

## Emerging Infectious Disease (5): Meningococcal Disease

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### Abstract

Meningococcal disease is a serious, potentially life-threatening bacterial infection caused by *Neisseria meningitides*. The peak incidence of meningococcal disease occurs in the first year of life following the loss of maternal antibodies. Although most common in children, meningococcal disease also affects adults. The disease most commonly is expressed as either meningococcal meningitis, an inflammation of the membranes surrounding the brain and spinal cord or meningococemia, a presence of bacteria in the blood. *Neisseria meningitides* has become the leading cause of bacterial meningitis in older children and young adults in the United States. Meningococcal disease strikes about 3,000 Americans each year and the case-fatality ratio is between 10 and 15 percent. Of patients recovered, 10 to 15 percent have permanent brain damage, mental retardation, hearing loss, learning disability, limb amputation or renal failure. Rapid initiation of effective antimicrobial therapy results in significant decrease in mortality rates. Prevention of meningococcal disease can be made by the use of antibiotics for certain exposed persons and by immunization. A meningococcal polysaccharide vaccine provides protection against *Neisseria meningitides* serogroup A, C, Y and W-135. Meningococcal conjugate vaccines can provide immunization for children young than two years of age. (*Ann Disaster Med.* 2005;3 Suppl 2:S73-S78)

**Key words:** Meningococcal Disease; Meningitis; Meningococemia

### Introduction

Meningococcal disease refers to a variety of clinical signs and symptoms caused by the bacterium *Neisseria meningitides* or commonly referred to as meningococcus. *Neisseria meningitides* can cause both isolated cases and epidemics. The most common types of meningococcal disease are infections of the blood (meningococemia) and infections of the coverings around the brain and spinal cord (meningitis).<sup>1,2,3</sup> It also cause arthritis, vasculitis

and pericarditis.<sup>1,4,5</sup> Rare manifestations include conjunctivitis, episcleritis, endophthalmitis, sinusitis, nephritis, pleuritis, genital infection and pneumonia.<sup>1,4,5,6</sup>

Before 1993, an outbreak was defined as five cases of the same serotype in 100,000 people with at least three occurring within three months. From 1994 to present, 10 cases of the same serotype in 100,000 people with at least three occurring within three months constitute an outbreak. According to the information from

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WHO, the newest episode of an outbreak happened in India. As of 16th May 2005, 303 cases of meningococcal disease have been reported in Delhi with 26 deaths. The majority of cases and all deaths have occurred in young adult population between 16 -30 years of age. The National Institute of Communicable Diseases (NICD) has demonstrated the presence of *Neisseria meningitides* serogroup A in cerebrospinal fluid obtained from 18 cases.<sup>7</sup>

### **Incidence**

Meningococcal disease usually peaks in late winter and early spring. Approximately 500,000 cases of invasive meningococcal disease occur annually worldwide, of which more than 50,000 died.<sup>6,8</sup> Within the United States, the annual incidence is 0.9 to 1.5 cases per 100,000, and 98 percent of cases are sporadic.<sup>6</sup> An estimated 2,200 to 3,000 cases of invasive meningococcal infection occur annually in the United States and had caused about 300 deaths among them.<sup>9</sup> The incidence of meningococemia is highest among children from three to twelve months of age and declines among older age groups.<sup>5,9,19</sup> Although most common in children, meningococcal disease also affects adults.<sup>6,10</sup> Close contacts of persons with meningococcal disease are at highest risk for acquiring the disease.

### **Serogroup**

The type of sugar material forming the outer coat or capsule of an organism determines the serogroup. There are 13 serogroups of *Neisseria meningitides* but only 5 serogroups, including groups A, B, C, Y and W-135, are associated most frequently with serious disease in humans.<sup>9</sup> Serogroups B, C, and Y each account for approximately 30 percent of reported

cases and serogroups A and W-135 were extremely rare.<sup>6,9</sup> Serogroup distribution may vary according to age, geographic location and time<sup>8</sup>. Group A has been associated frequently with epidemic disease elsewhere in the world, primarily in Saharan Africa and Asia but rare in the United States.<sup>9</sup>

### **Pathogen**

*Neisseria meningitides* has a characteristic coffee bean shape under a regular light microscope. The cytoplasm of the meningococcus is surrounded by a cell envelope consisting of three layers: an inner layer called the cell membrane, a middle layer composed of peptidoglycans, and an outer layer called the cell wall. The cell wall is made up of sugar-like molecules and outer membrane proteins, giving the bacterium its shape. Meningococci also have a polysaccharide capsule, which is attached to the outer cell wall and protects it from ingestion and killing by certain white blood cells<sup>5</sup>. The meningococcal cytoplasm contains water, salts, deoxyribose nucleic acid, ribose nucleic acid, various structures, proteins, enzymes and other substances necessary for life.

### **Pathophysiology**

When a person is exposed to meningococcus from an infected person's secretions, through coughing, sneezing or close contact, the meningococcal organisms adhere to the cells lining the upper respiratory tract, including the throat and nose. Oral contact with shared items such as cigarettes or through intimate contact such as kissing could put a person at risk for acquiring the infection.<sup>6,11</sup> The body's defense mechanisms usually are able to keep the organisms from spreading to other parts of the body. This

localization results in colonization of the nose and throat and is referred to as the carrier state.<sup>5,11</sup> Colonization by meningococci may persist for several weeks to months. Meningococci do not survive well outside their human host and have no alternate host because the lining of a person's nose and throat is the only natural reservoir of *Neisseria meningitides*.

The more serious event that may occur following exposure to meningococci is systemic disease. In most instances, the body is able to localize the meningococcal organisms. But occasionally, organisms spread from the throat to other parts of the body and result in disease.<sup>5,11</sup> When meningococci pass through the lining of the nose or throat and into the bloodstream (meningococcemia), organisms may spread to the coverings of the brain and spinal cord (meningitis) and less frequently to other parts of the body. During the early phase of colonization, persons are at greatest risk of developing disease when the body's immune system has not produced specific antibodies against the colonizing meningococcal strain. It is at this time that the organisms can spread to the blood and brain.

Endotoxin, the lipopolysaccharide component of the Gram-negative outer membrane, is critical in the pathogenesis of systemic meningococcal infections.<sup>5,9</sup> It can initiate a cascade, including activation of complement, release of cytokines and anaphylotoxins, leading to endothelial cell injury, capillary leak, loss of vasomotor tone, myocardial depression and circulatory collapse. Renal failure, pulmonary edema, gastrointestinal ischemia and brain impairment may be developed.<sup>11</sup> Initial plasma endotoxin levels correspond with morbidity and mortality.<sup>10,11,12,13</sup>

## Symptoms and Signs

*Neisseria meningitides* usually cause meningococcemia, meningitis, or both. Meningitis alone is presented in about half of patients with meningococcal disease, septicemia alone is presented in about 10 percent, and 40 percent have a mixed picture.<sup>2,4,6</sup> The disease can easily be misdiagnosed as something less serious, because symptoms are similar to the flu.<sup>2</sup> Meningococcemia is characterized by acute fever, headache, chills, malaise, low back, abdominal and thigh pain, generalized muscle aches, and a rash that occurs in about 75 percent of patients.<sup>2,6,10</sup> Meningococcal meningitis may induce fever, headache, neck stiffness, confusion, nausea, vomiting, lethargy, a petechial rash over 50 percent of cases and seizure at presentation in up to 20 percent of cases and is usually difficult to distinguish from meningitis caused by other bacteria.<sup>2,6</sup> Every child with fever and petechiae should be assumed to have meningococcal disease until proven otherwise. If not treated, the disease can progress rapidly and can lead to shock and death within hours of the onset.<sup>2,5,9</sup> The sequelae occur in 10 to 15 percent of cases and include brain damage, mental retardation, hearing loss, learning disability, limb amputation or kidney failure.<sup>8,9</sup>

## Risk Group

Meningococcal disease can affect people at any age. Persons who have certain medical conditions are at an increased risk for acquiring meningococcal infections. The disease is more common among persons with defects in certain parts of their immune system,<sup>5,11</sup> persons receiving immunosuppressive drugs, persons with autoimmune diseases, those in close contact with

a known case, persons traveling to endemic areas of the world, college freshmen who live in dormitories, the military recruits, microbiologists who work with isolates of *Neisseria meningitides* and people exposed to active and passive tobacco smoke.<sup>6</sup>

### Diagnosis

Cultures of blood and cerebral spinal fluid should be obtained in all patients with suspected invasive meningococcal disease. Confirmed diagnosis can be made when isolation of *Neisseria meningitides* from a usually sterile site including blood, cerebral spinal fluid, synovial joint fluid, pleural fluid, pericardial fluid and petechial or purpuric lesion (skin rash).<sup>6</sup> Detection of *Neisseria meningitides* from nose or throat is not helpful in making decisions about treatment because *Neisseria meningitides* can colonize there without causing disease.<sup>5,11</sup>

### Management

It is important to start treatment early in the course of the meningococcal disease. Aggressive early treatment can reduce mortality.<sup>2</sup> Laboratory results are not usually available rapidly enough to help in the initial clinical diagnosis. Even if available, laboratory results may not be helpful in distinguishing meningococcal disease from viral disease, particularly as in early infection. It is necessary to provide immediate management in suspected cases because profound clinical deterioration within hours may occur.<sup>2,10</sup> Antibiotics are the most important therapy for meningococcal infections and have resulted in a significant decrease in mortality rates among patients with invasive meningococcal disease.<sup>2,6</sup> Bacterial meningitis can be treated with a number of effective antibiotics and high-

dose penicillin is the drug of choice used to treat persons with invasive meningococcal infections. However, penicillin-resistant strains have been reported. Current first-line antibiotics therapy is cefotaxime or ceftriaxone.<sup>6,10</sup> Rapid initiation of antimicrobial therapy, early and aggressive fluid resuscitation and supportive intensive care including management of blood electrolytes and oxygenation, steroids replacement for documented adrenal insufficiency and careful glyce-mic control are the mainstays of treatment of meningococcal sepsis.<sup>2,10,11,12</sup> High-dose steroids may be useful in patients with meningitis without evidence of shock.<sup>2,6</sup> Despite aggressive antimicrobial therapy and intensive unit care, mortality rate of meningococcal sepsis continue to be high.<sup>3,6,12,16</sup>

### Prevention

Prevention of meningococcal disease relies upon two strategies. One is the use of antibiotics for certain exposed persons (chemoprophylaxis or antibiotic prophylaxis) and the other is prevention of disease by immunization (immunoprophylaxis).<sup>10</sup>

#### **Antibiotics (chemoprophylaxis)**

Chemoprophylaxis of close contacts of sporadic cases of meningococcal disease is the primary method to prevent meningococcal disease.<sup>6,10</sup> They should receive antibiotics with a fluoroquinolone such as ciprofloxacin or levofloxacin, rifampin or ceftriaxone.<sup>6</sup> Close contacts include (a) household members, (b) child care center or nursery school contacts and (c) anyone directly exposed to a patient's oral secretions through kissing, sharing toothbrushes, unprotected contact during endotracheal intubation or mouth-to-mouth resuscitation. Appro-

priate precaution such as masks, gloves and gowns should be used by all involved health care workers.<sup>10</sup>

Since the majority of the episodes of secondary disease in close contacts is highest during the first few days after exposure and generally occurs within the first 14 days following exposure, chemoprophylaxis should be given to close contacts as soon as possible after the case is identified.

### ***Immunization (immunoprophylaxis)***

Immunization is the most effective way to reduce the incidence of death as a result of meningococcal infection and permanent sequelae of the disease.<sup>9</sup> Two meningococcal vaccines are available in the United States: meningococcal polysaccharide vaccine (MPSV4) that has been available since the 1970s and meningococcal conjugate vaccine (MCV4) that was licensed in 2005.<sup>14</sup> Meningococcal quadrivalent polysaccharide vaccine consists of four different meningococcal capsular sugars and provides protection against four of the most common strains of *Neisseria meningitides* including serogroup A, C, Y and W-135. A vaccine is not available to prevent disease from serogroup B.<sup>2,5,6,11</sup> About two to three weeks after receiving the meningococcal polysaccharide vaccine, the recipient develops antibodies to many or all of the four meningococcal serogroups in the vaccine. Unfortunately this vaccine cannot be used in children under two years of age because this age group does not respond to polysaccharide vaccines.<sup>9,15</sup> Meningococcal conjugate vaccines link the capsular sugars to a protein carrier and make it possible to immunize infants beginning at two months of age because the protein-sugar complex is a more potent stimu-

lus to the child's immune system.<sup>9</sup> Studies are underway to evaluate the ability to combine this vaccine with other vaccines to decrease the number of injections that children receive.

The serogroup A and C components of the polysaccharide vaccine are 85 to 100 percent effective in older children and adults.<sup>6</sup> The polysaccharide vaccine is safe and the adverse reactions to vaccine are mild and consist primarily of pain and redness at the site of injection for one to two days.<sup>9</sup> A short-lasting fever has been reported to develop in less than two percent of young children.

All military recruits routinely have received the A, C, Y, W-135 meningococcal polysaccharide vaccine since 1982<sup>9</sup>. This has resulted in a dramatic decrease in the previous high rate of meningococcal disease in this population. Routine meningococcal immunization of people not in the military service is not recommended because of its relative ineffectiveness in children less than two years of age and its short duration of protection.<sup>9,15</sup> In general, routine use of the meningococcal polysaccharide vaccine is recommended for persons who are in high-risk groups including: persons who have terminal complement deficiencies, any person who had spleen removed or who has a spleen that doesn't function properly, travelers to endemic countries, research and clinical laboratory personnel routinely exposed to *Neisseria meningitides* and control of serogroup C meningococcal disease outbreaks.<sup>6,9</sup>

As of October 20, 1999, the Advisory Committee on Immunization Practices (ACIP) of the United States Centers for Disease Control and Prevention (CDC) recommends that individuals who provide medical care to college freshmen, particularly those who live in or

plan to live in dormitories or residence halls, should provide information about meningococcal disease and the benefits of vaccination to these students and their parents. ACIP further recommends that immunization should be provided or made easily available to those who wish to reduce their risk for meningococcal disease.<sup>9</sup>

Some researches are ongoing to develop a meningococcal vaccine that is effective in preventing disease due to serogroup B.<sup>2,8</sup>

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