Prevention of Meningococcal Infection in the United States: Current Recommendations and Future Considerations

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ABSTRACT

Neisseria meningitidis is a common cause of bacterial meningitis and septicemia that can lead to permanent sequelae or death. N meningitidis is classified into serogroups based on the composition of the capsular polysaccharide, with serogroups A, B, C, W, X, and Y recognized as the major disease-causing organisms. The unpredictability of infection coupled with the poor prognosis for some patients suggests immunization as an effective preventive strategy. Importantly, four of the six disease-causing serogroups (A, C, Y, and W) may be prevented with available quadrivalent capsular polysaccharide–protein conjugate vaccines; these vaccines have been successfully implemented into immunization programs in the United States. Unfortunately, quadrivalent conjugate vaccines are not effective against serogroup B, now the most common cause of invasive meningococcal disease. Two recombinant protein vaccines recently were licensed for prevention of serogroup B disease. Recommendations for use of these serogroup B vaccines in the United States have been made by the Advisory Committee on Immunization Practices. This article will discuss all available meningococcal vaccines, current recommendations for use, lessons learned from previous experiences, and future considerations, with the hope of further understanding how use of these vaccines may help reduce incidence of meningococcal disease in the United States.

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secondary cases in individuals in close contact with an infected patient [10,11]; detailed guidelines for their use already are described [12]. This review will focus on immunization as a preventive strategy, with an in-depth discussion of the available meningococcal vaccines in the United States, current recommendations for their use, lessons learned from previous experiences, and future considerations.

Assessment of Meningococcal Vaccine Effectiveness

Because of the low incidence of IMD in the United States, generally <1 per 100,000 persons [13], large-scale Phase 3 vaccine efficacy studies are not feasible because of financial and logistic difficulties. Therefore, alternative in vitro functional assays that mimic the main mechanism of protection observed in vivo were developed to assess the potential efficacy of a meningococcal vaccine in a population. Specifically, complement-dependent bactericidal activity of antibodies derived from the serum of individuals after immunization with meningococcal antigens is used as a surrogate (or correlate) of protection [14]. This correlate is measured with an assay referred to as a serum bactericidal antibody assay and is performed using human complement (hSBA) [2]. hSBA assays are the U.S. Food and Drug Administration’s (FDA’s) accepted standard for estimating efficacy of a meningococcal vaccine; an hSBA titer of ≥1:4 is considered protective [14–17]. This threshold has been shown to correlate with effectiveness in postlicensure studies [18], and hSBA titers are used to demonstrate protection across meningococcal serogroups [14,19,20].

Vaccines Available for the Prevention of Invasive Meningococcal Disease

Serogroup A, C, W, and Y vaccines

Neisseria meningitidis is classified into serogroups based on the composition of their capsular polysaccharides (CPs) [6,21], with serogroups designated as A, B, C, W, X, and Y attributed to almost all cases of life-threatening, sporadic, and endemic disease globally [21–25]. Until recently, meningococcal vaccines approved in the United States only protected against IMD caused by four of the six disease-causing serogroups of N meningitidis: A, C, W, and Y.

Four different meningococcal vaccines containing purified CPs alone or CPs conjugated to a carrier protein are licensed in the United States for the prevention of IMD caused by serogroups A, C, W, and Y (Table 1). The quadrivalent CPs vaccine MPSV4 (Menomune [Meningococcal Polysaccharide Vaccine, Groups A, C, W, and Y combined]; Sanofi Pasteur Inc., Swiftwater, Pennsylvania) has been available since the 1970s for use in individuals

### Table 1

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Licensure (age; year)</th>
<th>ACIP recommendation, dose:population</th>
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<tr>
<td></td>
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<td>General population</td>
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<td>Category</td>
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<tr>
<td>MenACWY vaccines</td>
<td></td>
<td></td>
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<tr>
<td>MenACWY-D (Menactra; Sanofi Pasteur)</td>
<td>2–55 years; 2005</td>
<td>A</td>
</tr>
<tr>
<td>MenACWY-CRM (Menveo; GlaxoSmithKline)</td>
<td>2–55 years; 2010</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td>≥2 months; 2013</td>
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<tr>
<td>MenCY vaccines</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hib-MenCY-TT (MenHibrix; GlaxoSmithKline)</td>
<td>6 weeks–18 months; 2012</td>
<td>A</td>
</tr>
<tr>
<td>MenB vaccines</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bivalent rLP2086 (Trumenba; Pfizer Inc)</td>
<td>10–25 years; 2014</td>
<td>B</td>
</tr>
<tr>
<td>4CMenB (Bexsero; GlaxoSmithKline)</td>
<td>10–25 years; 2015</td>
<td>B</td>
</tr>
</tbody>
</table>

ACIP = Advisory Committee on Immunization Practices; N/A = not applicable.

* Individuals remaining at increased risk of meningococcal disease should receive a MenACWY booster 3 or 5 years after completing the primary immunization at age 2 months–6 years or ≥7 years, respectively. Boosters should be repeated every 5 years thereafter.

* Individuals traveling to locations or who are residents of countries where meningitis is hyperendemic or epidemic.

* Community outbreaks caused by a vaccine serogroup.

* Individuals with persistent complement deficiencies, including those being treated with eculizumab (Soliris).

* Individuals with functional or anatomic asplenia (including sickle cell disease).

* Individuals who are first-year college students aged ≤21 years living in residential housing.

* Microbiologists who routinely work with Neisseria meningitidis isolates.

* 4CMenB is licensed as a two-dose series, with doses administered ≥1 month apart; Bivalent rLP2086 is licensed as a three-dose series, with the second and third doses administered 1–2 and 6 months after the first dose. In addition to the three-dose schedule for bivalent rLP2086, recently the Food and Drug Administration has approved a two-dose series (0 and 6 months); the choice of schedule depends on the risk of exposure and the patient’s susceptibility to disease.
aged ≥2 years, with an extensive history of use in mass immunization programs in response to outbreaks among international travelers and in closed populations of adults at high risk for disease [6,13,29].

MPSV4 has been replaced by the quadrivalent CPS-protein conjugate vaccines MenACWY-D (Menactra; Sanofi Pasteur Inc., licensed 2005) and MenACWY-CRM (Menveo; GlaxoSmithKline Biologicals, Rixensart, Belgium; licensed 2010), collectively referred to here as MenACWY for use in individuals nine months through 55 years of age and individuals 2 months through 55 years of age, respectively [30,31] (Figure 1). A bivalent CPS-protein conjugate vaccine, Haemophilus influenzae b-Neisseria meningitidis serogroups C and Y (Hib-MenCY-TT; MenHibrix; GlaxoSmithKline Biologicals), was approved in 2012 for use in individuals six weeks through 18 months of age [32]. These vaccines differ from MPSV4 vaccine in that their CPSs are conjugated to a protein carrier; this carrier protein presents the CPS to the immune system, resulting in a T-cell response and the likely added benefits of immunologic memory at re-exposure, nasopharyngeal carriage reduction, and herd immunity [13,29].

Serogroup B vaccines

There is a need for a broadly protective MnB vaccine for use in the United States, as MnB is responsible for approximately 30%–40% of all IMD cases in this country [33,34]. Moreover, serogroup B caused the recent outbreaks observed at several university campuses [28], further emphasizing the need for an effective MnB vaccine as a preventive measure in this circumstance. Unfortunately, the CPS of MnB does not elicit immune response owing to its similarity to peptides on human neural tissue [35].

To develop a broadly protective MnB vaccine, identification of surface proteins that elicit a sufficient immune response, that are present in a majority of disease strains, and that have limited immunologic variability across diverse serogroup B isolates was necessary. A conserved surface-exposed bacterial lipoprotein and hSBA factor H binding protein (fHBP; also known as LP2086) were identified as a promising vaccine target [36,37]. Two protein-based serogroup B vaccines that contain fHBP have been developed: bivalent rLP2086 (Trumenba [MenB-FHbp]; Pfizer Inc, Philadelphia, Pennsylvania) and 4CMenB (Bexsero [MenB-4C]; GlaxoSmithKline, Brentford, Middlesex, United Kingdom; Table 1).

These vaccines employ two different strategies to address broad coverage across diverse MnB strains. Specifically, 4CMenB includes four unrelated meningococcal protein components: subfamily B fHBP, neisserial adhesin A, neisserial heparin-binding antigen, and a porin A (PorA) outer membrane vesicle (Figure 2A). Although none of these proteins address the full antigenic diversity across all MnB strains, 4CMenB aims to provide breadth of serogroup B strain coverage by including multiple antigens with the expectation that at least one of the antigens

Figure 1. Development of serogroup MenACWY polysaccharide conjugate vaccines.
Figure 2. Development of serogroup B recombinant protein vaccines (A), 4CMenB (B). E. coli = Escherichia coli; NadA = neisserial adhesin A; NHBA = neisserial heparin-binding antigen.
will be present across divergent strains. In contrast, bivalent rLP2086 has only one protein (fHBP) but includes both of its antigenic variants: fHBP subfamily A and fHBP subfamily B (Figure 2B). Breadth of strain coverage is accomplished by the ability of these two proteins to cover the antigenic variability of fHBP found in all serogroup B strains. Unlike the fHBP subfamily B variant found in 4CMenB, both of the fHBP variants in bivalent rLP2086 are modified by addition of a lipid group, similar to the naturally occurring protein [36].

Bivalent rLP2086 was licensed in the United States in October 2014 through an accelerated FDA process for use in people aged 10 through 25 years [38]. This was subsequently followed by accelerated FDA approval of 4CMenB in January 2015 in the same age group [39]. Not only do these two vaccines differ in antigen composition, but also they differ in methods used to estimate breadth of coverage across MnB strain diversity. Although surrogate methods may help predict the potential coverage of the two vaccines, true effectiveness cannot be determined until there is enough vaccine uptake to collect large-scale surveillance data.

**Recommendations for meningococcal immunization**

The Advisory Committee on Immunization Practices (ACIP) recommends immunization with MenACWY for everyone ages 11 through 18 years (Table 1). The first dose ideally should be given at 11–12 years of age, followed by a booster at age 16 years. A single dose may be given up until 21 years of age as a catch-up vaccination if a first dose has not been administered before the age of 16 [2]. MenACWY also is recommended routinely for all individuals age nine months through 55 years who are considered to be at high risk for IMD (Table 1) [2]. High-risk individuals should receive MenACWY in a one- or two-dose series, depending on the vaccine indication and age of the individual.

Recommendations of the ACIP were recently updated to include MenACWY for high-risk infants two through 23 months of age. Immunization should be administered in a four-dose series, with the first booster three years after the primary series, if necessary [26]. Hib-MenCY-TT also is recommended for high-risk infants two–18 months of age, with the first dose administered as early as age six weeks and the fourth dose given as late as age 18 months [2]. This vaccine can be co-administered with other routine infant vaccines. A booster dose of MenACWY, if needed, is recommended three years after the last dose of Hib-MenCY-TT.

Recently, the ACIP published vaccination recommendations for MnB using either 4MenB or bivalent rLP2086 [27,28]. A vaccination series also may be used in individuals 16 through 23 years of age, preferably between the ages of 16–18 years, after consultation with a health care provider to provide short-term protection against most strains of MnB (category B recommendation) [27]. Vaccination is recommended for individuals aged ≥10 years who are at high risk for MnB disease [28]. The implications of these recommendations are discussed in more detail in the following section.

**Lessons Learned From Past Experiences**

**Successful implementation of ACWY vaccines**

The overall success of a vaccine depends on coverage of the at-risk population, safety and effectiveness of the vaccine at preventing disease, and ideally, reduction in carriage acquisition so that indirect (herd) effects are achieved. Since its introduction, coverage for MenACWY vaccines in adolescents age 13 through 17 years has been steadily increasing, with rates starting at 11.7% in 2006 [40] and increasing to 79.3% in 2014 [41]. Coverage by state in 2014 ranged from 46.0% (Mississippi) to 95.2% (Pennsylvania) [41]. As vaccine coverage in this age group increased, IMD incidence for the vaccine serogroups simultaneously decreased, with rates (95% confidence interval [CI]) per 100,000 people of .27 (.17–.39) from 2004 to 2005 and .05 (.02–.12) from 2010 to 2011 [2].

Although direct effects of the immunized population were evident, incidence did not decrease in other age groups, suggesting no evidence of protection in the unimmunized population (i.e., herd effects); however, herd effects from meningococcal vaccines have been demonstrated in other countries when coverage approaches 90% [42]. A case-control study evaluating vaccine effectiveness began in January 2006 [43]. As of May 2012, a total of 151 case patients and 200 controls were enrolled. The overall estimate of vaccine effectiveness in adolescents was 66% (95% CI, 24%–84%) in those vaccinated 0–6 years earlier. Vaccine effectiveness also decreased over time; however, the overlapping CIs observed must be taken into account when interpreting this decrease. Specifically, vaccine effectiveness was estimated at 79% (95% CI, 47%–92%) for adolescents immunized <1 year earlier, 73% (95% CI, 34%–89%) for adolescents immunized one to <2 years earlier, 44% (95% CI, 17%–74%) for adolescents immunized 2 to <3 years earlier, and 41% (95% CI, 19%–71%) for adolescents immunized 3 to <6 years earlier.

Important lessons can be garnered from our experiences with MenACWY vaccines in the United States. Specifically, vaccine effectiveness is high in the first or second year after primary immunization; it is likely that herd effects will not be seen until first dose coverage approaches 90%. However, long-term effectiveness after the primary dose is disappointingly short-lived; this waning effectiveness led to a policy change in adolescents from a single primary dose to a single primary dose plus a booster dose [44]. The decision to include a booster dose also took into consideration other factors such as health care provider access to adolescents, changing disease epidemiology, and cost-effectiveness. For herd effects to extend through all of adolescence, second dose coverage, which is currently approximately 30% [45], must increase substantially.

Although these results are encouraging, it should be noted that the number of cases of IMD caused by all serogroups diminished significantly even before the first A,C,W,Y conjugate vaccine was recommended for adolescents in 2005 [34]. Reasons for this decrease are not completely understood but may be attributed to the cyclical nature of disease [13,34]. The demonstrated effectiveness in adolescents also provides an encouraging example that strongly supports the continued use of immunization to reduce disease burden of serogroups A, C, W, and Y. Whether similar results will be observed after serogroup B vaccine implementation remains to be determined.

**Use of serogroup B vaccine on college campuses in the United States**

MnB has been responsible for several outbreaks on U.S. college campuses since 2013 (Table 2). Given the unpredictability of meningococcal outbreaks, immunization is a strategy for reducing meningococcal disease incidence and, in combination with chemoprophylaxis, controlling outbreaks. The lack of an FDA-licensed serogroup B vaccine presented significant
challenges during the first two outbreaks on the campuses of Princeton University and the University of California, Santa Barbara [51]. The outbreak at Princeton University lasted a full year (March 2013–March 2014), with nine cases resulting in one death. This lengthy outbreak was punctuated by some unusually long gaps between cases; the reason for this remains unclear. Several cases related to this outbreak also occurred off of the Princeton campus, including a student at a nearby college [46]. The outbreak at the University of California, Santa Barbara included four cases that occurred within a few weeks in November 2013. This was a more typical outbreak, with short intervals between cases. Further examination of cases led to the discovery of a related case that occurred on the campus seven months earlier. The four students survived, but one student suffered bilateral foot amputations [47].

Since no FDA-licensed serogroup B vaccine was available at the time of these outbreaks, 4CMenB, on an investigational new drug protocol in collaboration with the Centers for Disease Control and Prevention, was used to control these two outbreaks [47]. A two-dose immunization series with 4CMenB was recommended for approximately 7,500 undergraduates, faculty, and staff at Princeton and for 20,000 individuals at the University of California, Santa Barbara [52]. Approximately, 90% of the target population at Princeton University received both doses of 4CMenB; two-dose uptake was 37% at the University of California, Santa Barbara [47,53]. Differences in uptake at these two college campuses is likely multifactorial, including differences in campus structure, timing of immunization relative to serogroup B cases, and perceived risk among students and parents. It should be noted that these universities did a remarkable job managing their outbreak situation. In the future, it would be best to have protection before college entrance. Even if an MnB vaccine series was completed before entering college, it is unknown whether the protection would last through graduation. Further studies are needed to determine the ideal path forward to provide protection against serogroup B IMD in college students.

Finally, a fourth serogroup B outbreak at the University of Oregon has been actively managed since the beginning of 2015, with seven cases reported as of May 2015; one student died [48,55]. A four-day campus-based mass immunization clinic to administer bivalent rLP2086 was held in early March 2015 for 22,000 students, faculty, and staff. Almost 10,000 students received their first three doses of bivalent rLP2086 during the March clinic, but the second immunization clinic, which was held in May, was attended by only 2,700 individuals; a third clinic was held in October 2015 [49,50,56]. The total number of students vaccinated is unknown, but it is estimated that >15,000 doses of vaccine have been administered to students through a combination of university-sponsored clinics and vaccination at local pharmacies [56].

Through experiences with outbreaks on U.S. college campuses, it has been demonstrated that great effort can assure good uptake, at least for the initial vaccine dose; however, current MnB vaccine formulations require two or three doses, months apart, to provide protection, a fact that obviously is not ideal in an outbreak situation. In the future, it would be best to have protection before college entrance. Even if an MnB vaccine series was completed before entering college, it is unknown whether the protection would last through graduation. Further studies are needed to determine the ideal path forward to provide protection against serogroup B IMD in college students.

<table>
<thead>
<tr>
<th>University/college</th>
<th>Date of outbreak</th>
<th>Confirmed cases, n</th>
<th>Deaths/amputations, n</th>
<th>Vaccine used</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Princeton University [46–48]</td>
<td>March 2013–March 2014</td>
<td>9</td>
<td>1/0</td>
<td>4CMenB</td>
<td>• Lengthy outbreak with uncharacteristically long gaps between cases • Several cases occurred off campus • Lack of licensed MnB vaccine at time of outbreak presented significant challenges • FDA approved the use of 4CMenB as an investigational new drug; two-dose series recommended for &gt;5000 students; uptake was low</td>
</tr>
<tr>
<td>University of California, Santa Barbara [47,48]</td>
<td>November 2013</td>
<td>4</td>
<td>0/1</td>
<td>4CMenB</td>
<td>• Lengthy outbreak with uncharacteristically long gaps between cases • Several cases occurred off campus • Lack of licensed MnB vaccine at time of outbreak presented significant challenges • FDA approved the use of 4CMenB as an investigational new drug; two-dose series recommended for 20,000 students; uptake was low</td>
</tr>
<tr>
<td>Providence College [45,48]</td>
<td>January 2015</td>
<td>2</td>
<td>0/0</td>
<td>Bivalent rLP2086</td>
<td>• University moved rapidly to implement a mandatory campus-based mass immunization campaign; uptake of Dose 1 was high • Cases being actively managed • A high percentage of students received Dose 1; uptake of Dose 2 was much lower</td>
</tr>
<tr>
<td>University of Oregon [49,50]</td>
<td>January 2015–present</td>
<td>7</td>
<td>1/0</td>
<td>Bivalent rLP2086</td>
<td>• University moved rapidly to implement a mandatory campus-based mass immunization campaign; uptake of Dose 1 was high • Cases being actively managed • A high percentage of students received Dose 1; uptake of Dose 2 was much lower</td>
</tr>
</tbody>
</table>

FDA = U.S. Food and Drug Administration; MnB = meningococcal serogroup B.
Future Considerations

Implications of a category B Advisory Committee on Immunization Practices recommendation

These recent outbreaks of serogroup B IMD on college campuses illustrate why the ACIP recommends routine use of an MnB vaccine as a control measure. However, the burden of serogroup B IMD in older adolescents and young adults 18–23 years of age in the United States is low (i.e., an estimated 15–30 cases annually [57]). Among this age group, the incidence of MnB is estimated at .14 per 100,000 [27]. Taken together with the considerable cost of a routine immunization program targeting all individuals of this age group (i.e., college students [one third of serogroup B IMD cases in this age group [57]] and individuals not attending college) and the paucity of safety data the ACIP does not currently routinely recommend MnB vaccines in young adults [27]. Rather, the recent recommendation that the MnB vaccine may be administered to adolescents and adults aged 16 through 23 years for short-term protection is a “Category B” recommendation, which leaves the decision to immunize an individual in this age group up to physicians and parents/patients [27].

The permissive nature of Category B recommendations may potentially result in lower vaccine uptake compared with a “routine” or “Category A” recommendation. Category B recommendations rely on both the physician advising parents/patients that the MnB vaccine could be given and the availability of the vaccine in the doctor's office if the decision to vaccinate is made; thus, only time will allow us to determine vaccine uptake. Meanwhile, it is important to determine the potential effect of these MnB vaccines on meningococcal carriage, and duration of protection, as well as the effectiveness of different vaccination strategies and their costs.

Recent projections indicate that 29 cases and five deaths are potentially preventable with an MnB vaccination series administered at age 11, 16, and 18 years [27]; these numbers decrease to nine and one, respectively, if only college students are vaccinated. Estimates for the number needed to vaccinate to prevent one case and one death suggest fewer patients would need to be vaccinated to achieve positive outcomes by implementing an MnB vaccination series at earlier ages (i.e., number needed to vaccinate to prevent one case and one death: 102,000 and 638,000, respectively, for a vaccine series at age 11, 16, and 18 years; 368,000 and 2,297,000, respectively, for college student vaccination). Projections also indicate that the cost per quality-adjusted life years is lower ($3.7 vs. 9.4 million, respectively) when an MnB vaccination series is implemented at a younger age [27].

Continued monitoring of the incidence of endemic serogroup B disease is essential; IMD is currently at a historic low in the United States [2] although this could change with introduction of new clones. All these data, albeit challenging to collect given the low burden of disease, will be needed if the ACIP is to revisit the Category B recommendation in the future. Meanwhile, it will be a necessary but enormous task to effectively educate the public and providers about these new vaccines and how best to implement the associated recommendations.

A vaccine that protects against major meningococcal disease—causing serotypes

Currently, one meningococcal vaccine targets serogroups A, C, W, and Y and another targets only serogroup B. The availability of a single vaccine that could protect against all five serogroups would simplify the meningococcal immunization schedule and potentially increase meningococcal vaccine uptake. A pentavalent meningococcal A, B, C, W, and Y vaccine formulation is not yet available but has been developed and was recently examined in a small study in adolescents [58–60]; larger safety and immunogenicity studies are in progress [61]. Preliminary results, identifying the most optimal formulation for future studies, suggest all formulations tested have robust responses against all five meningococcal serogroups, albeit responses were somewhat higher for vaccine formulations containing outer membrane vesicles (OMVs). No safety concerns have been identified thus far. Because recommendations currently list serogroup A, C, W, Y vaccines as Category A versus the Category B recommendation for serogroup B vaccines in persons 16 through 23 years without increased risk conditions, whether the availability of a pentavalent vaccine would qualify it for a Category A recommendation remains to be determined. Moreover, it should be noted that although development of such a vaccine is underway, the actual availability of a pentavalent vaccine for inclusion into the immunization schedule is years away. The dynamic nature of IMD limits predictions of how this type of vaccine could actually change the immunization landscape when it is FDA-licensed and available for use.

Education

Continued educational programs will be needed to inform physicians and the general public about the risks of IMD, available vaccines, strategies for prevention, and approaches to improve vaccine uptake. Effective interventions include setting up systems in health care clinics to facilitate parental and provider reminders of upcoming and overdue immunizations, development of state laws for primary/secondary school and college entry, educating providers on how to talk to parents, and elucidating the best practices for implementation of old and new vaccine recommendations, including the need for a booster dose of the ACWY conjugate vaccine and immunization with the new MnB vaccine.

Protecting infants

Infants represent an age group with some of the highest incidence rates of IMD in the United States across disease-causing serogroups although the majority (60%) of disease in this age group is caused by serogroup B [2,62]. Routine vaccination of infants for meningitis is not a standard practice in the United States; however, MenACWY-D, MenACWY-CRM, and Hib-MenCY-TT are recommended for use in high-risk infants (Table 1). At present, neither of the MnB vaccines is currently FDA-licensed or ACIP-recommended for use in infants. In studies evaluating both currently available MnB vaccines in infants, reactogenicity, in particular high fever, was common [63–65]; although most cases were mild to moderate in intensity and short-lived. If immunization in infants is not possible owing to considerable reactogenicity [63–65], infants must rely on either maternally transmitted protective antibodies from their immunized mother or on indirect protection (or herd immunity) from their immunized contacts. However, at present, there are no data available to suggest these are viable options.

Although beyond the scope of this review, it is important to acknowledge that other countries besides the United States...
recommend routine meningococcal vaccination for infants as part of their national immunization programs [29]. Opportunity may exist to learn from the experiences of these countries with regards to infant vaccination.

IMD is a rapid and unpredictable illness, leaving substantial morbidity and mortality among those who are afflicted. Although implementation of MenACWY immunization recommendations was accompanied by a substantial decrease in the incidence of *N meningitidis* infection in adolescents age 11–18 years, protection was short lived, requiring a booster dose to protect through late adolescence [2,43]. Furthermore, a critical gap in the prevention of MnB disease remained, especially among infants. Whether the recent approval of two serogroup B vaccines effectively fills this gap in coverage remains to be determined. In the interim, some optimism is needed for their potential effectiveness. Further complicating their potential effectiveness, the recent Category B recommendation for the use of MnB vaccines may prove difficult to implement. Whether these recommendations are enough to promote uptake adequately to prevent outbreaks or to provide herd protection to unvaccinated individuals needs to be determined.

The recent outbreaks of MnB disease on college campuses in the United States serve as cruel reminders of the devastating effects that outbreaks have in a community. Going forward, we must heed the lessons learned from these experiences should future outbreaks occur. Prevention of serogroup B disease in infants remains an ongoing priority, but doing so will be challenging. Increasing awareness among clinicians and the public regarding meningococcal immunization in high-risk individuals in all age groups and those age groups with the highest disease burden remains essential for success.

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