.3-3 cases per 100,000 in the US, Australia, Europe, and South America)” (14) (28). Nearly all countries in Africa were considered to have high endemic rates reaching up to almost 300 per 100,000; while the US ranked amongst the lowest (post-vaccination) in 2009 with a rate at 0.3 per 100,000 (31). Most recently there was an outbreak in Ghana beginning in late 2015 that has since spread to Togo (29). Since early 2016, 548 cases with 93 deaths have been reported in Ghana and over 800 cases with 70 deaths in Togo (29).

Works Cited


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