

Meningococcal Vaccination:

An Update on Meningococcal Vaccine Recommendations for the Primary Care Physician

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Abstract

Neisseria meningitidis is an aerobic, gram-negative, diplococcus bacterium that is a leading cause of meningitis and sepsis in the United States. Particularly at-risk groups include those with complement deficiencies, people using complement inhibitors, individuals with anatomic or functional asplenia, patients with HIV infection and travelers to endemic countries. There are currently three quadrivalent meningococcal vaccines (Serogroups A, C, W, Y) and two recombinant serogroup B vaccines available for use in the United States, and recommendations for vaccine use have changed rapidly in the past 10-15 years. This article summarizes updated ACIP recommendations for meningococcal vaccination for the primary care provider.

Introduction

Neisseria meningitidis is an aerobic, gram-negative, diplococcus bacterium with a polysaccharide capsule that is a leading cause of meningitis and sepsis in the United States (figure 1). There are twelve unique polysaccharide capsules that have been discovered that define specific serogroups of the bacteria. There are six serogroups—A, B, C, W, X and Y—that cause the vast majority of invasive meningococcal disease around the world.² The capsule of the bacterium allows *N. meningitidis* to evade typical immune responses such as phagocytosis and complement-mediated destruction.

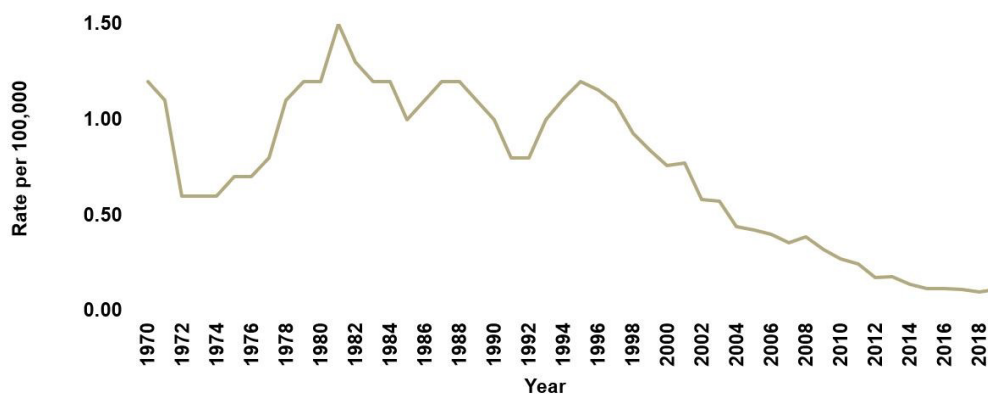
Figure 1: *N. meningitidis* colonies on a chocolate agar plate¹



In the United States, meningitis is the most common clinical presentation of invasive meningococcal disease, occurring in about 50% of cases; other presentations include bacteremia

and pneumonia.² Invasive meningococcal disease carries a high mortality (10-15%) and morbidity (20%) rate despite appropriate treatment.² Common co-morbidities include hearing loss, vision loss, neurologic deficits and amputation. The incidence of meningococcal disease peaked in the late 1990s in the United States and has been declining since (figure 2). In 2019, the total incidence of meningococcal disease cases in the United States was 0.11 per 100,000 persons⁴ (a total of 375 cases). Ninety-nine of these cases (26.4%) were caused by serogroup B infection, while C was the second-most common serogroup with 85 cases (22.7%). Among the 41 cases in the 18-24 year old age group, about half (51.2%) were attending college at the time. Serogroup B infection caused 12 out of the 21 cases identified among college attendees. Amongst cases of serogroup B in college attendees, 56.3% had received one or more doses of MenB vaccine.⁴

Figure 2. Meningococcal Disease Incidence, United States, 1970-2019³



There are several important risk factors that increase the risk of meningococcal infection. General risk factors include smoking, a preceding viral infection, and crowded living conditions (including dorm rooms, military members). Particularly at risk groups include those with complement deficiencies (as complement-mediated destruction is an important defense mechanism against invasive disease), people using complement inhibitors (such as eculizumab), individuals with anatomic or functional asplenia, patients with HIV infection and travelers to endemic countries.⁵

Types of Vaccinations

There are currently three quadrivalent meningococcal vaccines (Serogroups A, C, W, Y) and two recombinant serogroup B vaccines available for use in the United States.²

MenACWY-D (Menactra, Sanofi Pasteur, licensed in 2005) is a polysaccharide diphtheria toxoid conjugate vaccine for use in nine months to 55 years of age. MenACWY-CRM (Menveo, GlaxoSmithKline, 2010) is an oligosaccharide diphtheria CRM197 conjugate vaccine approved for ages two months to 55 years old. Lastly, MenACWY-TT (MenQuadfi, Sanofi Pasteur, 2020) is a polysaccharide tetanus toxoid conjugate approved for use in any patient two years or older.⁵

MenB-FHbp (Trumenba, Pfizer, 2014) and MenB-4C (Bexsero, GlaxoSmithKline, 2015) are the two meningitis B vaccines available in the United States. Both vaccines are approved for use in 10-25 year old patients.⁵ Notably, due to low incidence of meningococcal disease in the U.S.,

vaccine licensing approval has been based off demonstration of laboratory immune response to vaccine and not on randomized trials assessing clinical efficacy.

MenACWY Vaccination Recommendations

The Advisory Committee on Immunization Practices (ACIP) acts as an advisory committee for the Centers for Disease Control and Prevention in providing immunization recommendations.⁵

Routine Vaccination

Routine vaccination with any MenACWY vaccine is recommended for all adolescents 11-12 years old with a booster dose given at 16 years old if the first dose was received before their 16th birthday. Booster doses were recommended due to laboratory evidence of waning immunity in older adolescents. Routine vaccination is only recommended for adolescents 11-18 years old, but MenACWY may be given to patients 19 to 21 years old who have not yet received a dose after their 16th birthday. Minimum interval between doses is eight weeks.⁵

Special Circumstances

Vaccination for individuals two months old or greater is recommended for those at increased risk of meningococcal disease. These include persons with anatomic or functional asplenia, patients with complement deficiencies or use of complement inhibitors, or people with HIV. Additional reasons for early vaccination include those exposed to an outbreaks of meningococcal disease or travel to an endemic country. Notably, only MenACWY-CRM (Menveo) is approved for use in the two to less than nine months age group.

For those with complement deficiencies, use of a complement inhibitor, asplenia (including sickle cell disease), or HIV infection, primary vaccination should start with MenACWY-CRM (Menveo) at two months of age with four doses at 2, 4, 6 and 12 months. Dosing schedule varies if initial vaccination occurs at three or more months of age. For those who complete a primary series in this age group, a booster is recommended as a single dose for those less than seven years old three years after primary vaccination and every five years afterward. If vaccination starts at nine months or later, then MenACWY-D (Menactra) can be used. Menactra can be used as a 2-dose series starting at nine months for those with complement deficiency; however, for those with anatomic or functional asplenia or HIV infection, Menactra is not recommended from 9-23 months of age, but may be used at age 24 months or older as a 2-dose series at least eight weeks apart. Notably, Menactra must be administered at least four weeks after completion of PCV13 series.⁵ Various catch up schedules and primary vaccination schedules for this population are available from the CDC.⁵

Serogroup B meningococcal Vaccine Recommendations

Routine Vaccination

Both MenB vaccines MenB-FHbp (Trumenba) and MenB-4C (Bexsero) are licensed for use in patients ≥ 10 years of age. Trumenba is a 2-dose series (0 and 6 months), although a 3-dose series (0, 1-2 and 6 months) is recommended for those at increased risk of meningococcal disease. Bexsero is a 2-dose series at least one month apart. The same vaccine type should be used for a patient's entire vaccine series.

MenB series is recommended as a primary vaccination for those 16-23 years old on the basis of shared decision making. While no definitive recommendation exists for administration for college freshman or military recruits, it is important to note that serogroup B infections, while rare, are currently the most common individual serogroup for invasive meningococcal disease in college attendees.⁴ A 2019 study published in the journal *Pediatrics* examined the incidence and relative risk of meningococcal disease in college-aged young adults (18 to 24 years old) from 2014-2016. In that time period, 166 cases of disease occurred with an annual incidence of 0.17 cases per 100,000 population. The relative risk of serogroup B disease in college versus non-college students was 3.54 (95% CI: 2.21-5.41) driven by six MenB disease outbreaks on college campuses during that time. The authors conclude that incidence of disease is low, but college students do have an increased risk for MenB disease.⁶ The AAP estimates that universal routine adolescent MenB vaccination would prevent 15 to 29 cases per year and 2 to 5 deaths per year.⁷ The AAP policy statement on MenB vaccination encourages pediatricians to educate families regarding the availability of MenB vaccines while acknowledging low incidence of disease and lack of efficacy data (as trials were based on antibody response).⁷

Special Circumstances

For those with complement deficiencies, complement inhibitor use or anatomic or functional asplenia (including sickle cell disease), primary vaccination with either vaccine type should be started at age 10. The ACIP recommends booster vaccines to be given at one year after completion of primary vaccination, then every 2-3 years. However, only primary vaccine series are licensed for use in the United States and booster dose use is off label.⁵ Healthy persons deemed to be at risk due to a local MenB disease outbreak should receive the MenB vaccine series. This decision should be made in consultation with state or local health departments.

The American Academy of Pediatrics released a policy statement in 2016 stating their agreement with ACIP on MenB vaccine recommendations.⁷

Vaccine Safety

The most common adverse events with MenACWY-D (Menactra) vaccination were injection site pain, erythema, swelling, myalgias, fatigue, headache and gastrointestinal symptoms. Post-vaccine cases of Guillain-Barre syndrome were reported to VAERS (vaccine adverse events reporting system) after initial licensing; however, subsequent analyses have not shown an increased risk of GBS and ACIP removed precautions for patients with a history of GBS from their recommendations, though the package insert still has this precaution listed.⁵

MenACWY-CRM (Menveo) side effects include injection site pain, erythema, headaches, myalgias and fatigue. Post-licensing data showed a statistically significant increased risk for Bell's palsy in patients 11-21 years old when Menveo was given with other vaccines but not when given alone. However, among the eight patients noted to have Bell's palsy, several may have had other conditions that could be associated with Bell's palsy. In the 2 month to 10 years age group, no increased risk was noted. Subsequent VAERS data did not show an increased signal of Bell's palsy risk.⁵

MenACWY-TT (MenQuadfi) is a newly licensed vaccine and showed common adverse effects of erythema, swelling, injection site pain, malaise, myalgias, and fever. Adverse events were mild to moderate and no major adverse safety signals were identified.⁵

In clinical trials, most common MenB vaccine side effects were pain at injection site, fever, headache, fatigue, muscle pain and joint pain.⁷ MenB-FHbp (Trumenba) did not show any obvious safety signals for autoimmune or renal disease. No major adverse safety concerns were identified. MenB-4C (Bexsero) also did not show any major safety concerns in post-marketing VAERS data.⁵ Bexsero did show mild increase in symptoms of underlying disease in patients taking complement inhibitors (as the vaccine itself can activate complement). Vaccination is recommended to occur prior to administration of complement inhibitors when possible. Neither of the MenB vaccines have been evaluated in pregnancy or breastfeeding.⁷

Conclusion

Though overall incidence is declining, invasive meningococcal disease still carries a high morbidity and mortality and often affects young, healthy adults. Individuals with complement deficiency, complement inhibitor use, anatomic or functional asplenia, patients with HIV, and persons living in crowded conditions are at particularly high risk. Vaccination is an important preventative modality to help alleviate the burden of disease. Two major subtypes of vaccine exist which cover five of the six major serotypes that cause disease in humans. MenACWY vaccines are recommended as part of the routine adolescent vaccination schedule, while MenB vaccines can be given as part of a shared decision making process with patients and their families.

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References

1. Centers for Disease Control and Prevention. (2011). Chapter 7: Identification and Characterization of *Neisseria meningitidis*. In Mayer L., *Laboratory Methods for the Diagnosis of Meningitis*, 2nd ed. Centers for Disease Control and Prevention. <https://www.cdc.gov/meningitis/lab-manual/chpt07-id-characterization-nm.html>
2. Mbaeyi, S., Duffy, J., & McNamara, L. A. (2021). Chapter 14: Meningococcal Disease. In Hall E., Wodi A.P., Hamborsky J., et al., *Epidemiology and Prevention of Vaccine-Preventable Diseases*, 14th ed (pp. 207-224). Centers for Disease Control and Prevention. Washington, D.C. Public Health Foundation.
3. Centers for Disease Control and Prevention. Meningococcal Disease. 2021. <https://www.cdc.gov/meningococcal/images/meningococcal-disease-incidence.jpg>
4. Centers for Disease Control. (2019). National Center for Immunization and Respiratory Diseases, Office of Infectious Diseases. Enhanced Meningococcal Disease Surveillance Report, 2019. <https://www.cdc.gov/meningococcal/downloads/NCIRD-EMS-Report-2019.pdf>
5. Mbaeyi, S. A., Bozio, C. H., Duffy, J., Rubin, L. G., Hariri, S., Stephens, D. S., & MacNeil, J. R. (2020, September 25). Meningococcal Vaccination: Recommendations of the Advisory Committee on Immunization Practices, United States, 2020. *MMWR Recom Rep*, 69(9), 1–41. [PubMed](#)
6. Mbaeyi, S. A., Joseph, S. J., Blain, A., Wang, X., Hariri, S., & MacNeil, J. R. (2019, January). Meningococcal disease among college-aged young adults: 2014–2016. *Pediatrics*, 143(1), e20182130. [PubMed https://doi.org/10.1542/peds.2018-2130](https://doi.org/10.1542/peds.2018-2130)

7. Committee on Infectious Diseases. (2016, September). Recommendations for serogroup B meningococcal vaccine for persons 10 years and older. *Pediatrics*, 138(3), e20161890. [PubMed https://doi.org/10.1542/peds.2016-1890](https://doi.org/10.1542/peds.2016-1890)

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