Report from the Advisory Committee on Immunization Practices (ACIP): Decision Not to Recommend Routine Vaccination of All Children Aged 2--10 Years with Quadrivalent Meningococcal Conjugate Vaccine (MCV4)

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At its February 2008 meeting, the Advisory Committee on Immunization Practices (ACIP) decided not to recommend routine vaccination of children aged 2--10 years against meningococcal disease unless the child is at increased risk for the disease. This report summarizes the deliberations of ACIP and the rationale for its decision and restates existing recommendations for meningococcal vaccination among children aged 2--10 years at increased risk for meningococcal disease. ACIP continues to recommend routine vaccination against meningococcal disease for all persons aged 11--18 years and those persons aged 2--55 years who are at increased risk for meningococcal disease (*1*--*3*).

On October 17, 2007, the Food and Drug Administration added approval for use of quadrivalent meningococcal conjugate vaccine (MCV4) (Menactra®, Sanofi Pasteur, Swiftwater, Pennsylvania) in children aged 2--10 years to existing approval for use in persons aged 11--55 years (*4*). Before licensure of MCV4, quadrivalent meningococcal polysaccharide vaccine (MPSV4) (Menomune®, Sanofi Pasteur) was the only meningococcal vaccine available in the United States. MPSV4 was recommended for routine use only among persons at increased risk for meningococcal disease (*1*). Because clinical efficacy trials were not feasible in the United States, MCV4 licensure was based on clinical trials in which the safety and immunogenicity of MCV4 was compared with MPSV4. Immunogenicity was measured by serum bactericidal activity (SBA), a correlate of protection. Rates of most solicited local and systemic adverse events after MCV4 vaccination were comparable to rates observed after administration of MPSV4 (*5*). The proportion of children aged 2--10 years who did not have detectable SBA (titer <1:8) at day 0 and seroconverted (titer >1:32) by day 28 after MCV4 vaccination was 98.6% for serogroup A, 87.9% for serogroup C, 86.2% for serogroup Y, and 96.0% for serogroup W-135, similar to MPSV4 for all serogroups (Table) (*5*). Hence, MCV4 was found to be safe and noninferior to MPSV4 for all serogroups.

During June 2007--February 2008, the ACIP Meningococcal Vaccine Workgroup considered use of MCV4 among children aged 2--10 years by reviewing data on MCV4 immunogenicity and safety in this age group, the epidemiology and burden of meningococcal disease, cost-effectiveness of various vaccination strategies, and programmatic implications. These data, expert opinion of workgroup members, and feedback from partner organizations were presented by the workgroup to the full ACIP at the October 2007 and February 2008 ACIP meetings for its deliberation regarding a potential recommendation to vaccinate only those children at increased risk for meningococcal disease, among children aged 2--10 years.

Summary of ACIP Deliberations and Rationale

ACIP evaluated data to determine the anticipated duration of protection from a single dose of MCV4 in children aged 2--10 years. The duration of protection of MPSV4 is considered to be short (3--5 years), especially in young children, based on substantial declines in measurable levels of antibodies against group A and C polysaccharides by 3 years after vaccination (*6,7*). Although SBA titers at 28 days and 6 months after vaccination were significantly higher in children aged 2--10 years who received MCV4 compared with children who received MPSV4 for all four serogroups ($p<0.001$) (*5*), the difference in magnitude of SBA titers between children in the two groups was not substantial (Table). Further, SBA activity among children aged 2--3 years who received MCV4 was lower than in children aged 4--10 years. Based on these data, ACIP concluded that evidence was insufficient to determine that 1 dose of MCV4 administered at age 2 years would provide protection against meningococcal disease through late adolescence and college entry.

ACIP also reviewed the burden of meningococcal disease among children aged 2--10 years. In the United States, during 1998--2007, overall rates of meningococcal disease were lower in children aged 2--10 years (0.68 per 100,000 population) than in infants aged <2 years and adolescents aged 11--19 years (3.9 and 0.81 per 100,000, respectively). Furthermore, 41% of cases in children aged 2--10 years occurred among children aged 2--3 years. In addition, among cases that occurred in children aged 2--10 years, 59% were caused by serogroups contained in MCV4 (A, C, Y, and W-135), compared with 77% of cases among youths aged 11--19 years. Annually, an estimated 160 cases of A/C/Y/W-135 disease and 13 deaths occur in children aged 2--10 years, compared with 250 cases and 15 deaths among youths aged 11--19 years (Active Bacterial Core Surveillance [ABCs], unpublished data, 1997--2006).

A cost-effectiveness analysis of vaccinating a cohort of U.S. children aged 2 years also was presented at the February 2008 ACIP meeting. A Monte Carlo simulation analysis was used in which multiple parameters were varied simultaneously over specified probability distributions. Data on age- and serogroup-specific meningococcal incidence rates during 1991--2005 and case-fatality ratios from ABCs were used, in addition to published estimates of meningococcal disease complications (e.g., hearing loss and limb amputations) and vaccine efficacy (*8*). Duration of protection of 10 years from vaccination was assumed. Using standard cost-effectiveness methods, the analysis estimated that 205 meningococcal cases and 14 premature deaths could be prevented by vaccinating a cohort of 4 million children aged 2 years at a cost of $160,000 per quality-adjusted life year (QALY) saved. For a program conducting routine vaccination of children aged 11 years, the analysis estimated a cost of $90,000 per QALY saved. Hence, vaccinating children aged 2 years was determined to be less cost-effective than vaccinating children aged 11 years (*8*).

Because approximately 75% of cases of disease in children aged 2 years occur at age 24--29 months, the effectiveness of routine MCV4 vaccination of children aged 2 years in reducing the burden of disease is dependent on achieving high coverage at age 24 months (ABCs, unpublished data, 2008). However, achieving high coverage with MCV4 at age 24 months might be challenging. For example, during 1999--2006, before licensure of hepatitis A vaccine for use in children aged 12--23 months, ACIP recommended administration of hepatitis A vaccine to children at age 2 years in states with historically high rates of hepatitis A. After that recommendation was in effect for 5 years in the 11 states where vaccination was recommended, 1-dose coverage was 54.4% (range by state: 8.6%--74.4%) among children aged 24--35 months (*9*).

ACIP Decision and Continuing Recommendations

Based on reviews of safety and immunogenicity data, the epidemiology of meningococcal disease, a cost-effectiveness analysis, and programmatic considerations, ACIP decided not to recommend routine vaccination against meningococcal disease for all children aged 2--10 years at its February 2008 meeting. ACIP continues to recommend vaccination for children aged 2--10 years at increased risk for meningococcal disease. These children include travelers to or residents of countries in which meningococcal disease is hyperendemic or epidemic, children who have terminal complement deficiencies, and children who have anatomic or functional asplenia. Health-care providers also may elect to vaccinate children aged 2--10 years who are infected with human immunodeficiency virus (HIV).* MCV4 is preferred to MPSV4 for children aged 2--10 years in these groups at increased risk and for control of meningococcal disease outbreaks. In addition, if health-care providers or parents elect to provide meningococcal vaccination to other children in this age group, MCV4 is preferred to MPSV4. Recommendations for use of MCV4 in persons aged 11--55 years, including a recommendation for routine vaccination with MCV4 of persons aged 11--18 years, have been published previously and remain unchanged (*1,3*).

For children aged 2--10 years who have received MPSV4 and remain at increased risk for meningococcal disease, ACIP recommends vaccination with MCV4 at 3 years after receipt of MPSV4. Children who last received MPSV4 more than 3 years before and remain at increased risk for meningococcal disease should be

vaccinated with MCV4 as soon as possible. For children at lifelong increased risk for meningococcal disease, subsequent doses of MCV4 likely will be needed. ACIP will monitor available data on duration of protection to determine whether recommendations for revaccination with MCV4 are indicated. Persons with a history of Guillain-Barré syndrome (GBS) might be at increased risk for GBS after MCV4 vaccination (*3*); therefore, a history of GBS is a precaution to administration of MCV4.

Effective meningococcal conjugate vaccines for infants might be available in the near future. Phase III clinical trials for meningococcal conjugate vaccine in infants are ongoing, and published data suggest these vaccines are safe and immunogenic (*10*). Vaccines that provide protection against meningococcal disease early in life have the potential to greatly reduce the burden of meningococcal disease, especially if they provide protection against serogroup B meningococcal disease.

References

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Table

TABLE. Percentage of children aged 2–10 years in clinical trials with no detectable serum bactericidal activity (SBA) (titer <1:8) at day 0 who seroconverted (titer >1:32) by day 28 by using baby rabbit complement (rSBA), and rSBA geometric mean titer (GMT) 28 days after vaccination with meningococcal conjugate vaccine (MCV4) and meningococcal polysaccharide vaccine (MPSV4)* — United States

	% who seroconverted				rSBA GMT			
	MCV4		MPSV4		MCV4		MPSV4	
Serogroup	%	(95% CI†)	%	(95% CI)	No.	(95% CI)	No.	(95% CI)
A	98.6	(96.4–99.6)	94.7	(91.4–97.0)	1,700	(1,512–1,912)	893	(791–1,009)
C	87.9	(83.9–91.2)	80.1	(75.6–84.0)	354	(308–407)	231	(198–270)
Y	86.2	(77.2–92.7)	75.0	(65.1–83.3)	637	(563–720)	408	(362–460)
W-135	96.0	(93.6–97.7)	89.6	(86.1–92.4)	750	(657–855)	426	(372–487)

SOURCE: Pichichero M, Casey J, Blatter M, et al. Comparative trial of the safety and immunogenicity of quadrivalent (A, C, Y, and W-135) meningococcal polysaccharide-diphtheria conjugate vaccine versus quadrivalent polysaccharide vaccine in two-to-ten-year-old children. Pediatr Infect Dis J 2005;24:57–62.
* Numbers of subjects with titer <1:8 at baseline, MCV4 group = 279 for serogroup A, 338 for serogroup C, 87 for serogroup Y, and 400 for serogroup W-135. Numbers of subjects with titer <1:8 at baseline, MPSV4 group = 281 for serogroup A, 366 for seroroup C, 96 for serogroup Y, and 402 for serogroup W-135.
† Confidence interval.

Return to top.