Meningococcal disease: A brief primer

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The Organism

Humans are the only natural reservoirs for *Neisseria meningitidis*, a gram-negative diplococcus. The bacteria colonize the nasopharynx without causing disease (carriage) in about 10% of the population at any given time (higher in crowded environments). Invasive infection can cause death or permanent disability with a sudden onset of nonspecific symptoms and rapid progression.[1,2]

Meningococcus is classified into 13 serogroups based on its polysaccharide capsule of which five are the primary pathogens seen in human disease (A, B, C, Y, and W135).[2] This outer membrane capsule, which protects the bacteria from the human immune system, consists of multiple antigens (polysaccharides and proteins). Effective vaccines that contain purified capsular polysaccharide(s) were initially developed against serogroups A and C, and later against Y and W-135.[3] The capsule of serogroup B has a unique structure that is poorly immunogenic containing proteins similar to human neuronal tissue. As a result, a vaccine targeting a B polysaccharide could potentially lead to an autoimmune response. Other capsular proteins, such as outer membrane vesicles (OMV), have been studied.[1] The recently licensed serogroup B vaccines target the proteins contained in the capsule, specifically factor H-binding protein (fHBP), *Neisseria* adhesin A (NadA), and neisserial heparin binding antigen (NHBA).[4]

The Disease

Meningococcal disease is a serious bacterial illness transmitted through direct exchange of large respiratory droplets and throat secretions of a carrier or person infected with *Neisseria meningitidis*. Once exposed, the bacteria attach and colonize on the mucosal epithelium of the nasopharynx.[4,5] Most human hosts simply remain carriers, whereas in others, *N. meningitidis* penetrates the mucosal epithelium, migrates to the blood stream, and overcomes the host's immune system using an array of virulence factors.[1,5,6]

Invasive meningococcal disease (IMD) has a wide range of clinical manifestations; meningitis, bacteremia, and sepsis (meningococcemia) are the most common and severe. Meningitis, which often presents with fever, stiff neck, and headache, occurs in 50% of cases.[2] In just hours, meningococcemia can progress from a sudden onset of fever and a rapidly progressive purpuric rash to hypotension, gangrene, multiorgan failure, shock, and death. This classic, nonblanching rash, a key clinical feature of IMD, will not develop in all patients. Most present with nonspecific symptoms that can range from fever to irritability.

Despite appropriate antibiotic therapy, mortality rates range from 10% to 40%. Of those who survive, 20% will have life-long sequelae such as hearing loss, amputation due to gangrene, or neurologic damage. Less severe meningococcal disease manifestations include pneumonia, septic arthritis, and otitis media.[5,7]

The Risk

Risk of infection increases when persons are in close or lengthy contact with *N. meningitidis* carriers. Individuals at high risk of contracting the disease include infants, adolescents, and young adults, people living or gathering together in close quarters (college students or military trainees), people with certain medical conditions (asplenia and complement component deficiency), smokers, and travelers to endemic areas of the world.[1,3]

Epidemiology

Meningococcal disease occurs around the world. Most cases are sporadic; however, outbreaks appear to occur in a pattern, favoring late winter and early spring, although it can occur year round. In the absence of widespread vaccination programs, meningococcal disease is cyclic in nature with occurrences peaking approximately every 7–10 years.[5,7]

Rates of disease due to all serogroups have been declining since the 1990s with 564 cases reported in the United States in 2013, down from approximately 2,800 cases in 1997. While vaccination against A-C-Y-W135 has contributed to this decline, the incidence of serogroup B has also declined spontaneously.[8] The incidence and distribution among the serogroups can vary greatly. The most common serogroups in the United States are B, C, and Y. Serogroup A is the most commonly seen type in Sub-Saharan Africa, "the meningitis belt," although C, W-135, and X are reported. Serogroups B and C dominate in Europe, and serogroups A and C are most common in Asia.[5]

Serogroup B accounts for 50% of meningococcal diseases in infants, while serogroups C, Y, and W-135 are more common in adolescents and adults.[3] Serogroup B has been

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responsible for recent outbreaks occurring at three U.S. universities. These outbreaks and the public health response was reviewed in a recent *JAPhA* Vaccine Update.[9] A meningococcal serogroup B vaccine was used through an Investigational New Drug (IND) application granted by the Food and Drug Administration (FDA).[9]

Prevention

Strict isolation and contact precaution must be observed when near a patient with active meningococcal disease. Anyone who is to come within 6 to 10 feet of the patient should wear a face mask at all times.[10] Chemoprophylaxis is recommended for individuals in close contact (duration ≥8 hours in close proximity of less than 3 feet). This would include: household members, roommates, college students living in dormitories, individuals at a child-day-care facility and individuals that have come in intimate contact of a suspected infected patient. Recommended antimicrobials are rifampin, ciprofloxacin, and ceftriaxone.[11]

Vaccination is the most effective method of prevention. Table 1 lists the vaccines available in the United States and the recommendations for their use offered by the Advisory Committee on Immunization Practices.

One quadrivalent polysaccharide vaccine (Menomune—Sanofi-Pasteur) and two quadrivalent conjugated meningococcal vaccines (Menactra—Sanofi-Pasteur; Menveo—Novartis), are indicated for prevention of infection caused by serogroups A, C, Y, and W-135. Additionally, one combination vaccine, Hib-MenCY (MenHibrix—GlaxoSmithKline), was approved for use in young children.[3]

FDA recently approved the use of two vaccines, Trumenba and Bexsero, for prevention of serogroup B meningococcal disease. Trumenba induces complement-mediated antibody-dependent killing by mimicking the antigenic properties of two fHBP proteins that allow the bacteria to avoid an immune response from the human host.[12] Bexsero protects through the production of antibodies against the surface proteins fHBP, NHBA, NadA, and PorA P1.4.[13] Both vaccines are inactivated and were fast-tracked for approval by the FDA based upon antibody response studies. Postlicensure evaluation will continue.

Treatment

Early recognition, rapid diagnostic evaluation, and antimicrobial treatment without delay are essential to decrease the morbidity and mortality of meningococcal disease. Empiric antibiotic therapy is initially started followed by antibiotics that are selected based upon culture and sensitivity testing.[14]

Conclusion

Pharmacists are involved in the provision of information, as well as medication, for many serious infectious diseases. As new guidelines, vaccines and treatments become available, pharmacists will continue to be an important part of the public health team in education, prevention, and treatment.

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Table 1. Meningococcal vaccines available in the United States and recommended schedules

Vaccines (manufacturer)/ antigens	Doses	ACIP recommendations[a]	FDA-approved indications
Menomune (Sanofi-Pasteur) ACYW135 (MPSV4)	0.5 mL SC	Not routinely recommended. Preferred in vaccine-naive individuals ≥ 56 years old.	Individuals 2 years and older.
Menactra (Sanofi-Pasteur) (MenACWY-D)	0.5 mL IM	Two doses for individuals 11–18 years of age: the first dose at 11 or 12 years of age, with a booster at age 16. If the first dose is given after the 16th birthday, a booster is not needed.	Individuals 9 months through 55 years of age.
Menveo (Novartis) (MenACWY-CRM)	0.5 mL IM	Same as Menactra	Individuals 2 months through 55 years of age
Menhibrix (GlaxoSmithKline) (HibMenCY)	0.5 mL IM	Not routinely recommended. For use when Hib vaccinations is also indicated.	Infants ≥6 weeks to 18 months of age: four-dose series at 2, 4, 6 and 12–15 months of age.
Bexsero (Novartis) (MenB)	0.5 mL IM	High-risk patients including those with complement deficiencies, persons taking eculizumab, asplenic patients, microbiologist and outbreaks	Individuals 10–25 years of age given as a two-dose series separated by at least 1 month.
Trumenba (Pfizer) (MenB)	0.5 mL IM	Same as Bexsero	Individuals 10–25 years of age administered in a three-dose series at 0, 2, and 6 months.

Abbreviations used: ACIP, Advisory Committee on Immunization Practices; FDA, Food and Drug Administration; IM, intramuscular; SC, subcutaneous.
[a] See ACIP schedules (http://www.cdc.gov/vaccines/schedules/index.html) for more details.