Prevention of Meningococcal Infections in the First 2 Years of Life

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Abstract

The spectrum of disease caused by *Neisseria meningitidis* includes bacteremia, fulminant sepsis (meningococcemia), meningitis, and pneumonia. The incidence of meningococcal infection has long been higher in infancy than adolescents or adults older than 65 years (a third group with an increased risk based on age). Five meningococcal serogroups (A, B, C, Y, and W135) cause the great majority of human disease. Serogroup B strains cause about two-thirds of disease in children younger than 6 years. For this reason, new meningococcal vaccine formulations have been developed and evaluated in children younger than 2 years.

Of four meningococcal vaccines currently licensed in the United States, two conjugate products, (MenACWY-D [Menactra], Sanofi Pasteur; HibMenCY-TT [MenHibrix], GlaxoSmithKline), are recommended for infants and toddlers younger than 2 years who have an increased risk for invasive meningococcal disease. High-risk conditions are complement deficiencies, community outbreaks, functional or anatomic asplenia, and travel to high-risk areas in which serogroup A infection is prevalent. Recommendations vary by age, dosing, and indication between these two products. Both licensed products are immunogenic and have side-effect profiles that are considered safe for use. In most cases, concomitant use with other recommended childhood vaccines does not interfere with responses to these vaccines.

As of yet, there has not been universal adoption of this immunization in the infant population by parents or providers. Factors that weigh against the implementation of a national routine infant program include the prevention of only 40 to 50 meningococcal cases, two to four deaths per year, and a relatively low case fatality among infants. Some argue that costs should not be considered a barrier because infant deaths and morbidity would be prevented. The availability of a serogroup B vaccine would improve impact and cost-effectiveness of a routine infant meningococcal vaccine program. Debate over the implementation of routine infant meningococcal vaccination in the United States is ongoing. This review focuses on vaccines for the prevention of *N. meningitidis* infection in infants and young toddlers in the first 2 years of life.
The spectrum of disease caused by *Neisseria meningitidis* includes bacteremia, fulminating sepsis (meningococcemia), meningitis, and pneumonia. The incidence of meningococcal infection has long been higher in infancy than adolescents or adults older than 65 years (a third group with an increased risk based on age). For this reason, new meningococcal vaccine formulations have been developed and evaluated in children younger than age 2 years.

Four meningococcal vaccines are currently licensed for use in the United States (see Table 1). Of these vaccines, two conjugate products, (MenACWY-D [Menactra], Sanofi Pasteur; HibMenCY- TT [MenHibrix], GlaxoSmithKline), are recommended for infants and toddlers younger than 2 years who have an increased risk for invasive meningococcal disease.

High-risk conditions are complement deficiencies, community outbreaks, functional or anatomic asplenia, and travel to high-risk areas in which serogroup A infection is prevalent. Recommendations vary by age, dosing, and indication between these two products. This review focuses on vaccines for the prevention of *N. meningitidis* infection in infants and young toddlers in the first 2 years of life.

**OVERVIEW OF MENINGOCOCCAL EPIDEMIOLOGY**

Humans are the only reservoir of *N. meningitidis*. Asymptomatic colonization of the nasopharynx by meningococcal strains is far more common than invasive disease. Meningococcal infection was cyclic in the United States during the 1900s but has declined since the most recent peak in the late 1990s. Incidence reached a historic low in 2005 before the introduction of the meningococcal conjugate vaccine that year (see Figure 1). Only 800 to 1,200 cases of *N. meningitidis* infection have occurred annually in the United States from 2005 to 2011.

The overall incidence in the United States was 0.4 cases per 100,000 population between 2002 and 2011 (see Table 2). The highest incidence occurs during the first 5 months of life (5.3 per 100,000) followed by 6- to 11-month-olds (3.4 per 100,000) (see Figure 2). Incidence among 11- to 24-year-olds (0.4 to 0.5 per 100,000) is more than 10-fold less than young infants (see Table 1). However, case fatality is lower among young children compared with adolescents and adults. A meta-analysis of 89 studies showed that nasopharyngeal carriage of *N. meningitidis* occurs in 4% to 5% of infants and rises gradually through childhood. A sharp increase in carriage begins in adolescence, peaks at 24% in 19-year-olds, and decreases to 13% by 30 years.

Case fatality rates of meningococcal infection have been stable for several decades at 10% to 15%. Long-term sequelae, such as neurologic disability or loss of limbs or digits occur in 11% to 19% of survivors. Case fatality is lower in infants; in a recent US study, 21% of adolescents 11 years or older died versus 5% of children younger than 11 years. Among children who survive serogroup B infections, about one-third have one or more deficits in physical, cognitive, or neuropsychological functioning, and 10% have major disabling deficits.

Five of 13 serogroups of *N. meningitidis* (A, B, C, Y, and W135) cause the great majority of human disease worldwide. Serogroups are defined by antigenic variation of the capsular polysaccharide. Four serogroups that elaborate sialic acid–based capsules (B, C, Y, and W135) are predominant in North and South America, Europe, and Australia. Serogroups B, C, and Y each account for about one-third of cases of invasive disease in the United States, but serogroup B strains caused 66% of disease in children younger than 6 years from 2002 through 2011. About 98% of cases in the United States are sporadic, but outbreaks caused by serogroup B or C strains occur occasionally.

Host risk factors for infections caused by *N. meningitidis* include genetic deficiencies in the common complement pathway. Deficiencies of C3, properdin, factor D, factor H, or any of the components of the C5-C9 terminal attack complex confer up to a 10,000-fold risk of meningococcal infection over the general population. Anatomic or functional asplenia increases the risk for meningococcal disease but less so than for invasive pneumococcal infections. Antecedent viral infections, household crowding, passive smoke exposure, and chronic underlying illness are other risk factors for meningococcal infection and could affect infants and toddlers.

**THE PATHWAY TO INFANT MENINGOCOCCAL VACCINES**

Once *N. meningitidis* is acquired in the nasopharynx, strain-specific serum bactericidal antibodies are typically detectable in serum within 2 weeks. The presence of serum antibodies against capsular polysaccharides or outer membrane proteins appears to be necessary and adequate for protection against meningococcal infection. Human complement-dependent serum bactericidal assays (hSBAs) are used to assess antibody responses in clinical trials. hSBA titers are considered protective when ≥ 1:4. Higher titers suggest a longer duration of immunity.

**Serogroups A and C**

Meningococcal vaccines based on capsular polysaccharide antigens for serogroups A, C, Y, and W135 have been
### TABLE 1.

**Recommendations for Use of the Meningococcal Vaccines Currently Licensed* in the United States in Children Younger than 2 Years**

<table>
<thead>
<tr>
<th>Vaccine Product</th>
<th>Vaccine Components</th>
<th>Current Status for Use in Children Younger than 2 Years</th>
<th>Dosing Schedule in Children Younger than 2 Years</th>
<th>Booster Dose Recommendations for Children Vaccinated Younger than 2 Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hib-MenCY-TT (MenHibrix, GlaxoSmithKline)</td>
<td>5-mcg serogroups C and Y capsular polysaccharides and 2.5-mcg Hib capsular polysaccharide conjugated to 5 mcg and 6.5 mcg and 6.25 mcg, respectively, for tetanus toxoid</td>
<td>Recommended for use only in high-risk children who:⁴  - Have persistent complement deficiencies⁵  - Are at risk during a community outbreak attributable to a vaccine serogroup  - Have functional or anatomic asplenia</td>
<td>4 doses at 2, 4, 6, and 12-15 months</td>
<td>Children who have ongoing increased risk of meningococcal infection who completed the primary dose or series at age: 2 months to 6 years: should receive an additional dose of MenACWY-D or MenACWY-CRM 3 years after the last dose of the primary series; boosters should be repeated every 5 years thereafter 7 years or older: should receive an additional dose of MenACWY-D or MenACWY-CRM 5 years after the last dose of the primary series; boosters should be repeated every 5 years thereafter</td>
</tr>
<tr>
<td>MenACWY-D (Menactra, Sanofi Pasteur)</td>
<td>4-mcg serogroups A, C, W135, and Y capsular polysaccharides conjugated to 48-mcg diphtheria toxoid</td>
<td>Recommended for use only in high-risk children who:⁴  - Have persistent complement deficiencies⁵  - Are at risk during a community outbreak attributable to a vaccine serogroup  - Travel to or are residents of countries where meningococcal disease is hyperendemic or epidemic</td>
<td>2 doses 12 weeks apart⁶</td>
<td>N/A</td>
</tr>
<tr>
<td>MenACWY-CRM (Menveo, Novartis)</td>
<td>10-mcg serogroup A capsular polysaccharide and 5-mcg serogroups C, W135, and Y conjugated to 33-64 mcg CRM197⁷</td>
<td>Not recommended for use in children younger than age 2 years at this time¹⁰</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>MPSV4 (Menomune, Sanofi Pasteur)</td>
<td>50-mcg serogroups A, C, W135, and Y capsular polysaccharides</td>
<td>Not recommended for use in children younger than age 2 years. May be considered for infants age 2 months to &lt; 9 months for potential protection against serogroup A infection when traveling to countries where meningococcal disease is hyperendemic or epidemic¹⁰,¹¹</td>
<td>Single dose when used for this travel scenario</td>
<td>N/A</td>
</tr>
</tbody>
</table>

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*Recommendations as of May 8, 2013. See www.cdc.gov/vaccines for possible updates to these recommendations.

⁴Infants and children who received Hib-MenCY-TT and are traveling to areas with high endemic rates of meningococcal disease such as the African “meningitis belt” are not protected against serogroups A and W135 and should receive a quadrivalent meningococcal vaccination licensed for children 9 months or older before travel.

⁵Includes persons who have persistent complement deficiencies of C3, C5 to C9, properdin, factor H, or factor D.

⁶Because of a high risk for invasive pneumococcal disease, children with functional or anatomic asplenia should not be immunized with MenACWY-D (Menactra) before 2 years to avoid interference with the immune response to the pneumococcal conjugate vaccine series.

⁷If an infant is receiving the vaccine before travel, two doses may be administered with the second dose given as soon as 8 weeks after the first dose.

⁸CRM197 is a naturally occurring, nontoxic form of diphtheria toxin from Corynebacterium diphtheriae.

⁹This product has been studied in clinical trials in children younger than 2 years old (see text).


¹¹Alternatives for infants younger than 9 months at this time are no vaccination or off-label use of a conjugate meningococcal vaccine containing serogroup A polysaccharide that is currently licensed for older age groups.

Adapted from Cohn et al.²
available since the 1970s. Efficacies of the serogroup A and C components are ≥ 90%. Antibody titers induced by the meningococcal quadrivalent (ACWY) polysaccharide vaccine (Menomune [MPSV4], Sanofi Pasteur) against serogroups Y and W135 are comparable with those of serogroups A and C. These polysaccharide antigens interact directly with B lymphocytes in a T-cell–independent manner. This induces an antibody response but does not generate a memory B-cell population sufficient for adequate anamnestic antibody responses.

The duration of immunity after MPSV4 is of short duration, 3 to 5 years at most even in adults. Infants respond poorly to these polysaccharide antigens. Antibody titers comparable with those in adults are not seen until 4 or 5 years. Some infants develop transient protective antibody titers with better responses against serogroup A than C.

Covalent coupling (conjugation) of a protein to the capsular polysaccharide changes the human immune response to a T-lymphocyte–dependent process. This produces memory B cells that can respond to future exposures of the antigen. Young infants also can mount such responses. The success of the conjugate Haemophilus influenzae type b (Hib) vaccine program led to the application of this approach for the development of conjugate meningococcal vaccines.

**Serogroup B**

The development of serogroup B meningococcal infections has been slow because this polysaccharide is structurally similar to sialic acid moieties expressed in human neural tissues and may function as an autoantigen. Antibodies against the group B capsule react in vitro with neural cell adhesion molecules in fetal brain tissue. The B polysaccharide also does not elicit serum bactericidal antibodies. Efforts to develop vaccines against serogroup B strains have focused on proteins that are exposed on the outer cell membrane of meningococci. Broad cross-protection has been difficult to achieve because of substantial antigenic variation in many N. meningitidis proteins from frequent recombination events with other strains and related species.

A vaccine based on outer membrane vesicles that contain porin proteins was used successfully to control a serogroup B outbreak in New Zealand. Whole genome analysis of serogroup B strains led to the identification of relatively conserved meningococcal proteins that elicit serum bactericidal antibodies. The human complement factor H binding protein and Neisseria adhesin A have been fused with minor genome-derived antigens 2091 and 1030, respectively, which improve their immunogenicity. These proteins have been combined with outer membrane vesicles in a serogroup B vaccine (Bexsero, Novartis) that was approved in Europe in November 2012 for use in people 2 months and older. Another bivalent factor H binding protein fHpb-based serogroup B vaccine is under evaluation in clinical trials in young children.

Because infections caused by N. meningitidis are generally uncommon, randomized clinical trials to determine vaccine efficacy commonly are not feasible because of the large sample sizes and costs that would be involved. The effectiveness of the currently licensed protein conjugate meningococcal vaccines has been inferred by comparing serum bactericidal assay measurements of antibody responses to the new vaccines compared with MPSV4 for people 2 to 55 years and by determining the magnitude of seroresponses among children between 2 and 23 months.

**Efficacy of Conjugate Meningococcal Vaccines**

Two years after the introduction of a conjugate serogroup C meningocc...
cal vaccination program among 0- to 18-year-olds in the United Kingdom in 1999, serogroup C disease was reduced by 81%. Among infants, for whom a 2-, 3-, and 4-month vaccine series was implemented, serogroup C disease decreased by 83%. Nasopharyngeal carriage of serogroup C strains decreased by 80% among 15- to 19-year-olds. Carriage of serogroups B, Y, and W135 remained stable with no evidence of serogroup replacement. Vaccine efficacy against serogroup C was estimated at 75%.30,31

A monovalent conjugate serogroup C vaccine program was introduced in Ontario, Canada, in 2001. A single dose was administered at 12 months of age with catch-up doses given to previously unvaccinated people at ages 12 or 15 to 19 years.32 From 2001 through 2006, the rate of serogroup C disease in Ontario decreased by 50%, whereas disease caused by other serogroups decreased by about 6%. The decline in the serogroup C incidence rate was much more substantial in children ages 1 to 14 years (77% decline; 95% CI, 63%-94%) than infants who were not vaccinated (25% decline; 95% CI, 5%-139%). Similar results occurred in other Canadian provinces.33

Breakthrough infections have occurred in some conjugate serogroup C vaccine recipients despite their ability to mount an anamnestic antibody response to the infection.34 When people with low or nonprotective antibody titers against serogroup C polysaccharide 12 months after vaccination were challenged with 50 mcg C polysaccharide intranasally, protective levels of antibodies in serum or mucosal surfaces did not appear until 7 days after challenge.35 These findings suggest that protection against meningococcal infection requires persisting antibody titers above a protective threshold, at least in some cases, rather than immunologic memory alone because meningococcal infection may outpace the anamnestic antibody response rate.

CURRENT RECOMMENDATIONS FOR VACCINATION

Routine vaccination against meningococcal infection is currently not recommended for children younger than 11 years in the United States.1 Of the four meningococcal vaccines currently licensed in the United States, two conjugate products are recommended for infants and toddlers younger than 2 years who have an increased risk for invasive

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### TABLE 2.

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Serogroup B</th>
<th></th>
<th></th>
<th>Serogroup C</th>
<th></th>
<th></th>
<th>Serogroup Y</th>
<th></th>
<th></th>
<th>Other</th>
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<th>Total</th>
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<tbody>
<tr>
<td>No.</td>
<td>Rate</td>
<td>No.</td>
<td>Rate</td>
<td>No.</td>
<td>Rate</td>
<td>No.</td>
<td>Rate</td>
<td>No.</td>
<td>Rate</td>
<td>No.</td>
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<td></td>
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<tr>
<td>&lt; 1 year</td>
<td>117</td>
<td>2.8</td>
<td>14</td>
<td>0.3</td>
<td>38</td>
<td>0.9</td>
<td>8</td>
<td>0.2</td>
<td>177</td>
<td>4.3</td>
<td></td>
<td></td>
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<tr>
<td>0 to 5 months</td>
<td>74</td>
<td>3.6</td>
<td>5</td>
<td>0.3</td>
<td>23</td>
<td>1.1</td>
<td>6</td>
<td>0.3</td>
<td>108</td>
<td>5.3</td>
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<tr>
<td>6 to 11 months</td>
<td>43</td>
<td>2.1</td>
<td>9</td>
<td>0.4</td>
<td>15</td>
<td>0.7</td>
<td>2</td>
<td>0.1</td>
<td>69</td>
<td>3.4</td>
<td></td>
<td></td>
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<tr>
<td>1 year</td>
<td>28</td>
<td>0.7</td>
<td>9</td>
<td>0.2</td>
<td>2</td>
<td>0.1</td>
<td>3</td>
<td>0.1</td>
<td>42</td>
<td>1.0</td>
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<tr>
<td>2 to 4 years</td>
<td>38</td>
<td>0.3</td>
<td>16</td>
<td>0.1</td>
<td>8</td>
<td>0.1</td>
<td>7</td>
<td>0.1</td>
<td>69</td>
<td>0.6</td>
<td></td>
<td></td>
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<tr>
<td>5 to 10 years</td>
<td>31</td>
<td>0.1</td>
<td>16</td>
<td>0.1</td>
<td>12</td>
<td>0</td>
<td>3</td>
<td>0</td>
<td>62</td>
<td>0.3</td>
<td></td>
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<tr>
<td>11 to 18 years</td>
<td>28</td>
<td>0.1</td>
<td>43</td>
<td>0.1</td>
<td>43</td>
<td>0.1</td>
<td>10</td>
<td>0</td>
<td>124</td>
<td>0.4</td>
<td></td>
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<tr>
<td>19 to 21 years</td>
<td>26</td>
<td>0.2</td>
<td>23</td>
<td>0.2</td>
<td>16</td>
<td>0.1</td>
<td>3</td>
<td>0</td>
<td>68</td>
<td>0.5</td>
<td></td>
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<tr>
<td>22 to 24 years</td>
<td>21</td>
<td>0.2</td>
<td>22</td>
<td>0.2</td>
<td>7</td>
<td>0.1</td>
<td>1</td>
<td>0</td>
<td>51</td>
<td>0.4</td>
<td></td>
<td></td>
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<tr>
<td>25 to 64 years</td>
<td>93</td>
<td>0.1</td>
<td>129</td>
<td>0.1</td>
<td>125</td>
<td>0.1</td>
<td>21</td>
<td>0</td>
<td>368</td>
<td>0.2</td>
<td></td>
<td></td>
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<tr>
<td>≥ 65 years</td>
<td>20</td>
<td>0.1</td>
<td>33</td>
<td>0.1</td>
<td>114</td>
<td>0.3</td>
<td>19</td>
<td>0.1</td>
<td>186</td>
<td>0.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>402</td>
<td>0.1</td>
<td>305</td>
<td>0.1</td>
<td>365</td>
<td>0.1</td>
<td>76</td>
<td>0</td>
<td>1,146</td>
<td>0.4</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Per 100,000 population.
†Active Bacterial Core Group (ABC) cases from 2002 to 2011 estimated in the US population with 18% correction for underreporting. In 2010, estimated case counts from ABCs were lower than cases reported to the National Notifiable Diseases Surveillance System and might not be representative.
‡Includes serogroup W135, nongroupable, and other serogroups.

(From Cohn et al9, with permission)
meningococcal disease (MenACWY-D [Menactra], Sanofi Pasteur; HibMenCY-TT [MenHibrix], GlaxoSmithKline). A third conjugate product has been studied in infants (MenACWY-CRM [Meneveo, Novartis]), and MPSV4 still has one potential role for some traveling infants (see Table 1). Other conjugate meningococcal vaccine formulations also have been investigated in infants.36,37

MenACWY-D

MenACWY-D is licensed for use as a two-dose series for children between 9 and 23 months for specific high-risk conditions1 (see Table 1). Four studies of this series included 2,577 children who received two doses according to protocol and 3,721 who were monitored for safety outcomes.36,39 More than 90% of infants who received doses at 9 and 12 months developed protective bactericidal antibody titers ≥ 1:4 in hSBA assays (≥ 97.3% for serogroup A, ≥ 98.9% for C, ≥ 95.1% for Y, and ≥ 91.0% for W135). Titters ≥ 1:8 were achieved in ≥ 90.5% for serogroup A, ≥ 97.8% for C, ≥ 95.1% for Y, and ≥ 81.2% for W135.

MenACWY-D does not appear to interfere with responses to measles, mumps, and rubella and varicella or measles, mumps, rubella, varicella vaccines of Hib vaccine when administered concurrently.38 Immunoglobulin G responses to the seven serotypes in the pneumococcal conjugate vaccine 7-valent vaccine exceeded the defined protective concentrations for all seven types in > 98% of 12-month-olds vaccinated concomitantly with MenACWY-D. However, noninferiority criteria for ratios of the upper bounds of the 95% CIs were not met for responses to serotypes 4, 6B, and 18C. For this reason, MenACWY-D is not recommended for the prevention of meningococcal infection in infants and toddlers with anatomic or functional asplenia given the much greater risk of pneumococcal infections in these patients1 (see Table 1).

Adverse Events

The vaccine is well tolerated. Injection site reactions such as tenderness, erythema, and swelling are noted to some degree in 47% of 9-month-olds after MenACWY-D alone and 44% at 12 months old after MenACWY-D plus other vaccines recommended for this age group.38 Systemic reactions such as irritability soon after vaccination are common but not excessive. Fever after MenACWY-D alone occurs in about 12% of infants, but high fever is uncommon.39

Initial concerns about the increased risk of Guillain-Barré syndrome (GBS) among adolescents after receipt of MenACWY-D soon after its licensure have not been confirmed by large population-based studies. No cases of GBS were identified within 42 days of vaccination with MenACWY-D among 889,684 recipients between 2005 and 2010. A history of GBS is no longer considered a precaution for receipt of meningococcal vaccines by the Centers for Disease Control and Prevention.38 Systemic reactions such as tenderness, erythema, and swelling are noted to some degree in > 90% of infants.

HibMenCY-TT

HibMenCY-TT is licensed for use as a four-dose series in children between 6 weeks and 18 months with specific high-risk conditions1 (see Table 1). It is the only product recommended for infants younger than 2 years with anatomic or functional asplenia. Approval was based on the results of six studies that included 6,686 children who received the four-dose series. hSBA antibody titers ≥ 1:8 against serogroup C were induced in ≥ 98.5% after three and four doses and against serogroup Y in 95.8% after three and 98.8% after four doses. Protective titers against both serogroups persisted between doses three and four in > 90% of infants.40-42

The coadministration of HibMenCY-TT does not interfere with antibody responses to antigens contained in other vaccines recommended in the 6-week to 18-month age groups.43,44 HibMenCY-TT also is well tolerated. Local injection site reactions and irritability are common, but frequencies are comparable with or less than in control subjects. Fever occurs in 19% to 26% after the first three doses and 11% after the fourth dose, but fever greater than 104°F is rare (≤ 0.3%).40,43

MenACWY-CRM

MenACWY-CRM is not currently recommended for use in children younger than 2 years.

MenACWY-CRM is not currently recommended for use in children younger than 2 years.36,37,39

MPSV4

MPSV4 is not formally recommended for use in infants, but travel safety guidance provided by the Centers for Disease Control and Prevention states that “the serogroup A polysaccharide in MPSV4 induces an antibody response in some children as young as 3 months. Thus, vaccinating infants traveling to high-risk areas can provide some degree
of protection.\(^{48}\) Therefore, MPSV4 may be considered for infants 3 months to younger than 9 months who are traveling from the United States to areas of high risk for exposure to serogroup A strains (eg, sub-Saharan Africa).\(^ {48}\) If a conjugate vaccine containing serogroup A antigen is approved for use in this age group, it would supplant MPSV4 in this scenario.

**DURATION OF IMMUNITY**

Antibody titers often wane rapidly in infants and young children.\(^ {38}\) Protective levels persisted in only about 50% of 2-year-olds 6 months after receipt of a single dose of MenACWY-D. Among infants vaccinated at 9 months and 12 to 15 months, < 50% maintained protective titers were 3 years after the second dose.\(^ {1}\) Five years after receipt of a four-dose series of Hib-MenCY-TT, hSBA titers were ≥ 1:8 against serogroups C and Y in 83% and 74% of infants, respectively.\(^ {5}\) Five years after receipt of a single dose of HibMenCY-TT at 12 to 15 months, hSBA titers were ≥ 1:8 against serogroups C and Y in 70% and 54% of infants, respectively.\(^ {49}\)

**ROADBLOCKS TO UNIVERSAL INFANT VACCINATION**

The implementation of routine vaccination against meningococcal infection for infants in the United States appears to have a straightforward rationale, because infants have the highest incidence of infection and vaccination for adolescents is routinely recommended. Costs per quality-adjusted life year saved are estimated to be similar for a four-dose infant program and one-dose adolescent program at $139,000 and $145,000 in US 2010 dollars, respectively.\(^ {1}\)

Several factors weigh against taking on the additional costs of a national routine infant program. Such a program likely would prevent only 40 to 50 meningococcal cases and two to four deaths per year because about 60% of cases in this age group are caused by serogroup B.\(^ {4,50}\) The current low incidence of meningococcal disease, the relatively low case fatality rate in infants, and the potential herd immunity-based reduction in infant cases from the adolescent program are other issues.\(^ {41}\) The routine recommendation of currently licensed products would further complicate decision making regarding which vaccine product lines to purchase at practice or system levels because of product differences in age recommendations, meningococcal strains covered, and the inclusion of the Hib antigen. An infant program also is unlikely to eliminate the need for the adolescent program because of waning antibody titers.

An increase in the incidence of meningococcal infection or a change in serogroup distribution among infants could influence cost considerations. Arguments also have been made that the cost of universal vaccination of infants with currently licensed meningococcal vaccines should not be considered excessive because a number of infant deaths would be prevented annually and others would not suffer lifelong morbidities.\(^ {41}\) The availability of vaccines to prevent serogroup B infections, especially if combined with vaccines against other serogroups, would substantially improve the impact of a routine infant meningococcal vaccine program and likely improve its cost-effectiveness. The multiprotein-antigen-based serogroup B vaccine recently approved in Europe should be effective against most (but not all) circulating strains of serogroup B in the United States.\(^ {24}\) The debate over high risk only versus routine vaccination of infants against meningococcal infections in the United States is ongoing.\(^ {51}\)

**REFERENCES**


17. Centers for Disease Control and Prevention. Prevention and control of meningococcal disease and control and prevention of serogroup C meningococcal disease: evaluation and


