Meningitis, an inflammation of the membrane layers covering the brain and spinal cord, often presents with a symptomatic triad of high fever, headache, and stiff neck in adults and children aged 2 years and older. Classic triad symptoms of meningitis onset can occur within hours or over several days. Fewer than 50% of patients have all three classic symptoms at presentation, but most patients present with at least one of these symptoms.\textsuperscript{1} Additional, less common symptoms include photophobia, confusion, sleepiness, nausea and vomiting.

Infants younger than age 2 years who have meningitis are usually lethargic and exhibit vomiting, irritability or lack an interest in feeding.\textsuperscript{2} Seizures and death may result at any age, particularly when meningitis is undiagnosed and patients are not promptly treated. Fatalities are most common with meningitis of bacterial etiology. Because of the potential for seizures and death, early diagnosis of bacterial meningitis is crucial, as is vaccination to prevent the disease.\textsuperscript{3}

**Pathophysiologic factors**

Meningococcal meningitis is caused by *Neisseria meningitidis*, a gram-negative, diplococcal bacterium commonly referred to as meningococcus.\textsuperscript{3,4} This microbe is part of the normal flora in the nose and throat for about 5%-10% of the population, primarily young adults and adolescents in the United States.\textsuperscript{5} While this bacteria is normal in the nose and throat, microtrauma or infections can expose the meningococcal bacteria under mucous membranes and below the dermal layer. This exposure permits meningococcus to grow in cerebral spinal fluid, blood, and meninges around the brain, developing meningitis.

Meningococcus serogroups (i.e., subtypes) are classified according to the types of polysaccharides in the capsule, the outer part of the bacterium that elicits the immune response during infection.\textsuperscript{3,4} Six meningococcus serogroups are responsible for almost all cases of meningococcal meningitis in humans—serogroups A, B, C, W-135, X, and Y.\textsuperscript{3,4} Immunity obtained from vaccination is based on exposure to a specific serogroup polysaccharide. Thus, a vaccine for one serogroup will confer immunity only for that specific type of meningococcus.

Currently available commercial vaccines provide exposure and adaptive immunity to meningococcus serogroups A, C, W-135, and Y. Serogroup X is rarely a concern in terms of aggressive meningococcal meningitis. However, aggressive meningococcal meningitis infections are associated with serogroup B, for which a commercial vaccine is not available in the United States.\textsuperscript{4}

**Demographic factors**

Meningococcal meningitis affects approximately one out of every 100,000 people in the United States, accounting for 1,200-2,800 cases of meningitis each year with the highest rates of disease in children less than 2 years old.\textsuperscript{3} The incidence of meningococcal meningitis peaks during December and January. Serogroups B, C, and Y are responsible for the majority of meningococcal meningitis cases in the United States—each accounting for about 30% of cases; serogroups B and C occur in sporadic
Adults at high risk should
- CDC recommends routine use
- Indicated in individuals age 2-55.

In children, antibodies decrease
- Adults and adolescents at high risk should be revaccinated in three-to-five year intervals.
- In children, antibodies decrease considerably two-to-three years after vaccination.

**MPSV4—Meningococcal Polysaccharide Vaccine, Tetravalent**
- Indicated in individuals older than age 2 years—especially for travelers to countries having highly endemic or epidemic diseases, for residents of confined communities, and for individuals at high risk of acquiring meningococcal infection.
- CDC recommends routine use in adults at high risk after age 55 years.
- Adults and adolescents at high risk should be revaccinated in three-to-five year intervals.
- In children, antibodies decrease considerably two-to-three years after vaccination.

**MCV4—Meningococcal Polysaccharide Diphtheria Toxoid Conjugate Vaccine, Tetravalent**
- Indicated in individuals age 2-55.
- CDC recommends routine use in individuals age 11-18.
- Children at high risk should be revaccinated three years after first vaccination, then once every five years.
- Adults at high risk should be revaccinated once every five years.

**Figure. Indications and Centers for Disease Control and Prevention (CDC) recommendations for use of Menomune (Sanofi Pasteur Inc, Swiftwater, Pennsylvania), known by the acronym MPSV4 (meningococcal polysaccharide vaccine, tetravalent), Menactra (Sanofi Pasteur Inc, Swiftwater, Pennsylvania), known by the acronym MCV4 (meningococcal polysaccharide diphtheria toxoid conjugate vaccine, tetravalent).**

### Case scenario

A 19-year-old man has a throbbing headache and high temperature, and he feels fatigued. Earlier in the day, he felt nauseous and had only a slight headache, which he attributed to stress and over-studying for finals at the end of his first semester of college.

Now, the student is unable to nod his head, and he experiences intense pain when tightly closing his eyes. His headache continues to worsen, even after he takes several ibuprofen tablets. His dormitory roommate becomes concerned and takes his temperature, which registers 103.8°F (39.9°C).

The roommate phones the residence hall assistant (RA) for the dorm and describes the symptoms. The RA is a fourth-year pre-medical senior student who learned to recognize dormitory-related medical conditions during his RA training. The RA quickly dials 911 to report a possible meningitis outbreak in the dorm. Within several minutes, the febrile student is in the back of an ambulance headed for the regional emergency department—and he is feeling deep regret for not completing his vaccinations before beginning college.

### Vaccination

Unfortunately, events similar to the preceding case scenario are common in colleges, universities and other public places where there is frequent, close interpersonal contact. Every year, thousands of Americans are diagnosed as having meningitis, mostly from viral or bacterial infections. Although viral meningitis is typically limited in severity, bacterial meningitis is usually severe, causing permanent hearing loss, cognitive disabilities, or brain damage. In most cases, viral and bacterial meningitis are diagnosed with laboratory findings from a lumbar puncture.

Bacterial meningitis is often contagious, spreading from close, prolonged interpersonal contact. Most cases of transmitted bacterial meningitis have pneumococcal or meningococcal origins. Pneumococcal vaccines are available and generally recommended for all children under two and adults over 64. Meningococcal vaccines are also available, and were first introduced in the early 1980s. Since 2005, advances in meningococcal vaccines have expanded immune coverage for children and adults.

**MPSV4—A good first vaccine**

In 1981, the first multivalent vaccine for meningococcal meningitis was licensed in the United States under the trade name Menomune (Sanofi Pasteur Inc, Swiftwater, Pennsylvania). Known by the acronym MPSV4 (meningococcal polysaccharide vaccine, tetravalent), Menomune contains polysaccharide antigens from meningococcus serogroups A, C, W-135, and Y—yielding protection against four of the six infectious serogroups, including two of the three most common serogroups in the United States. Menomune is administered as a subcutaneous injection in a single dose.

Possible adverse reactions to MPSV4 include tenderness and erythema at the...
injection site, a brief fever (5% of patients), and allergic and neurologic reactions (less than 0.0001% of patients). The vaccine produces adequate short-term immunity, for three to five years, in approximately 85% of adults and adolescents. In children, however, antibodies decrease considerably two to three years after vaccination. Individuals at high risk for meningococcal meningitis should be revaccinated in three- to five-year intervals.

Menomune is indicated for active immunization in adults and children older than age two (See Figure 1). Vaccination should especially be considered for travelers to countries recognized as having highly endemic or epidemic diseases, for residents of confined communities, and for individuals at high risk of acquiring meningococcal infection.

The federal US Centers for Disease Control and Prevention (CDC) recommends routine use of MPSV4 for adults who are at increased risk for meningococcal meningitis after age 55. Using MPSV4 is a contraindication for using the vaccine known as MCV4—described in the next section—particularly in patients with a history of Guillain-Barré, syndrome.

**MCV4—A vaccine upgrade**

In January 2005, a modified version of MPSV4 was released under the trade name Menactra (Sanofi Pasteur Inc, Swiftwater, Pennsylvania). Known by the acronym MCV4 (meningococcal polysaccharide diphtheria toxoid conjugate vaccine, tetravalent), Menactra produces an increased length of immunity, compared to MPSV4, as a result of its conjugation with diphtheria toxin. The diphtheria toxin itself elicits a strong cell-mediated immune response. Therefore, conjugating polysaccharides with the toxin boosts the scope of stimulation and resultant immunity, particularly in adults and adolescents.

Like MPSV4, MCV4 provides protection against meningococcus serogroups A, C, W-135, and Y; unlike MPSV4, MCV4 is administered as an intramuscular injection in a single dose. Possible adverse reactions to MCV4 are similar to those of MPSV4. However, MCV4 also carries an increased risk for development of Guillain-Barré syndrome because of the presence of the diphtheria toxin and cell-mediated immune stimulation.

Menactra is indicated for active immunization in individuals aged 2 through 55 (See Figure 1). The CDC’s Advisory Committee on Immunization Practices recommends routine vaccination with MCV4 for all people between ages 11 and 18. A preadolescent pediatric clinical visit, at age 11 or 12, is the ideal point of initial immunization. Alternatively, vaccination at the earliest possible time between the ages of 13 and 18 is recommended.

Individuals at increased risk of meningococcal exposure are college students living in dormitories, military personnel living in barracks, microbiologists working with meningococcus, frequent travelers to areas with endemic meningococcal disease, and those with immune system compromise. Adults at high risk for meningococcal meningitis should receive MCV4 revaccination every five years. Children at high risk should be revaccinated three years after their first vaccination and, thereafter, once every five years.

**Further considerations**

Although effective vaccine coverage exists for several meningococcus serogroups, no vaccine is presently available in the United States for serogroup B. This serogroup is one of the three leading infectious types of meningococcus in the United States—and the most fatal type in infants.

A meningococcus serogroup B vaccine was developed at the Finlay Institute in Cuba during the 1980s, after a meningococcal B meningitis epidemic swept the country. While efficacious in Cuba, this vaccine was not made available in the United States. But as
meningococcal B meningitis in United States became a more prevalent cause of death in infants, a solution was necessary.

In 1999, the United States Treasury Department granted one pharmaceutical company a license to develop the meningococcal B vaccine in the United States. This encouragement for the new vaccine has encouraged other pharmaceutical companies to pursue developing meningococcal B vaccines as well. One pharmaceutical company has shown promising Phase II clinical trials developing meningococcal B (MenB) vaccine for infants since May 2008, with a tentative plan to bring the vaccine to the global market by 2011.

Meningococcal vaccination has undergone continuous development since the introduction of the first meningococcal vaccine in the early 1980s. The 2005 release of conjugate vaccine substantially increased patients’ immune stimulation to four important meningococcal serogroups, and the meningitis B vaccine in development will prevent meningococcal disease in the future. It is clear the meningococcal vaccines are important to prevent potentially life threatening infections and the related complications of meningitis.

The recommended subpopulations for the Menactra vaccine include children over 2 years old at increased risk of meningitis; adolescents before or during high school; and military personnel. The Menomune vaccine is recommended for adults over age 55 who are at increased risk for meningitis, and for adults over age 70 regardless of risk. These suggestions follow current trends in the literature recommendations to yield the best vaccination coverage for each age group in preventing meningococcal disease and protecting patient health.

References


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