Prevention of Meningococcal Disease

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Invasive disease caused by *Neisseria meningitidis* has an average annual incidence of one case per 100,000 in the United States. The disease can be rapidly fatal or result in severe neurologic and vascular sequelae despite antibiotic therapy. Antibiotic chemoprophylaxis with rifampin, ciprofloxacin, or ceftriaxone is required for household and other close contacts. Although the majority of cases of meningococcal disease are sporadic, outbreaks can occur, and vaccination of the affected population often is necessary. Serogroup B accounts for the highest incidence of disease in young infants but is not contained in any vaccine licensed in the United States. Adolescents and young adults 15 to 24 years of age have a higher incidence of disease and a higher fatality rate than other populations. Because 70 to 80 percent of these infections in the United States are caused by meningococcal serogroups C, Y, and W-135, which are contained in the tetravalent meningococcal vaccines, they are potentially preventable. The U.S. Food and Drug Administration recently approved a meningococcal conjugate vaccine containing serogroups A, C, Y, and W-135. This T-cell–dependent vaccine induces bactericidal antibody production and promotes immunologic memory that should result in a longer duration of immunity. The Advisory Committee on Immunization Practices recommends that this vaccine be given to 11- and 12-year-old adolescents, to adolescents entering high school, and to college freshmen living in dormitories. The vaccine also may be given to persons 11 to 55 years of age who belong to certain high-risk groups. (Am Fam Physician 2005;72:2049-56. Copyright © 2005 American Academy of Family Physicians.)

▶ **See editorial on page 1978.**

Neisseria meningitidis infects only humans; it causes 1,400 to 2,800 cases of invasive disease in the United States each year, with an annual incidence of approximately one case per 100,000 persons.[1,2] *N. meningitidis* is the most common cause of bacterial meningitis in children and young adults in the United States and the second most common cause of community-acquired meningitis in adults.[3] Death occurs in 10 to 14 percent of patients despite treatment, and sequelae such as limb loss, neurologic disabilities, and hearing loss occur in another 11 to 19 percent.[1,2] New recommendations regarding prevention and chemoprophylaxis for meningococcal disease are emerging, and a tetravalent conjugate vaccine was recently approved.

Transmission

N. meningitidis is a gram-negative diplococcus that colonizes the upper respiratory tract of 10 percent or more of humans and is transmitted from person to person by aerosol droplets or contact with respiratory tract secretions (e.g., by kissing, sharing drinking glasses, mouth-to-mouth resuscitation, or intubation management).[4] Less than 2 percent of young children are asymptomatic carriers of *N. meningitidis*,[5] and children younger than two years have the highest rate of disease.[1] However, more than 60 percent of meningococcal cases in the United States occur in persons 11 years or older.[1] Most cases of meningococcal disease are sporadic and are not linked to outbreaks; however, outbreaks have occurred in communities and secondary schools.[6,7] The disease also has occurred in travelers returning from Mecca, Saudi Arabia;[8] in microbiology laboratory workers;[9] and in persons who had been on a long-distance flight.[10]

Changing Epidemiology

The 13 capsular serogroups of *N. meningitidis* shift over time, geographic location, and age group. Serogroups A, B, C, W-135, and Y cause almost all cases of human disease.[4] Serogroup A disease is rare in the United States, although it is the most common cause of meningococcal infection in sub-Saharan Africa.[2] Serogroup B is the most common cause of sporadic disease in some European countries, and has caused outbreaks

SORT: KEY RECOMMENDATIONS FOR PRACTICE

Clinical recommendations	*Evidence rating*	*References*	*Comments*
Prescribe antimicrobial chemoprophylaxis to household and other close contacts of patients with meningococcal disease.	B	1	Based on consistent data from observational studies
For meningococcal outbreaks caused by serogroups A, C, W-135, and Y, use MCV4 or MPSV4.	B	1	Based on consistent data from observational studies
Children 11 to 12 years of age, adolescents entering high school, and college freshmen living in dormitories should receive MCV4 routinely.	B	1, 35	Based on consistent data from observational studies
Military recruits, asplenic persons, and travelers to high-risk areas should receive MCV4.	C	1, 35	—

MCV4 = tetravalent meningoccocal polysaccharide-protein conjugate vaccine; MPSV4 = tetravalent meningococcal polysaccharide vaccine.

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, see page 1949 or http://www.aafp.org/afpsort.xml.

in Canada and the Pacific Northwest.[4] In the United States, serogroup B accounts for more than one half of meningococcal cases in infants younger than one year.[1,2,11] Serogroup Y caused only 2 percent of disease from 1989 to 1991, but accounted for 37 percent of cases from 1997 to 2002.[1] Serogroup Y causes a higher proportion of pneumonia than serogroups B and C (14 versus 2 percent). Serogroup Y also causes a higher percentage of meningococcal disease than other serogroups in blacks (50 versus 23 percent)[12] and in patients 65 years or older.[11] The median age of female patients with serogroup Y disease (42 years) is significantly higher than male patients with the disease (18 years).[12]

An outbreak is defined as three or more cases of meningococcal disease in less than three months occurring among persons in an organization or community who are not close contacts, and with a primary disease attack rate of at least 10 per 100,000 persons.[1] Outbreaks account for 2 to 3 percent of meningococcal disease.[13] Serogroup C caused 26 of 42 outbreaks reported to state health departments from 1994 to 1997.[14] During the 1990s, serogroup C also was associated with 47 percent of cases of meningococcal disease in persons 15 to 24 years of age in Maryland, whereas serogroups Y, B, and W-135 accounted for 31, 12, and 5 percent of cases, respectively.[15] In the same study,[15] serogroups C, Y, and B accounted for 57, 29, and 14 percent, respectively, of the 14 of 16 fatalities in which the serogroup was known.

Antimicrobial Chemoprophylaxis

Close contacts of patients with invasive meningococcal disease should receive antimicrobial chemoprophylaxis, regardless of whether the disease is sporadic or occurs in an outbreak setting.[1] Household contacts have a 500 to 800 times greater rate of disease and should be given prophylaxis, ideally within 24 hours after identification of the index patient.[1] Child

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TABLE 1
Antibiotic Prophylaxis for Exposure to Meningococcal Disease

Antibiotic	*Age range*	*Dosage and route*	*Duration*
Rifampin* (Rifadin)	Children younger than one month	5 mg per kg orally every 12 hours	2 days
	Children older than one month	10 mg per kg (up to 600 mg) orally every 12 hours	2 days
	Adults	600 mg orally every 12 hours	2 days
Ciprofloxacin† (Cipro)	Adults	500 mg orally	Single dose
Ceftriaxone (Rocephin)	Patients younger than 15 years	125 mg intramuscularly	Single dose
	Patients 15 years and older	250 mg intramuscularly	Single dose

**—Rifampin may decrease the effectiveness of other medications, including oral contraceptives, and alternative contraceptive methods are recommended during its use. Rifampin is not recommended for pregnant women because it is teratogenic in laboratory animals.*

†—Ciprofloxacin is not recommended for pregnant or lactating women and is not generally used in patients younger than 18 years; however, it can be used in children if no acceptable alternative therapy is available.

Adapted from Bilukha OO, Rosenstein N. Prevention and control of meningococcal disease. Recommendations of the Advisory Committee on Immunization Practices. MMWR Recomm Rep 2005;54(RR-7):16.

care center contacts and anyone exposed to the patient's oral secretions also should be given chemoprophylaxis *(Table 1)*.[1] Travelers seated next to an indexz patient on a flight lasting eight hours or more or those who had direct contact with an index patient's respiratory secretions also should receive prophylaxis.[1] Because penicillin does not eradicate nasopharyngeal carriage, patients with invasive meningococcal disease who are treated with penicillin also should receive prophylaxis before hospital discharge.[16]

High-Risk Groups

A study[17] of meningococcal disease in Maryland from 1992 to 1997 found that college students residing on campus had at least a three times greater relative risk for contracting meningococcal infection than students living off campus. A subsequent 1998 to 1999 nationwide survey[13] of state health departments and college health centers found that the incidence of meningococcal disease for freshman living in dormitories was 5.1 per 100,000, compared with 0.7 per 100,000 for all undergraduates combined and 1.4 per 100,000 18- to 23-year-old patients in the general population. Serogroups C (48 percent), B (28 percent), Y (19 percent), and W-135 (1 percent) were responsible for the infections.[13]

Dormitory or barracks-style living brings persons together from different geographic areas with diverse strains of meningococci, some highly virulent. A British university study[18] found that the carriage rates for meningococci increased rapidly among students living in dormitories (from 6.9 percent on day 1 to 23.4 percent on day 4). Average carriage rates increased from 14 percent in October to 34 percent by December.[18] Male sex, smoking, visits to bars in dormitories and nightclubs, intimate kissing, and coeducational halls also were identified as risk factors for acquisition of meningococci.[18] Other potential risk factors for meningococcal disease among students include white race, use of radiator heat, and recent upper respiratory infection.[17,19]

The risk of meningococcal disease is increased at least threefold among freshmen living in college dormitories.

Approximately 70 to 80 percent of the serogroups most likely to cause meningococcal disease in adolescents and young adults are potentially preventable by the tetravalent meningococcal vaccine. The

majority of U.S. states mandate education about meningococcal disease and vaccines for students attending public (and private, in some states) colleges and universities or for all full-time students residing on campus.[1,20]

Meningococcal Vaccines

Meningococcal vaccines can be polysaccharide or conjugated. Polysaccharide vaccines are T-cell independent and stimulate mature B lymphocytes that produce antibodies but not immunologic memory. Conjugated vaccines covalently link the polysaccharide to a carrier protein, making them T-cell dependent and capable of stimulating immunologic memory that results in a greater and longer lasting immunity. Characteristics of the two types of vaccines are summarized in *Table 2*.[4,21,22]

Conjugated vaccines are capable of stimulating immunologic memory and provide greater and longer-lasting immunity to meningococcal disease.

TETRAVALENT MENINGOCOCCAL POLYSACCHARIDE VACCINE

The tetravalent meningococcal polysaccharide vaccine (MPSV4 [Menomune]) contains polysaccharide antigens to meningococcal groups A, C, Y, and W-135. It is T-cell independent and not effective in children younger than two years but has effectiveness as high as 85 percent for serogroups A and C in school-age children and in adults.[1] Immunity decreases about three years after initial administration. This is measured by declining antibody levels to groups A and C, especially in children younger than five years.[23] The serogroup B antigen is not contained in the vaccine because its capsular polysaccharide is poorly immunogenic in humans,[16] and serogroup B anticapsular antibodies have poor complement bactericidal activity.[4] The capsular polysaccharide of serogroup B also has structural homology to human embryonic neural tissue.[24] Consequently, MPSV4 does not confer protection against serogroup B disease, which is responsible for about 30 percent of all invasive meningococcal disease in the United States.[1]

A single immunizing dose is 0.5 mL given subcutaneously. The multidose formulation of the vaccine contains thimerosal and should not be given to anyone sensitive to this or any other vaccine constituent.[23] Pain, tenderness, and redness at the injection site are the most common local reactions; fever, malaise, and headache occur in a small per-

TABLE 2
Characteristics of Polysaccharide and Conjugate Meningococcal Vaccines

Characteristic	*Polysaccharide vaccine*	*Polysaccharide-protein conjugate vaccine*
Immunogenicity in adults	High	High
Immunogenicity in young children	Poor	High*
Antibody quality in children		
Avidity to elicit complement	Low	High*
Bactericidal activity	Low	High*
Response to booster	Poor†	High*
Induction of immunologic memory	No	Yes*
Effect on nasopharyngeal carriage	Transient and incomplete	Decreases[21]
Promotion of herd immunity	Transient or not at all	Probable[22]

**—Qualities improved by T-cell dependent properties of conjugate vaccine.*

†—Repeated immunization of young children elicits booster responses to group A polysaccharide but hyporesponsiveness to group C polysaccharide.

Adapted with permission from Granoff DM, Feavers IM, Borrow R. Meningococcal vaccines. In: Plotkin SA, Orenstein WA, eds. Vaccines. 4th ed. Philadelphia: Saunders, 2004:973, with additional information from references 21 and 22.

centage of patients.[23] Severe adverse events including allergic reactions, seizures, and paresthesias are rare, occurring in fewer than 0.1 out of 100,000 doses.[14]

MENINGOCOCCAL C CONJUGATED VACCINES

Meningococcal conjugate vaccines containing serogroup C or serogroups C and A are safe and stimulate immunologic memory, although they are not available in the United States.[25-27] In November 1999, the United Kingdom began an immunization program using meningococcal serogroup C conjugate (MCC) vaccine, resulting in a 76 percent reduction of group C cases in adolescents between January 1 and September 30, 2000.[28] Vaccine effectiveness was estimated at 97 percent for adolescents and 92 percent overall for toddlers and adolescents.[28] A four-year follow-up study[29] demonstrated vaccine effectiveness of greater than 82 percent in all children who had received MCC vaccines in the catch-up program at five months to 18 years of age. Vaccination was 66 percent effective in infants vaccinated at two to four months of age, but immunity waned after one year.[29] By November 2000, more then 70 percent of persons younger than 18 years in the United Kingdom had been immunized against meningococcal serogroup C.[21] Oropharyngeal samples obtained from students 15 to 17 years of age demonstrated a 66 percent decrease in carriage of serogroup C meningococci from 1999 to 2000, but there was no significant change in carriage of serogroups B, Y, and W-135.[21] Another study[22] subsequently estimated an overall 67 percent reduction in the rate of confirmed meningococcal serogroup C disease in unvaccinated children and estimated vaccine effectiveness at 96 percent. Although the confidence intervals for the younger age groups were relatively wide, this study supports the development of herd immunity with the MCC vaccine.[22]

TETRAVALENT MENINGOCOCCAL CONJUGATE VACCINE

A meningococcal vaccine containing polysaccharide serogroups A, C, Y, W-135 conjugated to diphtheria toxoid (MCV4 [Menactra]) has been approved by the U.S. Food and Drug Administration for active immunization of adolescents and adults 11 to 55 years of age.[30] A small study[31] of this vaccine demonstrated it to be immunogenic in adults and acceptably tolerated. A study[32] comparing vaccine doses of 1, 4, and 10 mcg for each of the four polysaccharide serogroups conjugated to diphtheria toxoid found it to be modestly immunogenic in infants, with 47 to 83 percent experiencing some redness, induration, or pain at the injection site after one or more primary series doses. There was no increase in local reaction rates with increasing numbers of primary doses, and most reactions were mild or moderate.[32] Studies by the manufacturer indicate that the most commonly reported adverse reactions with MCV4 in adolescents (11 to 18 years of age) and adults (18 to 55 years of age) were local pain, headache, and fatigue.[33] Local reactions other than redness in adults were more common in MCV4 recipients than MPSV4 recipients, but most reactions were mild.[33]

Immunizing adolescents once at 11 years of age is projected to prevent 270 cases of meningococcal disease and 36 deaths at a cost of $121,000 per year of life saved.

A recent U.S. study[34] compared MCV4 with MPSV4 in two- to 10-year-old children. The MCV4 had a similar safety profile and produced a higher and more persistent serum bactericidal antibody response against serogroups A, C, Y, and W-135 than did MPSV4.[34] Protective antibody levels usually are obtained seven to 10 days after vaccination.[1] *Table 3*[23,33] compares the composition and administration of MPSV4 and MCV4.

Indications

Table 4[1,35] summarizes the 2005 recommendations from the Advisory Committee on Immunization Practices (ACIP) of the Centers for Disease Control and Prevention (CDC).[1] It is recommended that MCV4 be given at the 11- to 12-year-old preadolescent visit, to adolescents entering high school, and to college freshman living in dormitories.[1] Although recommendations for catch-up vaccinations have not been made, it is the goal by 2008 that all adolescents will be vaccinated with MCV4 beginning at 11 years of age.[1]

TABLE 3
Comparison of MPSV4 and MCV4

	MPSV4 (Menomune)	*MCV4 (Menactra)*
Antigenic components A, C, Y, W-135 purified polysaccharides	50 mcg each polysaccharide	4 mcg each polysaccharide conjugated to 48 mcg diphtheria toxoid protein carrier
Preparation	Lyophilized	Liquid
Preservative or adjuvant	Thimerosal 1:10,000 added as preservative to diluent in multidose vial; single dose is preservative-free.	None; only single-dose vials
Dosage and administration	0.5 mL subcutaneously	0.5 mL intramuscularly
Cost*	$103	$98
Storage	Between 2°C and 8°C (35°F and 46°F)[23]	Between 2°C and 8°C[33]

MPSV4 = tetravalent meningococcal polysaccharide vaccine; MCV4 = tetravalent meningococcal polysaccharide-protein conjugate vaccine.

**—Estimated cost to the pharmacist based on average wholesale prices (rounded to the nearest whole dollar) in Red Book. Montvale, N.J.: Medical Economics Data, 2005. Cost to the patient will be higher, depending on prescription filling fee.*

Information from references 23 and 33.

TABLE 4
Indications for Use of Meningococcal Vaccines

Population classification	*Approximate age*	*Preferred vaccine type*
Routine vaccination		
Adolescents at routine checkup	11 to 12 years	MCV4 (Menactra)
Adolescents (who have not previously received MCV4) before high school entry	15 years	MCV4
Patients at increased risk for meningococcal disease		
College freshmen living in dormitories	17 to 24 years	MCV4 (MPSV4 [Menomune] acceptable)
Military recruits	18 years or older	MCV4 (MPSV4 acceptable)
Microbiologists routinely exposed to *Neisseria meningitidis*	Adult	MCV4 (MPSV4 acceptable)
Persons with anatomic or functional asplenia or terminal complement deficiencies	Two to 10 years of age or older than 55 years	MPSV4
	11 to 55 years of age	MCV4
Travelers to countries where *N. meningitidis* is hyperendemic or epidemic, especially sub-Saharan Africa or Saudi Arabia	Two to 10 years of age or older than 55 years	MPSV4
	11 to 55 years of age	MCV4
Patients with HIV*	11 years[35] or older (elective)	MCV4 or MPSV4

NOTE: MCV4 is licensed and preferred for persons 11 to 55 years of age; however, MPSV4 is an acceptable alternative. Only MPSV4 may be used in persons two to 10 years of age or those older than 55 years.

MCV4 = tetravalent meningococcal polysaccharide-protein conjugate vaccine; MPSV4 = tetravalent meningococcal polysaccharide vaccine; HIV = human immunodeficiency virus.

**—Efficacy of MCV4 among patients infected with HIV is unknown. Revaccination with MCV4 is not indicated unless vaccination with MPSV4 occurred three to five years previously and the person still remains at increased risk for meningococcal disease.*

Adapted from Bilukha OO, Rosenstein N. Prevention and control of meningococcal disease. Recommendations of the Advisory Committee on Immunization Practices. MMWR Recomm Rep 2005;54(RR-7):14, with additional information from reference 35.

Cost-Effectiveness

A recent study[36] analyzed the cost-effectiveness of immunizing different age groups in the United States with MCV4. Comparisons were made among immunizing infants at two, four, and six months of age; toddlers at one year of age; and preadolescents with one dose at 11 years of age. The last strategy was projected to prevent 270 cases and 36 deaths over 22 years at a cost of $633,000 per meningococcal case prevented and $121,000 per life-year saved.[35,36] However, the devastation of the disease and the anxiety that often accompanies the presence of the disease in the community are thought to justify the cost of prevention.

Update

The Vaccine Adverse Event Reporting System has received notification of five cases of Guillain-Barré syndrome (GBS) that have occurred in individuals 17 to 18 years of age within 14 to 31 days of receiving MCV4. The CDC states that there is not sufficient evidence at this time to determine a causal relationship between GBS and MCV4, and no changes have been made to current recommendations. However, it may be reasonable to withhold the vaccine in low-risk individuals who have a history of GBS. The CDC recommends that adolescents and their parents or guardians be informed of this ongoing investigation as part of the consent process for vaccination with MCV4.

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