An Update on Meningococcal Vaccination

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ABSTRACT

Neisseria meningitidis bacterial infection can cause severe life-threatening meningitis. Individuals who survive may be left with profound sequelae. In epidemic regions such as the meningitis belt of Africa, the case rate is drastically higher than in nonepidemic regions and is due to distinct outbreak serogroups. Two highly effective conjugate meningococcal vaccine against serogroups A, C, W and Y are licensed and indicated for prevention in childhood vaccination schedules and for travelers to outbreak regions. In the US, meningococcus serogroup B is the main cause of outbreaks, in areas with crowding such as college dorms. It has taken over 40 years to develop a meningitis type B vaccine and now there are 2 brands available for children and teens. All college-bound individuals should complete schedules of both conjugate ACWY serotypes and meningitis B vaccine series. This paper reviews details on who to vaccinate and how to use the currently available meningococcal meningitis vaccines.

KEYWORDS: meningitis vaccine, *Neisseria meningitidis*, serogroups ACWY, meningitis serogroup B, conjugate meningococcal vaccination

Neisseria meningitidis causes a wide range of clinical presentations, from asymptomatic carriage to severe life-threatening meningitis. When it presents with clinical disease, *N meningitidis* causes meningitis in over 50% of cases; other presentations include pneumonia and bacteremia. Person-to-person transmission of bacteria occurs through close personal contact with respiratory secretions or saliva of infected persons. Colonization is common – at any given time 5–10% of the population may be carriers of the organism. In contrast, invasive disease is rare in non-epidemic areas, occurring at a rate of 0.5 to 10 cases per 100,000. However, in epidemic regions such as the meningitis belt of Africa, the case rate can be drastically higher, up to 1,000 cases per 100,000, particularly during peak season. There are six major serogroups associated with human disease: A, B, C, X, Y, and W-135. *N meningitidis* is found worldwide, with some regional differences in serogroup distribution and prevalence.[1,2,3]

Though prevalence of clinical disease is low in non-epidemic regions, the severity of meningococcal disease when present, and the high mortality associated with *N meningitidis* meningitis, have led to recommendations for vaccination of key populations. Two types of meningococcal vaccines are available in the U.S. currently, one type covering serogroups A, C, Y, and W-135, and the other covering serogroup B. (**Table 1**)

For serogroups A, C, Y, and W-135, two similar vaccines are available: MenACWY-D (Menactra) and MenACWY-CRM (Menveo). Both are conjugate vaccines. The previously available quadrivalent polysaccharide vaccine (MPSV4, or Menomune) was discontinued in August 2017. The conjugate A, C, Y, and W-135 vaccines are approved for age 9 months and older (MenACWY-D) or 2 years and older (MenACWY-CRM) through the age of 55 years, though most authorities advise off-label usage if otherwise indicated in individuals over

Table 1.

VACCINE	TRADE NAME	AGE OF VACCINE INITIATION	DOSE	ROUTE	INTERVAL SINCE FIRST DOSE	BOOSTER
Conjugate Meningococcal A,C,W and Y vaccine	Menveo	2 mo	0.5 mL	IM	0,2,4, 10 mo	If at continued risk
		7–23 mo	0.5 mL	IM	0, 3 mo (2nd dose administered in 2nd year of life)	
		≥ 2 y	0.5 mL	IM	1 dose if traveling, then 2 doses given 8 weeks apart	
	Menactra	9–23 mo	0.5 mL	IM	0, 3 mo	If at continued risk
		≥ 2 y	0.5 mL	IM	1 dose	
Meningitis B vaccine	Trumenba	10–25 y	0.5 mL	IM	0, 1–2, 6 mo or 0, 6 mo The 3-dose schedule is preferred for groups at increased risk where more rapid protection is desired	None
	Bexsero	10–25 y	0.5 mL	IM	0, ≥ 1 mo	None

the age of 55 as, with the withdrawal of MPSV4, there is no approved vaccine for this age group. In polysaccharide vaccines only the sugar part of the bacteria, the capsule, is included as the antigen to stimulate the immune response. In conjugate vaccines the sugar is joined to a carrier protein to trigger a stronger and more long-lasting response. With the quadrivalent conjugate vaccines, protective antibody levels against all four serogroups develop within 10–14 days after vaccination, and protection of 90–95% is estimated. The duration of protection is shorter in children younger than 5 years of age, but generally considered to be 5 years in adolescents and adults. Conjugate vaccines carry the advantage over the older polysaccharide vaccine of eliciting stronger immunologic memory (generally with recommended revaccination only every 5 years in adults), a reduction in nasopharyngeal carriage, and more effective interruption of transmission and establishment of population protection.[3,4]

Meningitis B vaccinations have been more recently developed, as vaccine development against this serogroup was so challenging that it took over 40 years. The serogroup B polysaccharide resembles a human neural cell adhesion molecule, which raised concern about inducing autoimmunity. Outer membrane vesicle vaccines were developed and effective in outbreak settings, but were limited against the diversity of worldwide B strains. The current approved meningitis B vaccines in the US are recombinant protein-based and were developed through "reverse vaccinology" to identify target preserved proteins, and are widely protective against most meningitis B strains. Both approved in 2015, MenB-4C (Bexsero) and MenB-FHbp (Trumenba) are recommended as equivalent by the ACIP. They are approved for usage in individuals ages 10 through 25.[4] Meningitis B accounts for 40% of the meningitis cases in the US, and 10 university campus outbreaks were associated with this serogroup between 2013 and 2018.[5]

The ACIP now recommends meningitis vaccination routinely to adolescents and meningitis ACWY vaccination routinely in children between the ages of 11 and 18. MenACWY vaccination is administered as a two-dose series, separated by a minimum of 8 weeks, starting at 11–12 years of age, with a booster at age 16. Meningitis B vaccination is recommended, based on shared clinical decision-making, between the ages of 16 and 23 years (preferred ages 16–18). MenB-4C is administered as a 2-dose series separated by at least 4 weeks; MenB-FHbp is administered as a two-dose series separated by at least 6 months (a third dose at least 4 months later is recommended if dose #2 is administered prematurely). Patients should complete the series with the same vaccine as the original dose. Common reactions include pain and redness at the injection site and mild fever for 1 to 2 days. [6,7,8,9]

Other populations are encouraged to pursue vaccination due to increased risk. Vaccination against MenACWY is recommended in patients with functional or anatomic asplenia, patients with HIV infection, persistent complement deficiency, or use of a complement inhibitor (e.g. celuizumab, ravulizumab). It is also recommended in first-year college students and military recruits who were not previously vaccinated. MenACWY vaccination is additionally recommended in travelers to countries with high risk of sporadic outbreaks, particularly the so-called "meningitis belt" across sub-Saharan Africa, which includes a number of countries as well as parts of other African nations. (**Table 2**) Further, all persons entering Saudi Arabia for the Hajj and Umrah **require** MenACWY due to outbreak risk related to crowding. MenB vaccination is recommended outside of the standard dose interval described above in the setting of anatomic or functional asplenia, complement deficiency, and use of complement inhibitors. [6,7,8,9] During outbreak settings, vaccination of affected populations is recommended. A number of outbreaks in men who have sex with men in the past 10 years have led municipalities to offer MenACWY vaccination to these populations as well. [10]

Table 2.

Countries in the "Meningitis Belt"	Other African nations with increased meningococcal outbreak risk
Senegal	Uganda
Gambia	Mauritania
Guinea-Bissau	Mali
Guinea	Burkina Faso
Sudan	Côte d'Ivoire
South Sudan	Ghana
Eritrea	Togo
Ethiopia	Benin
Northwest Kenya	Nigeria
	Niger
	Cameroon
	Chad
	Central African Republic,
	Democratic Republic of Congo

Adapted from CDC website: www.cdc.gov/meningococcal

Though a rare disease, meningococcal disease can be associated with high morbidity and mortality. With the availability of effective vaccinations against most serogroups, including effective vaccines for serogroup B added in 2015, we have a new ability to prevent outbreaks and individual infections. Clinicians should remember to offer these vaccinations to all adolescents, but also remember key higher risk populations, including travelers to sub-Saharan Africa, individuals embarking on the Hajj or Umrah, and immunocompromised patients including people living with HIV. Meningococcal disease prevalence in the US is decreasing, in part due to increased vaccination, but further progress can be made by remembering and counseling adolescents, their parents, and high-risk individuals.

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