Prevention of Meningococcal Disease: Current Use of Polysaccharide and Conjugate Vaccines

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Invasive meningococcal disease (IMD), although uncommon, is difficult to diagnose and can be rapidly fatal, even in healthy young persons. IMD is cyclic, and serogroups responsible for disease vary by age group, although the prevalence of the serogroups changes over time and by geographical location. Two quadrivalent vaccines are licensed in the United States to prevent IMD caused by serogroups A, C, Y, and W-135, and the US Centers for Disease Control and Prevention recommends routine vaccination with quadrivalent meningococcal conjugate vaccine of adolescents 11–18 years of age and vaccination of persons 2–55 years of age who are at elevated risk of IMD. Efforts to prevent IMD remain challenging, because there is neither an immunogenic vaccine for infants nor a vaccine to prevent serogroup B disease that is currently licensed. Obstacles to achieving optimal vaccine coverage among adolescents persist, and strategies are needed to address these shortcomings.

Although widespread use of conjugate vaccines has dramatically reduced the incidence of meningitis caused by *Streptococcus pneumoniae* [1] and *Haemophilus influenzae* type b [2], *Neisseria meningitidis* remains a leading cause of meningitis and septicemia in the United States. Invasive meningococcal disease (IMD) caused by *N. meningitidis* is relatively uncommon, but the consequences can be devastating. Even when treated in an otherwise healthy person, IMD can be fatal within 48 h. Case-fatality rates exceed 10%, and up to 20% of survivors sustain permanent sequelae, including neurologic complications, loss of limbs, hearing loss, and paralysis [3, 4]. This review summarizes current recommendations for vaccine prevention of meningococcal disease and strategies to improve vaccine coverage among adolescents.

EPIDEMIOLOGY

Humans are the sole host of *N. meningitidis,* which colonizes the nasopharynx and spreads through direct contact with respiratory secretions. Most IMD in the United States is caused by endemic disease, although the frequency of local outbreaks is increasing. The incidence of IMD is now ebbing, but meningococcal disease occurrence is cyclical and may affect as many as 3000 persons in the United States annually during peak periods [5]. The cyclical nature of IMD and the risk of local outbreaks underscore the need to remain vigilant about promoting prevention behaviors and immunization practices, even when incidence is low.

Currently, *N. meningitidis* serogroups A, B, C, Y, and W-135 are the most important clinically (Table 1) [6]. The serogroups responsible for meningococcal disease vary by age and can change rapidly, making coverage against as many serogroups as possible crucial to a successful vaccine strategy. For example, the occurrence of W-135 disease in Hajj pilgrims in 2000 resulted in global outbreaks when they returned home, even though many had been vaccinated against serogroups A and C. In the United States, the proportion of cases caused by serogroup Y increased from 2% to 37% from the early 1990s to the early 2000s [5].

The incidence of meningococcal disease is highest among children <2 years of age, adolescents, and the elderly, with the highest mortality occurring among infants and teens (Figure 1) [7]. About half of meningococcal disease in infants is caused by serogroup B,

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Table 1. Clinically Significant Serogroups of *Neisseria meningitidis.*

Serogroup	Characteristics
A	• Leading cause of epidemic meningitis worldwide • Most prevalent serogroup in Africa and China • Rare in Europe and the Americas
B	• Major cause of endemic disease in Europe and the Americas • No vaccine available
C	• Major cause of endemic disease in Europe and North America • Multiple outbreaks in schools and communities
Y	• Associated with pneumonia, particularly in the elderly • Increased during the 1990s in the United States • Has become more common among infants and adolescents in recent years
W-135	• Small percentage of infections worldwide • Outbreaks associated with Hajj pilgrims starting in 2000

NOTE. Derived from [6].

and 75% of disease occurring in persons >11 years of age is caused by C, Y, or W-135 [8, 9]. A multivariate analysis identified household crowding, recent respiratory illness, active and passive smoking, new school or residence, and Medicaid insurance as risk factors for IMD [5]. Local outbreaks of IMD have been associated with social and behavioral risk factors, such as bar patronage, alcohol use, and active and passive smoking [10, 11].

CURRENT VACCINES TO PREVENT MENINGOCOCCAL DISEASE

Two vaccines are licensed for use in the United States to prevent meningococcal disease, a quadrivalent polysaccharide vaccine and a quadrivalent conjugate vaccine (Table 2).

Quadrivalent Meningococcal Polysaccharide Vaccine (MPSV4)

Composition. MPSV4, licensed in the United States in 1981, contains 50 μg each of 4 purified bacterial capsular polysaccharides (A, C, Y, and W-135) [12]. MPSV4 is administered as a single dose subcutaneously and is available in single- or 10-dose vials. It is indicated for prophylaxis of meningitis against serogroups A, C, Y, and W-135; MPSV4 is not indicated for children <2 years of age, except for short-term protection against serogroup A in infants >3 months of age [12]. Currently, no vaccine is licensed in the United States for protection against infection caused by *N. meningitidis* serogroup B.

Immunogenicity and efficacy. Antibody responses to meningococcal serogroups A, C, Y, and W-135 are serogroup specific. The efficacy of *N. meningitidis* serogroup A polysaccharide was 89%–100% in clinical trials [13, 14]. Infants as young as 3 months develop antibodies to serogroup A polysaccharide vaccine, with short-term protection [15]. Serogroups A and C polysaccharides had efficacy of ~85% in clinical trials in settings where meningococcal disease is epidemic [16]. In infants and young children, the duration of vaccine protection is short against disease caused by polysaccharide serogroups A and C. In children <4 years of age, vaccine efficacy was shown to decrease from 100% to 8% in 3 years [17]. Vaccines using polysaccharides from serogroups Y and W-135 were immunogenic in children >2 years of age [18, 19].

Safety. Meningococcal polysaccharide vaccines have been used safely in a wide range of contexts, including during outbreaks and broad vaccination efforts and in travelers. Systemic or severe reactions to polysaccharide vaccine are uncommon, and most common adverse reactions are mild, such as pain and redness at the injection site [5].

Meningococcal Conjugate Vaccines

Although meningococcal polysaccharides can stimulate a B-lymphocyte response leading to functional antibody, they fail to stimulate T lymphocytes (Table 2). As a result, the response to polysaccharide antigen is short-lived and incapable of generating an anamnestic response when the recipient is later exposed to the same antigen. In addition, meningococcal polysaccharide vaccines are poorly immunogenic in infants and young children. The immune response to bacterial polysaccharide antigens can be enhanced by coupling them to a protein carrier, leading to T lymphocyte–dependent responses. Conjugate vaccines are generally believed to have greater immunogenicity and are capable of providing persistence and an anamnestic response. In contrast to polysaccharide vaccines, meningococcal conjugate vaccines are capable of reducing nasopharyngeal carriage of *N. meningitidis,* which is essential to herd immunity [20–22].

In the United Kingdom, experience with monovalent meningococcal conjugate vaccines against serogroup C showed that they are able to successfully decrease the incidence and carriage of *N. meningitidis.* In 1999, several conjugate vaccines were introduced on the basis of safety and immunogenicity data, although none had been evaluated for clinical efficacy [23]. In 2002, with >80% coverage, vaccine effectiveness was shown to be 88%–98%, and carriage decreased by 66% [24, 25]. In the context of high background population coverage with conjugate vaccine, the incidence of meningococcal disease among unvaccinated persons 1–17 years of age decreased by 67% [22].

Quadrivalent conjugate vaccine (MCV4). A quadrivalent meningococcal conjugate vaccine was licensed in the United States in 2005 (Table 3). Each dose contains 4 μg each of capsular polysaccharides (A, C, Y, and W-135) conjugated to

48 μg of diphtheria toxoid. MCV4 is available in single-dose vials only [26] and is administered intramuscularly.

Immunogenicity and efficacy. The immunogenicity of MCV4 was compared with that of MPSV4 in a randomized trial involving persons 11–18 years of age [27]. Immunogenicity was assessed by a serum bactericidal assay using baby rabbit complement (rSBA). For this immunologic correlate of protection, the criterion for establishing efficacy was a ⩾4-fold increase in rSBA level. The percentage of participants with at least a 4-fold increase in rSBA level 28 days after vaccination with MCV4 was 96.7%, 92.7%, 91.7%, and 81.8% for serogroups W-135, A, C, and Y, respectively. In another randomized trial comparing the immunogenicity of the polysaccharide vaccine with that of the conjugate vaccines in persons 18–55 years of age, the percentage of participants with at least a 4-fold increase in rSBA level 28 days after vaccination with conjugate vaccine was 89.4%, 80.5%, 88.5%, and 73.5% for serogroups W-135, A, C, and Y, respectively [28]. The efficacy of MCV4 was compared with that of MPSV4 in a randomized trial involving children aged 2–10 years [29]. The proportion of those seronegative at baseline who developed a ⩾4-fold increase in rSBA level 28 days after vaccination was significantly higher in the MCV4 group than in the MPSV4 group for serogroups A, C, Y, and W-135 ($P < .05$ for all).

Safety. In randomized trials, MCV4 was generally well tolerated, with a safety profile similar to that of MPSV4. Vaccine-related serious adverse events were uncommon, and similar rates of mild, local and systemic events were observed in the 2 vaccine groups. Fever (temperature, >37.7°C) was reported more frequently among MCV4 recipients aged 11–18 years or 18–55 years than among MPSV4 recipients aged 11–18 years (5.1% vs 3.1%) or 18–55 years (1.5% vs 0.5%) [27, 28]. Among persons 11–18 years of age, local adverse reactions were more common among those who received MCV4 than among those who received MPSV4. Thirteen percent of persons administered MCV4 reported movement-limiting pain in the injection arm, compared with 3% of those administered MPSV4.

Table 2. Characteristics of Meningococcal Polysaccharide and Protein-Conjugate Vaccines

Property	Polysaccharide	Conjugate
T cell–dependent response	No	Yes
Immune memory	No	Yes
Persistence of protection	No	Yes[a]
Booster effect	No	Yes
Reduction of carriage	No	Yes
Herd immunity	No	Yes

NOTE. Derived from [6].

[a] Duration of persistence of protection is currently unknown.

As of 2008, with >15 million doses of the MCV4 vaccine distributed, the Vaccine Adverse Event Reporting System received 26 reports of confirmed cases of Guillain-Barré syndrome (GBS) occurring within 6 weeks after receipt of vaccine [30]. These data are not sufficient to establish an increased risk of GBS associated with MCV4. The US Centers for Disease Control and Prevention (CDC) recommends continuation of current vaccination strategies as it investigates these cases. A personal history of GBS is a relative contraindication to administration of MCV4, and caution should be used for persons with a first-degree family member history of GBS [26, 31].

Meningococcal conjugate vaccine strategies. The potential public health impact of meningococcal conjugate vaccines has been studied using predictive models. In the absence of pop-

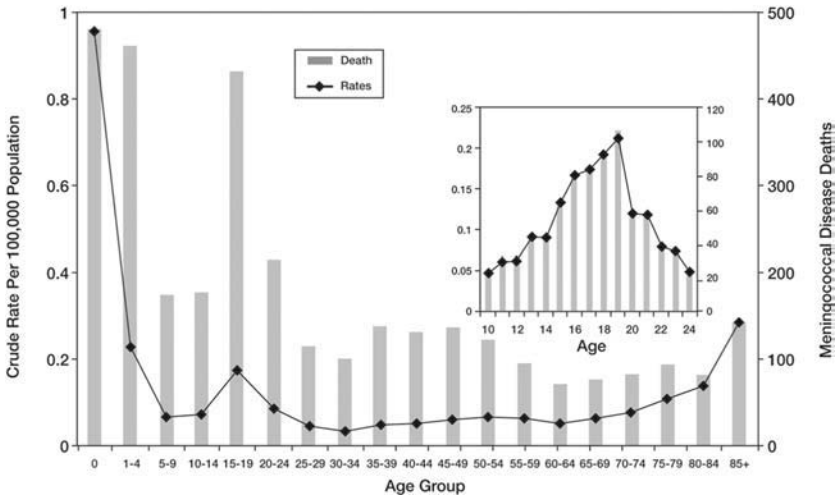

Figure 1. Number of deaths due to meningococcal disease and mortality rates, by age, United States, 1990–2002 [7]. The graph inset shows single-year age categories. Image used with permission from *Pediatric Infectious Diseases Journal,* 2006;25:191–194. Copyright © 2006 Wolters Kluwer Health.

Table 3. Meningococcal Vaccines Licensed in the United States

Characteristic	MPSV4	MCV4
US proprietary name	Menomune-A/C/Y/W-135	Menactra
Manufacturer	Sanofi Pasteur	Sanofi Pasteur
Polysaccharide components	A, C, W-135, Y	A, C, W-135, Y
Conjugate carrier	None	Diphtheria toxoid
Adjuvant	None	None
Preservative	Thimerosal	None
How supplied	Powder for solution (0.05 mg and 0.5 mg)	Suspension (16 μg/0.5 mL)
Route of administration	Subcutaneous only	Intramuscular only
Recommendations	Persons aged 2–55 years if MCV4 is unavailable, children aged 2–10 years with a history of GBS, persons >55 years of age	All adolescents aged 11–18 years, persons aged 2–55 years who are at increased risk
Dose	0.5 mL as a single dose, formulated to contain 50 μg each of A, C, Y, and W-135 of polysaccharide	0.5 mL as a single dose formulated to contain 4 μg each of A, C, Y, and W-135 of polysaccharide and 48 μg of diphtheria toxoid carrier
Revaccination	Persons aged 2–55 years who remain at increased risk for meningococcal disease 5 years after vaccination with MCV4 or MPSV4 should be revaccinated with MCV4; children who received their first MCV4 or MPSV4 at age 2–6 years and remain at risk should be revaccinated with MCV4 3 years after their first vaccine; college freshmen living in dorms who were previously vaccinated at age 11–18 years are not recommended for revaccination; use MCV4 for revaccination	Persons aged 7–55 years who remain at increased risk for meningococcal disease 5 years after vaccination with MPSV4 should be revaccinated with MCV4; children at high risk who received their first dose at ages 2–6 years should be revaccinated after 3 years
Precautions	Do not give with whole-cell pertussis or typhoid vaccines because of combined endotoxin content	Defer if acute moderate-to-severe febrile illness,[a] bleeding disorder or concomitant anticoagulant therapy, history of GBS in first-degree relative
Contraindications	Acute illness,[a] sensitivity to vaccine components or thimerosal,[b] sensitivity to latex (used in vial stopper)	Hypersensitivity to vaccine components, history of GBS, known hypersensitivity to latex (used in vial stopper)
Pregnancy category	C	C

NOTE. Derived from [5, 12, 26]. GBS, Guillain-Barré syndrome; MCV4, quadrivalent meningococcal conjugate vaccine; MPSV4, quadrivalent meningococcal polysaccharide diphtheria toxoid conjugate vaccine.

[a] Mild diarrheal or respiratory illnesses are not a contraindication to vaccination.

[b] In persons sensitive to thimerosal, administer with a single-dose using a 0.78-mL vial of preservative-free diluent.

ulation-based data on outcomes of vaccination programs, these models have been informative in identifying optimal immunization strategies. One study predicted a reduction in the incidence of IMD-related disease and mortality with use of several strategies in models of bivalent serogroup C and Y meningococcal conjugate vaccination [32]. Vaccination of infants, children, and adolescents reduced the cumulative incidence of meningococcal disease by 54%, 48%, and 25%, respectively. Vaccination of all 3 age groups was predicted to reduce the incidence of meningococcal disease by 50% and mortality by 64%. Another study used discrete modeling to assess the effect of routine vaccination of adolescents with a quadrivalent conjugate vaccine against serotypes A, C, Y, and W-135 [33]. Routine adolescent vaccination (71% coverage of persons aged 12 years) reduced mortality by >46% and decreased the prevalence of outbreaks by 74%. When accounting for the role of herd immunity, as demonstrated in the UK meningococcal vaccination program, this model suggests that the benefits of routine adolescent vaccination may be substantially greater than was previously predicted in economic models.

FUTURE DIRECTIONS

Several meningococcal vaccines in advanced development have the potential to fill current gaps in prevention. Although in the United States, there is currently no vaccine licensed to prevent serogroup B disease, novel vaccines containing recombinant human factor H binding protein are undergoing clinical trials [34, 35]. A novel quadrivalent meningococcal vaccine conjugated to a nontoxic mutant of diphtheria toxin (cross-reactive material [CRM_{197}]) has been shown to be safe and immunogenic [36]. MenACWY was compared with MCV4 in adolescents in a phase 3 clinical trial [37]. The human complement serum bactericidal assay geometric mean titers with MenACWY-CRM were higher than those with MCV4 (geometric mean titer ratios of 1.6, 1.3, 2.0, and 2.8 for serogroups A, C,

Table 4. Recommendations for Use of Meningococcal Vaccines in Persons Not Previously Vaccinated

	Age group, years				
Population	<2	2–10	11–19	20–55	>55
General population	Not recommended	Not recommended	A single dose of MCV4 is recommended at age 11–12 years at preadolescent visit or at high school entry	Not recommended	Not recommended
Groups at increased risk[a]	Not usually recommended	A single dose of MCV4 is preferred (MPSV4 is an acceptable alternative)	A single dose of MCV4 is preferred (MPSV4 is an acceptable alternative)	A single dose of MCV4 is preferred (MPSV4 is an acceptable alternative)	A single dose of MPSV4[b]

NOTE. Derived from [5]. MCV4, quadrivalent meningococcal conjugate vaccine; MPSV4, quadrivalent meningococcal polysaccharide diphtheria toxoid conjugate vaccine.

[a] See Table 5 for additional information on groups at increased risk.

[b] MCV4 is not licensed for persons >55 years of age.

W-135, and Y, respectively), meeting predetermined superiority criteria. When compared with MCV4, the proportion of study participants receiving MenACWY-CRM with postvaccination human complement serum bactericidal assay titers ⩾1:8 was superior for serogroups A, W-135, and Y and noninferior for serogroup C. MenACWY-CRM was well tolerated, and neither vaccine was associated with a serious adverse event. The MenACWY-CRM vaccine has been shown to be immunogenic in infants [38] and could potentially fill an important need in an age group in which the incidence of IMD is high and in groups for which no vaccine is available [39]. Another vaccine in advanced development combines *H. influenzae* type b with meningococcal serogroups C and Y conjugated to tetanus toxoid. This vaccine is immunogenic in infants and, if approved, may provide bivalent meningococcal coverage without adding to the number of required infant vaccines [40]. A comprehensive review of investigational meningococcal vaccines can be found in this Supplement [41].

Table 5. Persons at Increased Risk for Meningococcal Disease

Population
College freshmen living in dormitories
Certain travelers
Travelers to or near areas where *Neisseria meningitidis* infection is hyperendemic or epidemic or where there is an increased risk of exposure
Visitors to the "meningitis belt" of sub-Saharan Africa
Travelers to Saudi Arabia during the Hajj
Certain microbiologists and/or laboratory workers routinely exposed to *N. meningitidis*
Certain populations experiencing outbreaks (information on the use of vaccination in outbreak settings is available from the Centers for Disease Control and Prevention)
Military recruits
Persons with increased susceptibility
Persons with terminal complement-component deficiencies
Persons with anatomic or functional asplenia
Persons with HIV infection[a]

NOTE. Derived from [5].

[a] Vaccination is elective. The efficacy of MCV4 in HIV-infected patients is unknown.

RECOMMENDATIONS

Recommendations for vaccination to protect against meningococcal disease are based on several considerations. IMD can be serious and rapidly progressive. Within 24–48 h, IMD can cause precipitous disease in healthy young people, providing little time for diagnosis and treatment [3]. In the early stages, symptoms of meningococcal disease can be similar to those of viral illnesses. *N. meningitidis* is the most common agent causing bacterial meningitis among US children and adolescents, making prevention a public health priority.

Routine immunization. The Advisory Committee on Immunization Practices (ACIP) recommends routine vaccination with a single dose of MCV4 for all persons aged 11–18 years (Table 4). Ideally, vaccination occurs at the preadolescent health care visit at age 11–12 years; the ACIP, the American Academy of Pediatrics, and the Society for Adolescent Medicine recommend that persons in this age group receive vaccines and other preventive care services [5, 42, 43]. Persons who do not receive vaccine during a visit when they are aged 11–12 years should be offered the vaccine at the first appropriate health care visit or at preventive visits at ages 13–18 years [44].

Vaccination is also recommended for persons 2–55 years of age who are at elevated risk of meningococcal infection (Table 5). Although CDC recommendations for college-aged persons specify freshmen living in dormitories, the feasibility of targeting vaccination on campuses has led some schools to recommend vaccination of all incoming freshmen and other college students who wish to decrease their risk of meningococcal disease [5]. The American Academy of Pediatrics recommends that those at increased risk of meningococcal disease who received MPSV4 ⩾3 years previously should receive MCV4 [45].

Vaccine selection. MCV4 conjugate vaccine is preferred for vaccine recipients aged 2–55 years. In 2007, the US Food and

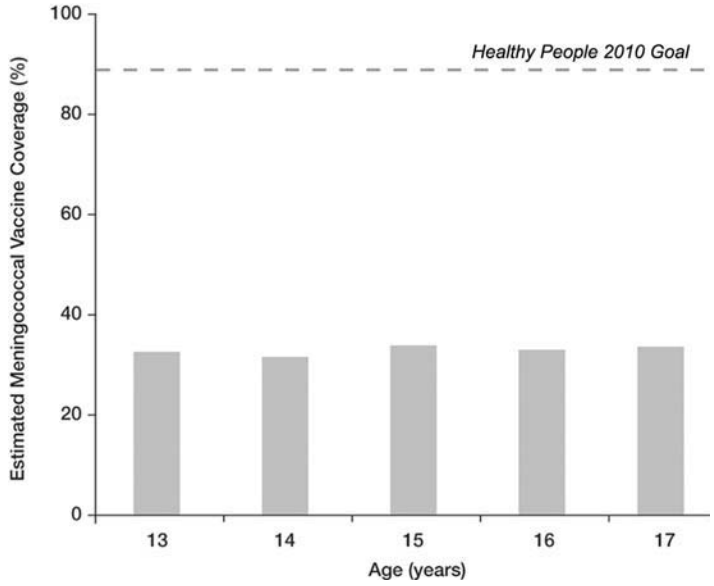

Figure 2. Meningococcal vaccine coverage among adolescents in the National Immunization Survey Teen Module [48].

Drug Administration approved MCV4 for use in children aged 2–10 years on the basis of results of clinical trials comparing MCV4 with MPSV4 in children [29]. MCV4 is not indicated for children <2 years of age. MPSV4 is the only meningococcal vaccine indicated for adults >55 years of age and is recommended for persons at increased risk of meningococcal disease who are >55 years of age.

Pregnancy. Studies have not shown adverse effects in women who receive MPSV4 during pregnancy or in their newborns [44, 45]. Although there are insufficient data on the safety of MCV4 during pregnancy, available data do not rule out the use of MPSV4 in pregnant women when indicated. Because of the short duration of protection conferred by MPSV4, the decision whether to vaccinate with MPSV4 during pregnancy or to wait until after delivery depends on the nature of the risk and the reasons for considering vaccination.

Immunosuppressed persons. MCV4 and MPSV4 are inactivated vaccines and may be considered for use in persons who are immunosuppressed because of disease or medication use. Depending on the nature of the immunosuppression, antibody response may be suboptimal. Patients undergoing elective splenectomy should receive meningococcal vaccination ⩾2 weeks before surgery [5].

Revaccination. Persons 2–55 years of age who remain at increased risk of meningococcal disease 5 years after vaccination (with MCV4 or MPSV4) should be revaccinated with MCV4. Children who first received MCV4 and MPSV4 at ages 2–6 years and remain at risk should be revaccinated with MCV4 3 years after receipt of their first meningococcal vaccine [46].

OPPORTUNITIES AND CHALLENGES OF ADOLESCENT IMMUNIZATION

Since 2005, the ACIP has made 4 new vaccine recommendations for adolescents: MCV4; tetanus, diphtheria, and acellular pertussis; human papillomavirus quadrivalent vaccine; and annual influenza vaccine [31]. In addition, the ACIP recommends that adolescents receive any incomplete or missing childhood vaccinations and be evaluated for vaccines on the basis of specific risk. In the future, other vaccines are likely to be added to the list of recommended adolescent vaccines [47].

Vaccine coverage of adolescents. Immunizations can significantly reduce morbidity and mortality among adolescents and provide an important bridge to a longer, healthier adulthood. Across the spectrum of health issues that young people face, vaccine-preventable diseases are among the few for which proven interventions exist, many of which are cost effective. Despite the resounding success of infant immunization programs in the United States, the health care system does not have well-developed methods for vaccinating adolescents, and vaccine coverage among persons 11–18 years of age remains alarmingly low. The CDC's 2007 National Immunization Survey Teen Module showed that, for all vaccines studied, none achieved the *Healthy People 2010* goal of 90% coverage [48]. Only 32% of adolescents had received 1 dose of MCV4 (Figure 2).

Strategies to improve adolescent immunization. There are many reasons why vaccine coverage is low among adolescents. Although ~86% of children aged 6–17 years had at least 1 visit to a health care provider in 2006 [49], only approximately one-

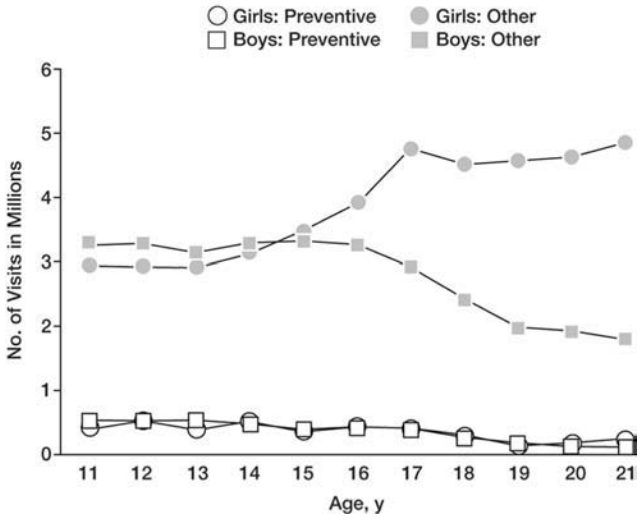

Figure 3. Number of preventive care visits for adolescents [51]. Used with permission from the *Archives of Pediatrics & Adolescent Medicine,* 2007; 161:252–259. Copyright © 2007 American Medical Association. All rights reserved.

third of adolescents access annual preventive services [50]. Data from the National Ambulatory Medical Care Survey showed that the number of preventive visits decreases dramatically after 13 years of age, and there is a precipitous decrease in the number of nonpreventive visits for male individuals aged >15 years (Figure 3) [51]. Nonpreventive visits provide an important opportunity to screen for immunization status and to administer needed vaccines. Recommended vaccines can be administered in the presence of minor illness, such as diarrhea or respiratory tract infection with or without fever [5].

Data clearly reveal that opportunities for vaccination are frequently missed. A survey of 1480 physicians found that, even among physicians who vaccinated adolescents during 95% of health-maintenance preventive visits, only 23% provided vaccines during nonpreventive encounters and fewer than half checked immunization status during follow-up visits [52]. Furthermore, only 21% of physicians used immunization tracking systems or recall. Another study found that family physicians and pediatricians who were aware of adolescent vaccinations were less likely to assess immunization status and to offer indicated vaccines to persons 14–21 years of age, compared with younger adolescents [53]. A study evaluated how frequently an indicated vaccine was administered among ~24,000 eligible adolescents enrolled in the Harvard Pilgrim Health Care system from 1997 through 2004 [54]. The results showed >87,000 opportunities when a needed vaccine was not given, or 4.8 missed opportunities per adolescent.

Remaining challenges. Adolescent care is a rapidly changing area of medicine. Although delivery of health care to adolescents is complex, the increasing number of recommended adolescent vaccines will continue to create opportunities to enhance access to preventive services [47].

Several aspects of adolescent immunization continue to challenge health care providers and policy makers. Knowledge of vaccines and vaccine-preventable diseases is crucial and requires enhanced education of providers, parents, and patients [53, 55]. Professional guidelines remain one of the strongest motivators for clinicians to recommend a vaccine [56]. The CDC's National Vaccine Advisory Committee recently reported its policy and health care infrastructure recommendations for success in the new era of adolescent vaccines [57]. Among the priorities that the CDC identified were improved adolescent access to existing venues of care, such as vaccination during acute or nonpreventive visits, and enhanced opportunities for alternative venues for vaccination. In addition, consent laws need to be clarified and standardized. School mandates have been proven to increase vaccination rates effectively [58, 59]. In 2008, 13 US states required meningococcal vaccine or waiver for incoming college and university students, and 23 states required education only [60]. Only 7 US states required meningococcal vaccine or waivers for students in elementary and secondary schools.

CONCLUSIONS

Meningococcal disease is a serious health threat. With rapid onset, nonspecific symptoms, and a high associated case-fatality rate even after treatment, life-threatening meningococcal infections are a priority for prevention. Although the shifting epidemiology and cyclic nature of IMD suggest that these illnesses will continue to challenge public health, they are preventable by vaccination. Meningococcal conjugate vaccine is routinely recommended for all persons 11–18 years of age and those 2–55 years of age who are at increased risk. The expanding recommendations for vaccinations during adolescence highlight the challenges of immunization for this population. Although preventive care visits are far less frequent for adolescents than for infants or toddlers, the majority of adolescents have at least 1 health care encounter annually, suggesting that opportunities for vaccinations are being missed. Strategies are needed to overcome barriers to preventive services in this age group. Capturing opportunities to administer vaccines during nonpreventive care visits is a strategy that can be used immediately to increase vaccine coverage. Future efforts are also needed to address other barriers, such as deficiencies in provider and parent education, adolescent communication, public awareness, consent laws, and lagging school mandates. Although current vaccine coverage among adolescents is inadequate, it is improving. New, safe, and effective vaccines hold promise for decreasing morbidity and mortality in this age

group and have the potential to provide a sound bridge to a healthy adulthood.

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