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Control and Prevention of Meningococcal Disease and Control and Prevention of Serogroup C Meningococcal Disease: Evaluation and Management of Suspected Outbreaks

Recommendations of the Advisory Committee on Immunization Practices (ACIP)

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
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Contents

Control and Prevention of Meningococcal Disease 1
Introduction 1
Meningococcal Polysaccharide Vaccine 2
Vaccine Efficacy 2
Duration of Efficacy 3
Recommendations for Use of Meningococcal Vaccine 3
Indications for Use 3
Primary Vaccination 5
Revaccination 5
Precautions and Contraindications 5
Reactions to Vaccination 5
Vaccination During Pregnancy 5
Prospects for New Meningococcal Vaccines 5
Antimicrobial Chemoprophylaxis 6
Conclusions 7
References 8

Control and Prevention of Serogroup C Meningococcal Disease: Evaluation and Management of Suspected Outbreaks 13
Introduction 13
Background 14
Endemic Disease 14
Control of Outbreaks 14
Outbreak Settings 14
Definitions 15
Case Definitions 15
Close Contacts 15
Primary, Secondary, and Co-Primary Cases 15
Organization- and Community-Based Outbreaks 15
Population at Risk 16
Vaccination Group and Seasonality of Outbreaks 16
Recommendations 16
Vaccine 20
Other Control Measures 20
Conclusions 21
References 21

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Control and Prevention of Meningococcal Disease: Recommendations of the Advisory Committee on Immunization Practices (ACIP)

Summary

These recommendations update information regarding the polysaccharide vaccine licensed in the United States for use against disease caused by Neisseria meningitidis *serogroups A, C, Y, and W-135, as well as antimicrobial agents for chemoprophylaxis against meningococcal disease (superseding* MMWR *1985;34:255–9). This report provides additional information regarding meningococcal vaccines and the addition of ciprofloxacin and ceftriaxone as acceptable alternatives to rifampin for chemoprophylaxis in selected populations.*

INTRODUCTION

Neisseria meningitidis causes both endemic and epidemic disease, principally meningitis and meningococcemia (*1*). As a result of the control of *Haemophilus influenzae* type b infections, *N. meningitidis* has become the leading cause of bacterial meningitis in children and young adults in the United States, with an estimated 2,600 cases each year (*2*). The case-fatality rate is 13% for meningitic disease (defined as the isolation of *N. meningitidis* from cerebrospinal fluid) and 11.5% for persons who have *N. meningitidis* isolated from blood (*2*), despite therapy with antimicrobial agents (e.g., penicillin) to which U.S. strains remain clinically sensitive (*3*).

The incidence of meningococcal disease peaks in late winter to early spring. Attack rates are highest among children 3–12 months of age and then steadily decline among older age groups (Figure 1). Based on multistate surveillance conducted during 1989–1991, serogroup B organisms accounted for 46% of all cases and serogroup C for 45%; serogroups W-135 and Y and strains that could not be serotyped accounted for most of the remaining cases (*2*). Recent data indicate that the proportion of cases caused by serogroup Y strains is increasing (*4*). Serogroup A, which rarely causes disease in the United States, is the most common cause of epidemics in Africa and Asia. In the United States, localized community outbreaks of serogroup C disease and a statewide serogroup B epidemic have recently been reported (*5,6*).

Persons who have certain medical conditions are at increased risk for developing meningococcal infection. Meningococcal disease is particularly common among persons who have component deficiencies in the terminal common complement pathway (C3, C5–C9); many of these persons experience multiple episodes of infection (*6*). Asplenic persons also may be at increased risk for acquiring meningococcal disease with particularly severe infections (*8*). Persons who have other diseases associated with immunosuppression (e.g., human immunodeficiency virus [HIV] and *Streptococcus pneumoniae*) may be at higher risk for acquiring meningococcal disease and for disease caused by some other encapsulated bacteria. Evidence suggests that HIV-infected persons are not at substantially increased risk for epidemic serogroup A meningococcal disease (*9*); however, such patients may be at increased risk for sporadic meningococcal disease or disease caused by other meningococcal

serogroups (*10*). Previously, military recruits had high rates of meningococcal disease, particularly serogroup C disease; however, since the initiation of routine vaccination of recruits with the bivalent A/C meningococcal vaccine in 1971, the high rates of meningococcal disease caused by those serogroups have decreased substantially and cases occur infrequently (*11*). Military recruits now routinely receive the quadrivalent A,C,Y, W-135 meningococcal vaccine.

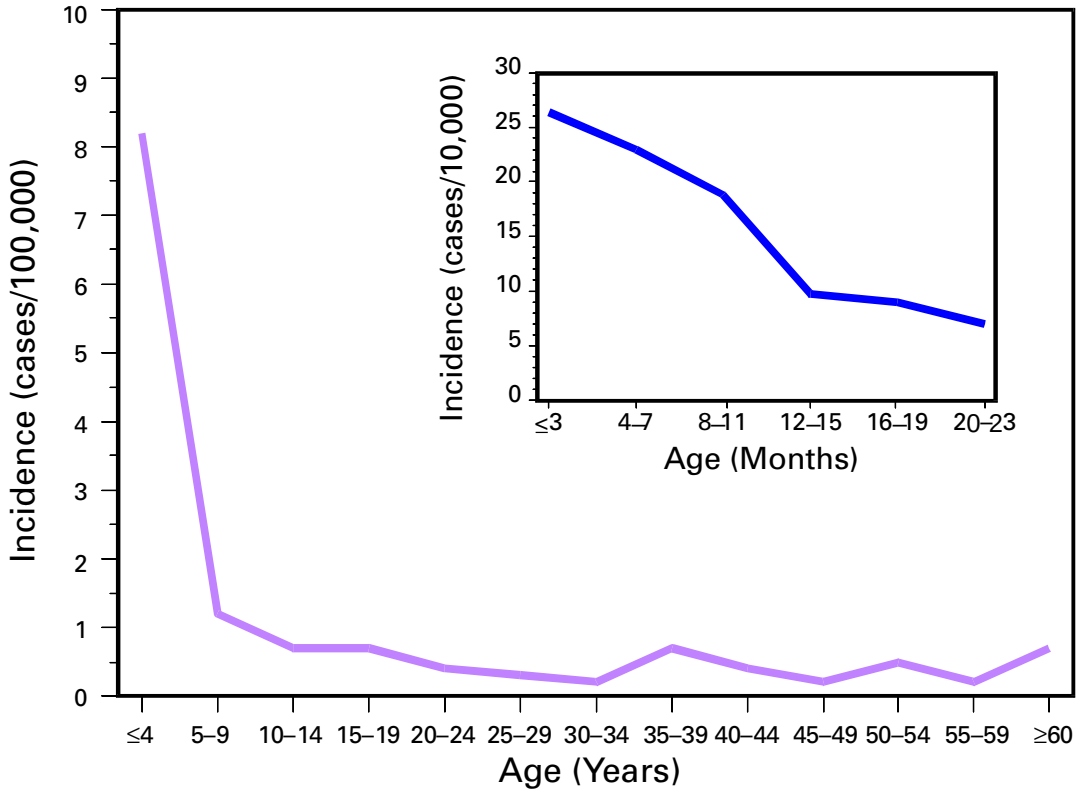
MENINGOCOCCAL POLYSACCHARIDE VACCINE

The quadrivalent A,C,Y,W-135 vaccine (Menomune®–A,C,Y,W-135, manufactured by Connaught Laboratories, Inc.) is the formulation currently available in the United States. The recommended dose of vaccine is a single 0.5-mL subcutaneous injection. Each vaccine dose consists of 50 µg each of the purified bacterial capsular polysaccharides. Menomune® is available in single-dose, 10-dose, and 50-dose vials.

Vaccine Efficacy

The immunogenicity and clinical efficacy of the serogroups A and C meningococcal vaccines have been well established. The serogroup A polysaccharide induces antibody in some children as young as 3 months of age, although a response comparable with that among adults is not achieved until 4 or 5 years of age; the serogroup C

FIGURE 1. Incidence of meningococcal disease, by age group — selected U.S. areas, 1989–1991



component is poorly immunogenic in recipients who are <18–24 months of age (*12,13*). The serogroups A and C vaccines have demonstrated estimated clinical efficacies of 85%–100% in older children and adults and are useful in controlling epidemics (*9,14–17*). Serogroups Y and W-135 polysaccharides are safe and immunogenic in adults and in children >2 years of age (*18–21*); although clinical protection has not been documented, vaccination with these polysaccharides induces bactericidal antibody. The antibody responses to each of the four polysaccharides in the quadrivalent vaccine are serogroup-specific and independent.

Duration of Efficacy

Measurable levels of antibodies against the group A and C polysaccharides decrease markedly during the first 3 years following a single dose of vaccine (*13,22–25*). This decrease in antibody occurs more rapidly in infants and young children than in adults. Similarly, although vaccine-induced clinical protection probably persists in schoolchildren and adults for at least 3 years, the efficacy of the group A vaccine in young children may decrease markedly with the passage of time: in a 3-year study, efficacy declined from >90% to <10% among children who were <4 years of age at the time of vaccination, whereas among children who were ≥4 years of age when vaccinated, efficacy was 67% 3 years later (*26*).

RECOMMENDATIONS FOR USE OF MENINGOCOCCAL VACCINE

Routine vaccination of civilians with the quadrivalent meningococcal polysaccharide vaccine is not recommended because of its relative ineffectiveness in children <2 years of age (among whom risk for endemic disease is highest) and its relatively short duration of protection. However, the polysaccharide meningococcal vaccine is useful for controlling serogroup C meningococcal outbreaks (*27*).

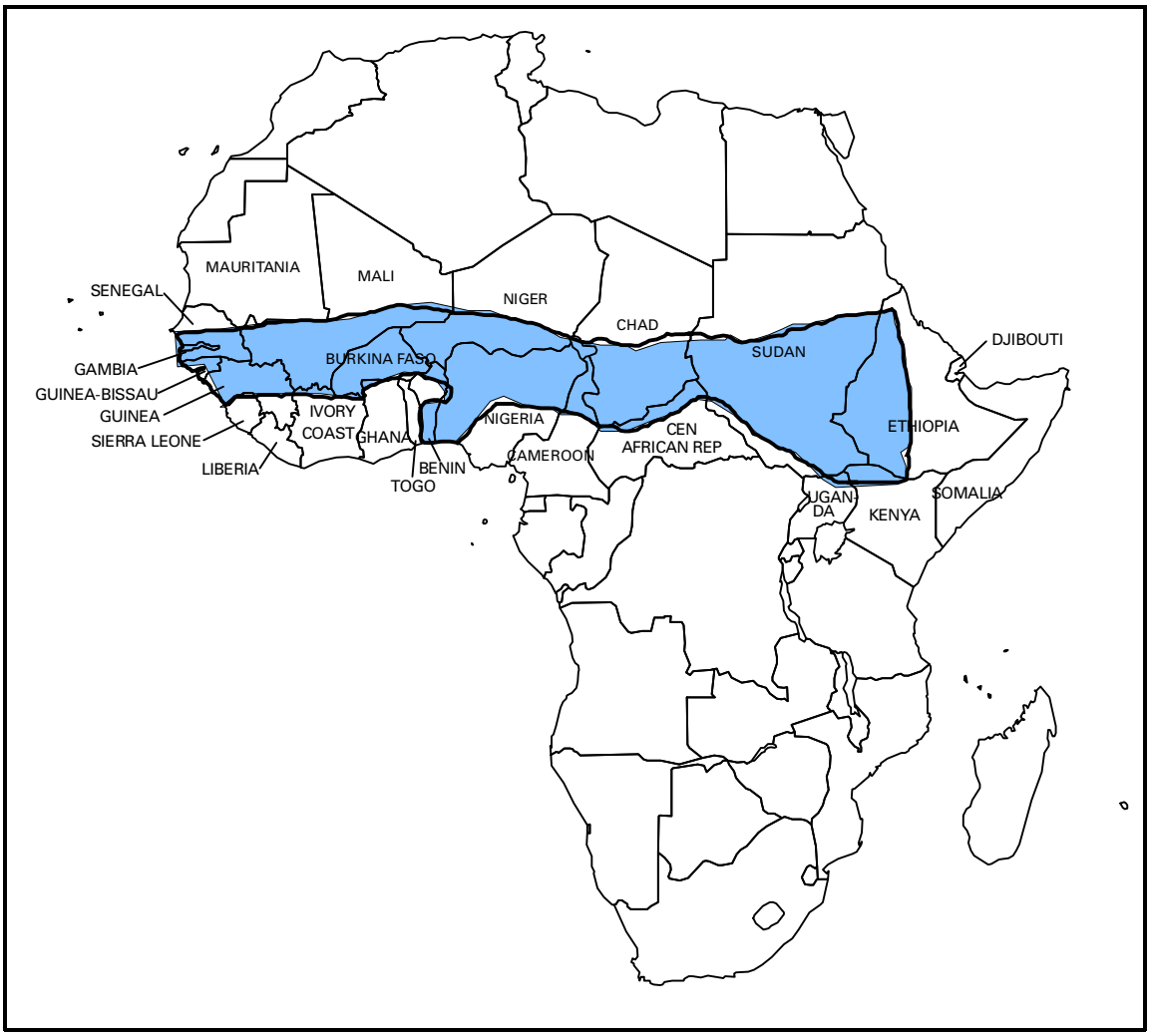
Indications for Use

In general, use of polysaccharide meningococcal vaccine should be restricted to persons ≥2 years of age; however, children as young as 3 months of age may be vaccinated to elicit short-term protection against serogroup A meningococcal disease (two doses administered 3 months apart should be considered for children 3–18 months of age) (*28*).

Routine vaccination with the quadrivalent vaccine is recommended for certain high-risk groups, including persons who have terminal complement component deficiencies and those who have anatomic or functional asplenia. Persons whose spleens have been removed because of trauma or nonlymphoid tumors and persons who have inherited complement deficiencies have acceptable antibody responses to meningococcal vaccine; however, the clinical efficacy of vaccination has not been documented for these persons, and they may not be protected by vaccination (*7,29*). Research, industrial, and clinical laboratory personnel who routinely are exposed to *N. meningitidis* in solutions that may be aerosolized should be considered for vaccination.

Vaccination with the quadrivalent vaccine may benefit travelers to and U.S. citizens residing in countries in which *N. meningitidis* is hyperendemic or epidemic, particularly if contact with the local populace will be prolonged. Single-dose vials of the quadrivalent vaccine are now available and may be more convenient than multidose vials for use in international health clinics for travelers (*30*). Epidemics of meningococcal disease are recurrent in that part of sub-Saharan Africa known as the "meningitis belt," which extends from Senegal in the west to Ethiopia in the east (Figure 2) (*31*). Epidemics in the meningitis belt usually occur during the dry season (i.e., from December to June); thus, vaccination is recommended for travelers visiting this region during that time. Epidemics occasionally are identified in other parts of the world and recently have occurred in Saudi Arabia (during a Haj pilgrimage), Kenya, Tanzania, Burundi, and Mongolia. Information concerning geographic areas for which vaccination is recommended can be obtained from international health clinics for travelers, state health departments, and CDC (telephone: [404] 332-4559).

FIGURE 2. Sub-Saharan meningitis belt



Primary Vaccination

For both adults and children, vaccine is administered subcutaneously as a single 0.5-mL dose. The vaccine can be administered at the same time as other vaccines but at a different anatomic site (i.e., deltoid muscle or buttocks). Protective levels of antibody are usually achieved within 7–10 days after vaccination.

Revaccination

Revaccination may be indicated for persons at high risk for infection (e.g., persons remaining in areas in which disease is epidemic), particularly for children who were first vaccinated when they were <4 years of age; such children should be considered for revaccination after 2–3 years if they remain at high risk. Although the need for revaccination of older children and adults has not been determined, antibody levels decline rapidly over 2–3 years, and if indications still exist for immunization, revaccination may be considered within 3–5 years.

PRECAUTIONS AND CONTRAINDICATIONS

Reactions to Vaccination

Adverse reactions to meningococcal vaccine are mild and consist principally of pain and redness at the injection site, for 1–2 days. Estimates of incidence of mild-to-moderate local reactions have varied, ranging from infrequent to >40% among vaccine recipients (*32,33*). Pain at the site of injection is the most commonly reported adverse reaction, and a transient fever might develop in ≤2% of young children.

Vaccination During Pregnancy

Studies of vaccination during pregnancy have not documented adverse effects among either pregnant women or newborns (*34,35*). In addition, these studies have documented high antibody levels in maternal and umbilical cord blood following vaccination during pregnancy. Antibody levels in the infants decreased during the first few months after birth; subsequent response to meningococcal vaccination was not affected (*35*). These observations have been confirmed in more recent studies of other polysaccharide vaccines administered during pregnancy (*36*). Based on data from studies involving use of meningococcal vaccines and other polysaccharide vaccines administered during pregnancy, altering meningococcal vaccination recommendations during pregnancy is unnecessary.

PROSPECTS FOR NEW MENINGOCOCCAL VACCINES

To enhance the immunogenicity and protective efficacy of A and C polysaccharides in infants and young children, methods similar to those used for *H. influenzae* type b conjugate vaccines have been applied to produce conjugate serogroups A and C vaccines (*37,38*). Capsular polysaccharides are being covalently linked to carrier proteins to convert the T-cell–independent polysaccharide to a T-cell–dependent antigen. The efficacy of these vaccines has not been evaluated.

Because the serogroup B capsular polysaccharide is poorly immunogenic in humans, vaccine development for serogroup B meningococci has focused on the outer membrane proteins as potential immunogens. The immunogenicity and protective efficacy of several outer membrane protein vaccines against several serogroup B meningococci have been evaluated recently. Evaluation of those vaccines documented estimated efficacies ranging from 57% to 83% in older children and adults (*39–41*). However, a subsequent study of one of these vaccines did not document efficacy in children <4 years of age, the group often at highest risk for disease (*42*). None of the currently available serogroup B meningococcal vaccines are licensed for use in the United States.

ANTIMICROBIAL CHEMOPROPHYLAXIS

Antimicrobial chemoprophylaxis of close contacts of sporadic cases of meningococcal disease is the primary means for prevention of meningococcal disease in the United States (Table). Close contacts include a) household members, b) day care center contacts, and c) anyone directly exposed to the patient's oral secretions (e.g., through kissing, mouth-to-mouth resuscitation, endotracheal intubation, or endotracheal tube management). The attack rate for household contacts exposed to patients who have sporadic meningococcal disease has been estimated to be four cases per 1,000 persons exposed, which is 500–800 times greater than for the total population (*43*). Because the rate of secondary disease for close contacts is highest during the first few days after onset of disease in the primary patient, antimicrobial chemoprophylaxis should be administered as soon as possible (ideally within 24 hours after the case is identified). Conversely, chemoprophylaxis administered >14 days after onset of illness in the index case-patient is probably of limited or no value. Oropharyngeal or nasopharyngeal cultures are not helpful in determining the need for chemoprophylaxis and may unnecessarily delay institution of this preventive measure.

Rifampin is administered twice daily for 2 days (600 mg every 12 hours for adults, 10 mg/kg of body weight every 12 hours for children ≥1 month of age, and 5 mg/kg every 12 hours for infants <1 month of age). Rifampin is effective in eradicating nasopharyngeal carriage of *N. meningitidis* (*44*). *Rifampin is not recommended for*

TABLE. Schedule for administering chemoprophylaxis against meningococcal disease

Drug	Age group	Dosage	Duration and route of administration*
Rifampin	Children <1 mo	5 mg/kg every 12 hrs	2 days
	Children ≥1 mo	10 mg/kg every 12 hrs	2 days
	Adults	600 mg every 12 hrs	2 days
Ciprofloxacin	Adults	500 mg	Single dose
Ceftriaxone	Children <15 yrs	125 mg	Single IM† dose
Ceftriaxone	Adults	250 mg	Single IM dose

*Oral administration unless indicated otherwise.
†Intramuscular.

pregnant women, because the drug is teratogenic in laboratory animals. Rifampin changes the color of urine to reddish-orange and is excreted in tears and other body fluids; it may cause permanent discoloration of soft contact lenses. Because the reliability of oral contraceptives may be affected by rifampin therapy, consideration should be given to using alternate contraceptive measures while rifampin is being administered.

In addition to rifampin, other antimicrobial agents are effective in reducing nasopharyngeal carriage of *N. meningitidis*. Ciprofloxacin in various dosage regimens is >90% effective in eradicating nasopharyngeal carriage (*45,46*). A single 500-mg oral dose of ciprofloxacin is a reasonable alternative to the multidose rifampin regimen. Ciprofloxacin levels in nasal secretions far exceed the MIC_{90} for *N. meningitidis* following oral dosing (*47*). Ciprofloxacin is not generally recommended for persons <18 years of age or for pregnant and lactating women because the drug causes cartilage damage in immature laboratory animals. However, a recent international consensus report has concluded that ciprofloxacin can be used for chemoprophylaxis of children when no acceptable alternative therapy is available (*48*).

When ceftriaxone was administered in a single parenteral dose (an intramuscular dose of 125 mg for children and 250 mg for adults), it was 97%–100% effective in eradicating pharyngeal carriage of *N. meningitidis* (*49,50*). Thus, ceftriaxone (diluted in 1% lidocaine to reduce local pain after injection) is also a reasonable alternative for chemoprophylaxis.

Systemic antimicrobial therapy of meningococcal disease with agents other than ceftriaxone or other third-generation cephalosporins may not reliably eradicate nasopharyngeal carriage of *N. meningitidis*. If other agents have been used for treatment, the index patient should receive chemoprophylactic antibiotics for eradication of nasopharyngeal carriage before being discharged from the hospital (*51*).

CONCLUSIONS

N. meningitidis is the leading cause of bacterial meningitis in older children and young adults in the United States. The quadrivalent A, C, Y, and W-135 meningococcal vaccine available in the United States is recommended for control of serogroup C meningococcal disease outbreaks and for use among certain high-risk groups, including a) persons who have terminal complement deficiencies, b) persons who have anatomic or functional asplenia, and c) laboratory personnel who routinely are exposed to *N. meningitidis* in solutions that may be aerosolized. Vaccination also may benefit travelers to countries in which disease is hyperendemic or epidemic. Conjugate serogroup A and C meningococcal vaccines are being developed by using methods similar to those used for *H. influenzae* type b conjugate vaccines, and the efficacies of several experimental serogroup B meningococcal vaccines have been documented in older children and young adults.

Antimicrobial chemoprophylaxis of close contacts of patients who have sporadic cases of meningococcal disease is the primary means for prevention of meningococcal disease in the United States. Rifampin has been the drug of choice for chemoprophylaxis; however, data from recent studies document that single doses of ciprofloxacin or ceftriaxone are reasonable alternatives to the multidose rifampin regimen for chemoprophylaxis.

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Control and Prevention of Serogroup C Meningococcal Disease: Evaluation and Management of Suspected Outbreaks: Recommendations of the Advisory Committee on Immunization Practices (ACIP)

Summary

Outbreaks of serogroup C meningococcal disease (SCMD) have been occurring more frequently in the United States since the early 1990s, and the use of vaccine to control these outbreaks has increased. These outbreaks are characterized by increased rates of disease among persons who may have a common organizational affiliation or who live in the same community. By using surveillance for SCMD and calculation of attack rates, public health officials can identify SCMD outbreaks and determine whether use of meningococcal vaccine is warranted. This report describes 10 steps for evaluation and management of suspected SCMD outbreaks. The principles described also apply to suspected outbreaks caused by meningococcal serogroups A, Y, and W-135. The effectiveness of mass chemoprophylaxis (administration of antibiotics to large populations) has not been demonstrated in most settings in which community and organizational outbreaks occur. However, in outbreaks involving small populations, administration of chemoprophylaxis to all persons within this group may be considered. The ability to validate some aspects of these recommendations is currently limited by incomplete reporting of serogroup information in most systems for meningococcal disease surveillance in the United States and by the relative rarity of SCMD and SCMD outbreaks.

INTRODUCTION

In the United States, outbreaks of serogroup C meningococcal disease (SCMD) have been occurring more frequently since the early 1990s, and the use of meningococcal vaccine to control these outbreaks has increased. During 1980–1993, 21 outbreaks of SCMD were identified, eight of which occurred during 1992–1993 (*1*). Each of these 21 outbreaks involved from three to 45 cases of SCMD, and most outbreaks had attack rates exceeding 10 cases per 100,000 population, which is approximately 20 times higher than rates of endemic SCMD. During 1981–1988, only 7,600 doses of meningococcal vaccine were used to control four outbreaks, whereas from January 1992 through June 1993, 180,000 doses of vaccine were used in response to eight outbreaks.

The decision to implement mass vaccination to prevent meningococcal disease depends on whether the occurrence of more than one case of the disease represents an outbreak or an unusual clustering of endemic meningococcal disease. Because the number of cases in outbreaks is usually small, this determination is not easily made without evaluation and analysis of the pattern of disease occurrence. Mass vaccination campaigns are expensive, require a massive public health effort, and can

create unwarranted concern among the public. However, mass vaccination can prevent unnecessary morbidity and mortality. This report provides public health professionals (i.e., epidemiologists in state and local health departments) with guidelines for determining whether mass vaccination should be implemented to prevent meningococcal disease.

BACKGROUND

Meningococcal disease is an infection caused by *Neisseria meningitidis*. Meningococcal disease manifests most commonly as meningitis and/or meningococcemia that can progress rapidly to purpura fulminans, shock, and death. *N. meningitidis* is transmitted from person to person via respiratory secretions; carriage is usually asymptomatic.

Endemic Disease

In the United States, rates of endemic SCMD have remained unchanged at approximately 0.5 cases per 100,000 population per year (*2*). Most of these cases are sporadic and are not epidemiologically associated with other SCMD cases. Secondary and co-primary SCMD cases sometimes occur among close contacts of persons with primary disease; however, such cases are rare, primarily because close contacts are administered chemoprophylaxis (*3*).

Control of Outbreaks

SCMD outbreaks represent a different epidemiologic phenomenon than does endemic SCMD. SCMD outbreaks are characterized by increased rates of disease among persons who may have a common organizational affiliation or who live in the same community yet do not have close contact. By using the guidelines contained in this report, public health officials can identify SCMD outbreaks and determine whether the use of meningococcal vaccine is warranted. Meningococcal vaccine is recommended for the control of SCMD outbreaks, which often affect older children and adults, for whom vaccination is effective.

The benefit of vaccination for control of SCMD outbreaks is difficult to assess because the pattern of disease occurrence is unpredictable and the numbers of cases are usually small. However, in three recent SCMD outbreaks in the United States during which vaccination campaigns were conducted, additional SCMD cases occurred only among nonvaccinated persons in the group targeted for vaccination (*1*), suggesting that additional SCMD cases probably were prevented by vaccination.

Outbreak Settings

In the United States, SCMD outbreaks have occurred in organizations and communities. In a community-based outbreak, identifying groups most likely to benefit from vaccination is more difficult because communities include a broad range of ages among whom risk for disease and vaccine efficacy vary. Thus, the recommendations for evaluation and management of organization-based and community-based outbreaks are considered separately.

DEFINITIONS

In this report, the following definitions for SCMD and other definitions are used (*4*):

Case Definitions

A **confirmed case** of SCMD is defined by isolation of *N. meningitidis* serogroup C obtained from a normally sterile site (e.g., blood or cerebrospinal fluid) from a person with clinically compatible illness. A **probable case** of SCMD is defined by the detection of serogroup C meningococcal polysaccharide antigen in cerebrospinal fluid (by latex agglutination or counterimmunoelectrophoresis) in the absence of a diagnostic culture from a person with clinically compatible illness.

Close Contacts

Close contacts of a patient who has meningococcal disease include a) household members, b) day care center contacts, and c) persons directly exposed to the patient's oral secretions (e.g., through mouth-to-mouth resuscitation or kissing) (*3*).

Primary, Secondary, and Co-Primary Cases

A **primary case** is a case that occurs in the absence of previous known close contact with another case-patient. A **secondary case** is defined as one that occurs among close contacts of a primary case-patient ≥24 hours after onset of illness in the primary case-patient. If two or more cases occur among a group of close contacts with onset of illnesses separated by <24 hours, these cases are considered to be **co-primary**.

Organization- and Community-Based Outbreaks

An **organization-based outbreak** of SCMD is defined as the occurrence of three or more confirmed or probable cases of SCMD during a period of ≤3 months in persons who have a common affiliation but no close contact with each other, resulting in a primary disease attack rate of at least 10 cases per 100,000 persons. In instances where close contact has occurred, chemoprophylaxis should be administered to close contacts. Organization-based outbreaks have recently occurred in schools, universities, and correctional facilities (*1*). Investigation of organization-based outbreaks may reveal even closer links between patients than suggested by initial reports. For example, data from an investigation of one outbreak at a school indicated that all persons who had meningococcal disease had ridden the same school bus (*5*).

A **community-based outbreak** of SCMD is defined as the occurrence of three or more confirmed or probable cases during a period of ≤3 months among persons residing in the same area who are not close contacts of each other and who do not share a common affiliation, with a primary attack rate of at least 10 cases per 100,000 population. Community-based outbreaks have occurred in towns, cities, and counties (*1*). Distinguishing whether an outbreak is organization-based or community-based is complicated by the fact that, in some instances, these types of outbreaks may occur simultaneously.

Population at Risk

The **population at risk** is defined as a group of persons who, in addition to close contacts, are considered to be at increased risk for SCMD when compared with historical patterns of disease in the same population or with the risk for disease in the general U.S. population. This group is usually defined on the basis of organizational affiliation or community of residence. The population at risk is used as the denominator in calculations of the disease attack rate.

Vaccination Group and Seasonality of Outbreaks

During a vaccination campaign, the group designated to be administered vaccine is called the **vaccination group**. In some instances, the vaccination group will be the same as the population at risk; however, in other instances, these groups may differ. For example, in an organization-based outbreak at a university in which all cases have occurred among undergraduates rather than graduate students, faculty, or other staff, undergraduates may be the vaccination group. In community-based outbreaks, cases often occur in persons within a narrow age range (e.g., only in persons <30 years of age) (*1*). Because the available vaccine is probably not effective in children <2 years of age, these children are not usually included in the vaccination group, and the vaccination group may be that portion of the population at risk who are 2–29 years of age.

In the United States, the incidence of meningococcal disease varies by season, with the highest rates of disease occurring in February and March and the lowest in September (*2*). For control of SCMD outbreaks, vaccination administered before or during the seasonal peak (i.e., fall and winter months) is more likely to prevent cases than vaccination administered during lower incidence periods (i.e., spring and summer).

RECOMMENDATIONS

The following recommendations regarding the evaluation and management of suspected SCMD outbreaks are based on experience with SCMD outbreaks in the United States. However, the principles described apply to outbreaks caused by the other vaccine-preventable meningococcal serogroups A, Y, and W-135.

- **Establish a diagnosis of SCMD.** Only confirmed and probable SCMD cases should be considered in the characterization of a suspected SCMD outbreak. Cases not fulfilling these criteria should be excluded from consideration.
- **Administer chemoprophylaxis to appropriate contacts.** Chemoprophylaxis should be administered to close contacts of patients. Administering chemoprophylaxis to persons who are not close contacts of patients has not been effective in preventing community outbreak-associated cases and usually is not recommended. Neither oropharyngeal nor nasopharyngeal cultures for *N. meningitidis* are useful in deciding who should receive chemoprophylaxis or when investigating suspected outbreaks (*3*).

- **Enhance surveillance, save isolates, and review historical data.** Most state and local health departments rely on passive surveillance for meningococcal disease, which may result in delayed or incomplete reporting of cases. When an SCMD outbreak is suspected, potential reporting sites should be alerted and encouraged to report new cases promptly. Reporting sites also should send all *N. meningitidis* isolates to a designated local or state laboratory until investigation of the suspected SCMD outbreak is completed. This action will ensure availability of isolates for confirmation of serogroup and application of other methods for subtyping.

  Information on the serogroup of *N. meningitidis* isolates is needed to fulfill criteria for confirmed and probable case definitions. This information should be obtained promptly with all meningococcal disease case reports in the United States. To ensure availability of serogroup information, health department laboratories should support laboratory facilities that do not routinely perform serogrouping on meningococcal isolates.

  Public health officials should review overall and serogroup-specific meningococcal disease rates for previous years in the same or comparable population(s) and in different regions within the state. These data should be compared with data currently reported for the population being evaluated to characterize both the geographic extent and magnitude of the outbreak.

- **Investigate links between cases.** In addition to demographic information, public health professionals should collect age-appropriate information concerning each SCMD patient (e.g., close contact with other case-patients, day care attendance, participation in social activities, participation in sports activities, and affiliation with organizations). This information will help identify secondary and co-primary cases and also may reveal links between cases that will help define the population at risk.

- **Consider subtyping.** Subtyping of *N. meningitidis* isolates, using methods such as multilocus enzyme electrophoresis or pulsed-field gel electrophoresis of enzyme-restricted DNA fragments, may provide information that will be useful in determining whether a group of cases represents an outbreak. SCMD outbreaks usually are caused by closely related strains. Subtyping data can allow identification of an "outbreak strain" and aid in better defining the extent of an outbreak. If strains from a group of patients are unrelated by subtyping, the group of cases most likely does not represent an outbreak. Although subtyping is potentially useful, it is time consuming and can be done only in specialized reference laboratories. In addition, results can sometimes be difficult to interpret. Initiation of outbreak-control efforts should not be delayed until subtyping results are available.

- **Exclude secondary and co-primary cases.** To calculate a primary disease attack rate, all confirmed and probable cases should be summed; secondary cases should be excluded and each set of co-primary cases counted as one case. Because the purpose of calculating attack rates is both to characterize the risk for disease among the general population and to determine whether overall rates have increased, related cases (i.e., secondary and co-primary cases) should not be included. Epidemiologically, secondary and co-primary cases can be considered as representing single episodes of disease with direct spread to one or more close contact(s), which is consistent with endemic disease. Because the risk for acquiring meningococcal disease is 500–800 times greater among close contacts of case-patients than among the total population, chemoprophylaxis is recommended for these persons (*3*). Because secondary and co-primary cases occur infrequently, they should represent a small portion of outbreak-associated SCMD cases in the United States.

- **Determine if the suspected outbreak is organization- or community-based.** Epidemiologic and laboratory investigations can reveal common affiliations among case-patients. Potential affiliations can be organizational, with all or most of the patients attending a particular day care center, school, or university; belonging to a sports team or club; or sharing an activity (e.g., riding a school bus). Alternatively, common affiliations can be geographic (e.g., residing in the same town, city, or county). Of 21 U.S. outbreaks identified between 1980 and mid-1993, 11 (52%) were organization-based and 10 (48%) were community-based. Eight (73%) of the 11 organization-based outbreaks occurred in schools (*1*). If a common organizational affiliation other than community can be identified, the outbreak is termed organization-based; otherwise, it is considered to be community-based.

- **Define population at risk and determine its size.** In *organization-based outbreaks*, cases are linked by a common affiliation other than a shared geographically delineated community. The population at risk is the group of persons who best represent that affiliation. For example, if the only association between patients was attending the same school or university, the population at risk would be all persons attending the school or university. Information concerning the size of the organization should be obtained from officials in the organization. In *community-based outbreaks*, there are no common affiliations among patients other than a shared, geographically defined community. The population at risk can be defined by the smallest geographically contiguous population that includes all (or almost all) case-patients. This population is usually a neighborhood, town, city, or county. The size of the population can be obtained from census information.

- **Calculate the attack rate.** If three or more SCMD cases have occurred in either an organization- or community-based outbreak in ≤3 months (starting at the time of the first confirmed or probable case), a primary disease attack rate should be calculated. Because of the small number of cases typically involved and the seasonal patterns of meningococcal disease, rate calculations should not be

annualized for use in this algorithm. The following formula can be used to calculate this attack rate:

> Attack rate per 100,000 = [(Number of definite and probable SCMD cases during a 3-month period)*/(Number of population at risk)] x 100,000
>
> If an attack rate exceeds 10 SCMD cases per 100,000 persons, vaccination of the population at risk should be considered.[†]

The actual attack rate at which the decision to vaccinate is made may vary. Public health personnel should consider the following factors: a) completeness of surveillance and number of possible SCMD cases for which bacteriologic confirmation or serogroup data are not available; b) occurrence of additional SCMD cases after recognition of a suspected SCMD outbreak (e.g., if the SCMD outbreak occurred 2 months previously and if no additional cases have occurred, vaccination may be unlikely to prevent additional SCMD cases); and c) logistic and financial considerations.

- **Select the target group for vaccination.** In most *organization-based outbreaks*, the vaccination group may include the whole population at risk provided all persons are >2 years of age. If a substantial proportion of patients are <2 years of age and, thus, not eligible to receive the current vaccine, patients <2 years of age may be excluded and, if at least three case-patients remain, an attack rate should be recalculated. If after recalculation the attack rate is still more than 10 cases per 100,000 persons, vaccination should be considered for some or all of the population at risk ≥2 years of age. In some organization-based outbreaks, a vaccination group larger than the population at risk may be designated. For example, in a high school in which all outbreak-associated cases occurred among students, authorities may decide to offer vaccine to staff. In *community-based outbreaks*, the vaccination group usually can be defined as a subset of the entire population at risk, based on a group ≥2 years of age (e.g., 2–19 or 2–29 years of age). This age range should contain all (or almost all) SCMD patients ≥2 years of age. If a large proportion of patients are <2 years of age and probably will not be protected with the current vaccine, patients <2 years of age may be excluded from calculation of an attack rate.[§]

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*Secondary cases should be excluded, and co-primary sets should be counted as one case.

[†]Calculation of attack rates for organization-based SCMD outbreaks is most useful for large organizations (e.g., some universities). However, in most organization-based SCMD outbreaks with three cases of disease, the rate will exceed 10 cases per 100,000 population. Thus, occurrence of three cases in these settings should prompt consideration of vaccination. In some situations, public health officials also may wish to consider vaccination after only two SCMD cases are identified.

[§]Because community-based outbreaks often affect a broader age distribution than organization-based outbreaks, it may be appropriate to include patients <2 years of age in the calculation of an attack rate even though persons in this age group are unlikely to benefit from vaccination.

In some situations, the entire population ≥2 years of age, without other age restriction, might be the most appropriate vaccination group. For example, in a small town in which several cases have occurred among children ≥2 years and adults >29 years of age, it may be most appropriate to select all persons ≥2 years of age as the vaccination group. For larger populations, this decision would be costly in terms of finances and human resources and restricting the vaccination group to the persons in age groups with the highest attack rates may be more appropriate. Age-specific attack rates can be calculated by using the formula previously provided and restricting the numerator and denominator to persons within specific age groups (e.g., persons 2–19 years of age). Many recent immunization programs have been directed at persons who are 2–19 years of age or who are 2–29 years of age (*1*). The 10 steps are summarized as follows:

Summary of 10 steps in the evaluation and management of suspected outbreaks of serogroup C meningococcal disease (SCMD)

1. Establish a diagnosis of SCMD.
2. Administer chemoprophylaxis to appropriate contacts.
3. Enhance surveillance, save isolates, and review historical data.
4. Investigate links between cases.
5. Consider subtyping.
6. Exclude secondary and co-primary cases.
7. Determine if the suspected outbreak is organization- or community-based.
8. Define the population at risk and determine its size.
9. Calculate the attack rate.
10. Select the target group for vaccination.

Vaccine

Quadrivalent meningococcal vaccine is available in single, 10- or 50-dose vials. Fifty-dose vials are designed for use with jet-injector devices. Questions about vaccination or use of jet-injector devices should be addressed to the National Immunization Program, CDC (telephone: [404] 639-8257) (*6*).

From 7 to 10 days are required following vaccination for development of protective levels of antimeningococcal antibodies. Cases of SCMD occurring in vaccinated persons within 10 days after vaccination should not be considered vaccine failures.

Other Control Measures

Mass chemoprophylaxis (i.e., administration of antibiotics to large populations) is not effective in most settings in which community-based or organization-based outbreaks have occurred. Disadvantages of widespread administration of antimicrobial drugs for chemoprophylaxis include cost of the drug and administration, difficulty of ensuring simultaneous administration of chemoprophylactic antimicrobial drugs to large populations, side effects of the drugs, and emergence of resistant organisms. In most outbreak settings, these disadvantages outweigh the possible (and unproven) benefit in disease prevention. However, in outbreaks involving small populations (e.g., an outbreak in a small organization, such as a single school), administration of chemoprophylaxis to all persons within this population may be considered. If mass chemoprophylaxis is undertaken, it should be administered to all members at the same time. In the United States, measures that have *not* been recommended for control of SCMD outbreaks include restricting travel to areas with a SCMD outbreak, closing schools or universities, or cancelling sporting or social events.

Educating communities, physicians, and other health-care workers about meningococcal disease is an important part of managing suspected SCMD outbreaks. Educational efforts should be initiated as soon as an SCMD outbreak is suspected.

CONCLUSIONS

The ability to validate some aspects of these recommendations is currently limited by both incomplete reporting of serogroup information in most systems for meningococcal disease surveillance in the United States and the infrequency of SCMD cases and SCMD outbreaks. As additional information becomes available from ongoing surveillance projects, these recommendations may be revised.

Consultation on the use of these recommendations or other issues regarding meningococcal disease is available from the Childhood and Respiratory Diseases Branch, Division of Bacterial and Mycotic Diseases, National Center for Infectious Diseases, CDC (telephone: [404] 639-2215 or [404] 639-3311 outside normal working hours).

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