

# Meningococcal Disease

## Meningococcal Disease

Meningococcal disease is an acute, potentially severe illness caused by the bacterium *Neisseria meningitidis*. Illness believed to be meningococcal disease was first reported in the 16th century. The first definitive description of the disease was by Vieusseux in Switzerland in 1805. The bacterium was first identified in the spinal fluid of patients by Weichselbaum in 1887.

*Neisseria meningitidis* is a leading cause of bacterial meningitis and sepsis in the United States. It can also cause focal disease, such as pneumonia and arthritis. *N. meningitidis* is also a cause of epidemics of meningitis and bacteremia in sub-Saharan Africa. The World Health Organization has estimated that meningococcal disease was the cause of 171,000 deaths worldwide in 2000.

The first monovalent (group C) polysaccharide vaccine was licensed in the United States in 1974. A quadrivalent polysaccharide vaccine was licensed in 1978. Meningococcal conjugate vaccine has been licensed in United Kingdom since 1999 and has had a major impact on the incidence of type C meningococcal disease. A quadrivalent conjugate vaccine was first licensed in the United States in 2005.

### *Neisseria meningitidis*

*N. meningitidis*, or meningococcus, is an aerobic, gram-negative diplococcus, closely related to *N. gonorrhoeae*, and to several nonpathogenic *Neisseria* species, such as *N. lactamica*. The organism has both an inner (cytoplasmic) and outer membrane, separated by a cell wall. The outer membrane contains several protein structures that enable the bacteria to interact with the host cells as well as perform other functions.

The outer membrane is surrounded by a polysaccharide capsule that is necessary for pathogenicity because it helps the bacteria resist phagocytosis and complement-mediated lysis. The outer membrane proteins and the capsular polysaccharide make up the main surface antigens of the organism.

Meningococci are classified by using serologic methods based on the structure of the polysaccharide capsule. Thirteen antigenically and chemically distinct polysaccharide capsules have been described. Some strains, often those found to cause asymptomatic nasopharyngeal carriage, are not groupable and do not have a capsule. Almost all invasive disease is caused by one of five serogroups: A, B, C, Y, and W-135. The relative importance of each serogroup depends on geographic location, as well as other factors, such as age.

- Neisseria meningitidis***
- Severe acute bacterial infection
  - Cause of meningitis, sepsis, and focal infections
  - Epidemic disease in sub-Saharan Africa
  - Current polysaccharide vaccine licensed in 1978
  - Conjugate vaccine licensed in 2005

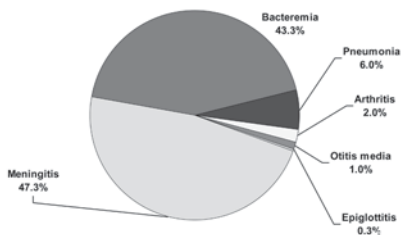
- Neisseria meningitidis***
- Aerobic gram-negative bacteria
  - At least 13 serogroups based on characteristics of the polysaccharide capsule
  - Most invasive disease caused by serogroups A, B, C, Y, and W-135
  - Relative importance of serogroups depends on geographic location and other factors (e.g. age)

# Meningococcal Disease

## Meningococcal Disease Pathogenesis

- Organism colonizes nasopharynx
- In some persons organism invades bloodstream and causes infection at distant site
- Antecedent URI may be a contributing factor

## *Neisseria meningitidis* Clinical Manifestations\*



## Meningococcal Meningitis

- Most common pathologic presentation
- Result of hematogenous dissemination
- Clinical findings
  - fever
  - headache
  - stiff neck

## Meningococcemia

- Bloodstream infection
- May occur with or without meningitis
- Clinical findings
  - fever
  - petechial or purpuric rash
  - hypotension
  - multiorgan failure

For instance, serogroup A is a major cause of disease in sub-Saharan Africa but is rarely isolated in the United States.

Meningococci are further classified on the basis of certain outer membrane proteins. Molecular subtyping using specialized laboratory techniques (e.g., pulsed-field gel electrophoresis) can provide useful epidemiologic information.

## Pathogenesis

Meningococci are transmitted by droplet aerosol or secretions from the nasopharynx of colonized persons. The bacteria attach to and multiply on the mucosal cells of the nasopharynx. In a small proportion (less than 1%) of colonized persons, the organism penetrates the mucosal cells and enters the bloodstream. The bacteria spread by way of the blood to many organs. In about 50% of bacteremic persons, the organism crosses the blood–brain barrier into the cerebrospinal fluid and causes purulent meningitis. An antecedent upper respiratory infection may be a contributing factor.

## Clinical Features

The incubation period of meningococcal disease is 3–4 days, with a range of 2–10 days.

**Meningitis** is the most common presentation of invasive meningococcal disease and results from hematogenous dissemination of the organism. Meningeal infection is similar to other forms of acute purulent meningitis, with sudden onset of fever, headache, and stiff neck, often accompanied by other symptoms, such as nausea, vomiting, photophobia (eye sensitivity to light), and altered mental status.

Meningococci can be isolated from the blood in up to 75% of persons with meningitis.

**Meningococcal sepsis** (bloodstream infection or meningococcemia) occurs without meningitis in 5%–20% of invasive meningococcal infections. This condition is characterized by abrupt onset of fever and a petechial or purpuric rash, often associated with hypotension, shock, acute adrenal hemorrhage, and multiorgan failure.

Less common presentations of meningococcal disease include pneumonia (5%–15% of cases), arthritis (2%), otitis media (1%), and epiglottitis (less than 1%).

The **case-fatality rate** of invasive meningococcal disease is 9%–12%, even with appropriate antibiotic therapy. The fatality rate of meningococcemia is up to 40%. As many as 20% of survivors have permanent sequelae, such as hearing loss, neurologic damage, or loss of a limb.

**Risk factors** for the development of meningococcal disease include deficiencies in the terminal common complement pathway and functional or anatomic asplenia. Persons with HIV infection are probably at increased risk for meningococcal disease. Certain genetic factors (such as polymorphisms in the genes for mannose-binding lectin and tumor necrosis factor) may also be risk factors.

Family members of an infected person are at increased for meningococcal disease. Antecedent upper respiratory tract infection, household crowding, and both active and passive smoking also are also associated with increased risk. In the United States, African Americans and persons of low socioeconomic status have been consistently at higher risk; however, race and low socioeconomic status are likely markers for differences in factors such as household crowding rather than risk factors. During outbreaks, bar or nightclub patronage and alcohol use have also been associated with higher risk for disease.

Cases of invasive meningococcal disease, including at least two fatal cases, have been reported among microbiologists. These persons have worked with *N. meningitidis* isolates rather than patient specimens.

Studies have shown that college freshmen living in dormitories are at modestly increased risk of meningococcal disease. However, U.S. college students are not at higher risk for meningococcal disease than other persons of similar age.

## Laboratory Diagnosis

Invasive meningococcal disease is typically diagnosed by isolation of *N. meningitidis* from a normally sterile site. However, sensitivity of bacterial culture may be low, particularly when performed after initiation of antibiotic therapy. A Gram stain of cerebrospinal fluid showing gram-negative diplococci strongly suggests meningococcal meningitis.

Kits to detect polysaccharide antigen in cerebrospinal fluid are rapid and specific, but false-negative results are common, particularly in serogroup B disease. Antigen tests of urine or serum are unreliable.

Serologic testing (e.g., enzyme immunoassay) for antibodies to polysaccharide may be used as part of the evaluation if meningococcal disease is suspected but should not be used to establish the diagnosis.

### *Neisseria meningitidis* Risk Factors for Invasive Disease

- **Host factors**
  - terminal complement pathway deficiency
  - asplenia
  - genetic risk factors
- **Exposure factors**
  - household exposure
  - concurrent upper respiratory tract infection
  - demographic and socioeconomic factors and crowding
  - active and passive smoking

### Meningococcal Disease Among Young Adults, United States, 1998-1999

•18-23 years old	1.4 /100,000
•18-23 years old not college student	1.4 /100,000
•Freshmen	1.9 /100,000
•Freshmen in dorm	5.1 /100,000

Bruce et al, *JAMA* 2001;286:688-93

### Meningococcal Disease Laboratory Diagnosis

- **Bacterial culture**
- **Gram stain**
- **Non-culture methods**
  - antigen detection in CSF
  - serology

# Meningococcal Disease

## ***Neisseria meningitidis*** **Medical Management**

- Initial empiric antibiotic treatment after appropriate cultures are obtained
- Treatment with penicillin alone recommended after confirmation of *N. meningitidis*

## **Meningococcal Disease** **Epidemiology**

- Reservoir Human
- Transmission Respiratory droplets
- Temporal pattern Peaks in late winter and early spring
- Communicability Generally limited

## **Medical Management**

The clinical presentation of meningococcal meningitis is similar to other forms of bacterial meningitis. Consequently, empiric therapy with broad-spectrum antibiotics (e.g., third-generation cephalosporin, vancomycin) should be started promptly after appropriate cultures have been obtained.

Many antibiotics are effective for *N. meningitidis* infection, including penicillin. Few penicillin-resistant strains of meningococcus have been reported in the United States. Once *N. meningitidis* infection has been confirmed, penicillin alone is recommended.

## **Epidemiology**

### **Occurrence**

Meningococcal disease occurs worldwide in both endemic and epidemic form.

### **Reservoir**

Humans are the only natural reservoir of meningococcus. As many as 10% of adolescents and adults are asymptomatic transient carriers of *N. meningitidis*, most strains of which are not pathogenic (i.e., strains that are not groupable).

### **Transmission**

Primary mode is by respiratory droplet spread or by direct contact.

### **Temporal Pattern**

Meningococcal disease occurs throughout the year. However, the incidence is highest in the late winter and early spring.

### **Communicability**

The communicability of *N. meningitidis* is generally limited. In studies of households in which a case of meningococcal disease has occurred, only 3%–4% of households had secondary cases. Most households had only one secondary case. Estimates of the risk of secondary transmission are generally 2–4 cases per 1,000 household members at risk. However, this risk is 500–800 times that in the general population.

# Meningococcal Disease

## Secular Trends in the United States

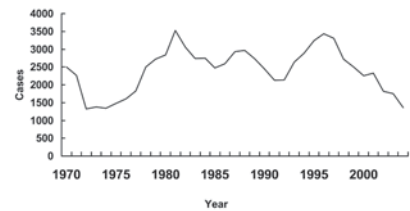
Approximately 2,000 to 3,000 cases of meningococcal disease are reported each year in the United States (0.8–1.3 cases per 100,000 population). In 2004, an estimated 125 deaths due to meningococcal disease occurred in the United States. Infants younger than 12 months of age have the highest rates of disease. Incidence of disease declines in early childhood, increases during adolescence and early adulthood, then declines among older adults. The rate of invasive disease among persons 17–20 years of age is approximately twice that of the overall U.S. population. Although incidence is relatively low, more cases occur in persons 23–64 years of age than in any other age group. The proportion of cases among adolescents and young adults has increased in recent years. During 1992–1998, 28% of reported case-patients were 12–29 years of age.

The proportion of disease caused by different serogroups has changed during the last 15 years. From 1988 to 1991, most cases of meningococcal disease in the United States were due to either serogroup C or B, and serogroup Y accounted for only 2% of cases. However, during 1996–2001, serogroup Y accounted for 21% of cases, with serogroups B and C accounting for 31% and 42%, respectively. Nongroupable strains accounted for 5% of cases. The proportion of cases caused by each serogroup also varies by age group. In 2001, 65% of cases among infants aged less than 1 year were caused by serogroup B, for which no vaccine is available in the United States. Among persons 18–34 years of age, 41% of cases were due to serogroup B, and 25% and 14% were due to serogroups C and Y, respectively.

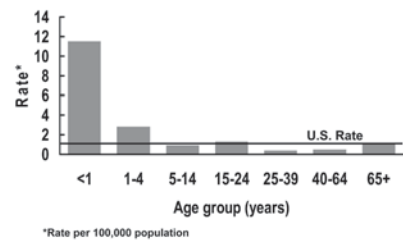
In the United States, **meningococcal outbreaks** account for less than 5% of reported cases (95%–97% of cases are sporadic). However, since 1991, the frequency of localized outbreaks has increased. Most of these outbreaks have been caused by serogroup C. Since 1997, localized outbreaks caused by serogroups Y and B have also been reported. See <http://www.cdc.gov/mmwr/PDF/rr/rr4605.pdf> for additional information on the evaluation and management of meningococcal outbreaks.

Large outbreaks of serogroup A meningococcal disease occur in the African “meningitis belt,” an area that extends from Ethiopia to Senegal. Rates of endemic meningococcal disease in this area are several times higher than in industrialized countries. In addition, outbreaks occur every 8–12 years with attack rates of 500–1000 cases per 100,000 population.

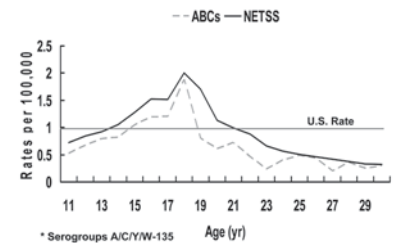
**Meningococcal Disease—United States, 1972-2004**



**Meningococcal Disease, 1998 Incidence by Age Group**



**Rates of Meningococcal Disease\* by Age, United States, 1991-2002**



## Meningococcal Disease in the United States

- Distribution of cases by serogroup varies by time and age group
- In 1996-2001:
  - 21% serogroup Y
  - 31% serogroup B
  - 42% serogroup C
  - 65% of cases among children <1 year of age due to serogroup B

## Meningococcal Outbreaks in the United States

- Outbreaks account for <5% of reported cases
- Frequency of localized outbreaks has increased since 1991
- Most recent outbreaks caused by serogroup C
- Since 1997 outbreaks caused by serogroup Y and B organisms have also been reported

## **Meningococcal Polysaccharide Vaccine (MPSV)**

- Menomune (sanofi pasteur)
- Quadrivalent polysaccharide vaccine (A, C, Y, W-135)
- Administered by subcutaneous injection
- 10-dose vial contains thimerosal as a preservative

## **Meningococcal Conjugate Vaccine (MCV)**

- Menactra (sanofi pasteur)
- Quadrivalent polysaccharide vaccine (A, C, Y, W-135) conjugated to diphtheria toxoid
- Administered by intramuscular injection
- Single dose vials do not contain a preservative

## **Meningococcal Vaccines**

### **Characteristics**

#### ***Meningococcal Polysaccharide Vaccine (MPSV)***

The first meningococcal polysaccharide vaccine (Menomune, sanofi pasteur) was licensed in the United States in 1974. The current quadrivalent A, C, Y, W-135 polysaccharide vaccine was licensed in 1978. Each dose consists of 50 mcg of each of the four purified bacterial capsular polysaccharides. The vaccine contains lactose as a stabilizer.

MPSV is administered by subcutaneous injection. The vaccine is available in single-dose and 10-dose vials. Fifty-dose vials are no longer available. Diluent for the single-dose vial is sterile water without preservative. Diluent for the 10-dose vial is sterile water with thimerosal added as a preservative. After reconstitution the vaccine is a clear colorless liquid.

No vaccine is available in the United States for serogroup B.

#### ***Meningococcal Conjugate Vaccine (MCV)***

Meningococcal conjugate vaccine (Menactra, sanofi pasteur) was first licensed in the United States in 2005. The vaccine contains *N. meningitidis* serogroups A, C, Y and W-135 capsular polysaccharide antigens individually conjugated to diphtheria toxoid protein. Each 0.5-mL dose of vaccine is formulated in sodium phosphate buffered isotonic sodium chloride solution to contain 4 mcg each of meningococcal A, C, Y, and W-135 polysaccharides conjugated to approximately 48 mcg of diphtheria toxoid protein carrier.

MCV is administered by intramuscular injection. It is supplied as a liquid in a single dose vial. The vaccine does not contain a preservative.

### **Immunogenicity and Vaccine Efficacy**

#### ***Meningococcal Polysaccharide Vaccine***

The characteristics of MPSV are similar to other polysaccharide vaccines (e.g., pneumococcal polysaccharide). The vaccine is generally not effective in children younger than 18 months of age. The response to the vaccine is typical of a T-cell independent antigen, with an age-dependent response, and poor immunogenicity in children younger than 2 years of age. In addition, no boost in antibody titer occurs with repeated doses; the antibody which is produced is relatively low-affinity IgM, and “switching” from IgM to IgG production is poor.

A protective level of antibody is usually achieved within 7–10 days of vaccination. Among infants and children younger than 5 years of age, measurable levels of antibodies against serogroup A and C polysaccharides decrease substantially during the first 3 years following a single dose of vaccine. In healthy adults, antibody levels also decrease, but antibodies are detectable as long as 10 years after vaccination. Although vaccine-induced protection likely persists in school-aged children and adults for at least 3 years, the efficacy of the group A vaccine in children younger than 5 years of age may decrease markedly within this period. In one study, efficacy declined from more than 90% to less than 10% 3 years after vaccination among children who were younger than 4 years of age when vaccinated. Efficacy was 67% among children who were older than 4 years of age at vaccination.

### **Meningococcal Conjugate Vaccine**

The approval of MCV was based on studies that compared the serologic response to a single dose the response of persons of similar age who received a single dose of meningococcal polysaccharide vaccine. In these studies a similar proportion of recipients achieved at least a fourfold rise in serum bactericidal antibody titer assay following MCV as those who received MPSV. The proportion of recipients in each group that achieved a titer of 1:128 (the titer considered to predict protection) was more than 98% in both groups.

Because the polysaccharides are conjugated to diphtheria toxoid for MCV, it is believed that this vaccine will have a longer duration of protection than for MPSV. In addition, MCV is expected to reduce asymptomatic carriage of *N. meningitidis* and produce “herd” immunity, as occurs for *Streptococcus pneumoniae* and *Haemophilus influenzae* type b following receipt of the respective vaccines. Pure polysaccharide vaccines have little or no effect on carriage of the vaccine organism.

## **Vaccination Schedule And Use**

### **Meningococcal Polysaccharide Vaccine**

For children 2 years of age and older and adults, MPSV is administered as a **single 0.5-mL dose**. The vaccine can be administered at the same time as other vaccines but should be given at a different anatomic site.

Routine vaccination of civilians with MPSV is not recommended because of its relative ineffectiveness in children younger than 2 years of age (the age group with the highest risk for sporadic disease) and because of its relatively short duration of protection. Use of MPSV should be limited to persons 2–10 years and older than 55 years of age, or when

#### **MPSV Recommendations**

- Approved for persons  $\geq 2$  years of age
- Not recommended for routine vaccination of civilians
- Should be used only for persons at increased risk of *N. meningitidis* infection who are 2-10 years or  $>55$  years of age, or if MCV is not available

# Meningococcal Disease

## MCV Recommendations

- Routinely recommended for:
  - all children at 11-12 years of age
  - unvaccinated children at entry to high school (age 15 years)
  - all college freshmen living in a dormitory
  - other persons 11-55 years of age at increased risk of invasive meningococcal disease

MMWR 2005; 54(RR-7);1-21

## Meningococcal Vaccine Recommendations

- Use of MCV is preferred for persons 11-55 years of age for whom meningococcal vaccine is recommended
- MPSV should be used for persons 2-10 years and >55 years
- Use of MPSV is an acceptable alternative for persons 11-55 years of age if MCV is not available

MMWR 2005; 54(RR-7);1-21

## Meningococcal Vaccine Recommendations

- Recommended for persons at increased risk of meningococcal disease:
  - microbiologists who are routinely exposed to isolates of *N. meningitidis*
  - military recruits
  - persons who travel to and U.S. citizens who reside in countries in which *N. meningitidis* is hyperendemic or epidemic
  - terminal complement component deficiency
  - functional or anatomic asplenia

MMWR 2005; 54(RR-7);1-21

## Meningococcal Endemic Areas 2004



MCV is not available. MPSV can be administered at the same visit as other indicated vaccines. All vaccines should be given at separate sites with separate syringes.

## Meningococcal Conjugate Vaccine

MCV should be administered to all children at 11–12 years of age as well as to unvaccinated adolescents at high school entry (age 15 years). Other adolescents who wish to decrease their risk for meningococcal disease may also be vaccinated. All college freshmen living in dormitories should also be vaccinated.

MCV if preferred for routine vaccination of adolescents and persons 11–55 years of age who are at increased risk of meningococcal disease. MPSV is an acceptable alternative for persons 11–55 years of age if MCV if not available.

Meningococcal vaccination is recommended for persons at increased risk for meningococcal disease, including microbiologists who are routinely exposed to isolates of *N. meningitidis*, military recruits, persons who travel to and U.S. citizens who reside in countries in which *N. meningitidis* is hyperendemic or epidemic, persons with terminal complement component deficiency, and persons with functional or anatomic asplenia.

For travelers, vaccination is especially recommended for those visiting countries in the sub-Saharan Africa “meningitis belt” (Ethiopia in the east to Senegal in the west). Epidemics in the meningitis belt usually occur during the dry season (i.e., from December to June). Therefore, vaccination is recommended for travelers visiting the region during this time. Vaccination is required by the government of Saudi Arabia for all travelers to Mecca during the annual Hajj. Information concerning geographic areas for which vaccination is recommended can be obtained from the CDC Travelers Health website at <http://www.cdc.gov/travel>.

MCV can be administered at the same visit as other indicated vaccines. All vaccines should be given at separate sites with separate syringes.

Both MCV and MPSV are recommended for use in **control of meningococcal outbreaks** caused by vaccine-preventable serogroups (A, C, Y, and W-135). An outbreak is defined by the occurrence of at least three confirmed or probable primary cases of serogroup C meningococcal disease during a period of 3 months or less, with a resulting primary attack rate of 10 or more cases per 100,000 population. For calculation of this threshold, population-based rates are used, and not age-specific attack rates, as have been calculated for college



students. These recommendations are based on experience with serogroup C meningococcal outbreaks, but these principles may be applicable to outbreaks caused by the other vaccine-preventable meningococcal serogroups.

## Revaccination

Revaccination may be indicated for persons previously vaccinated with MPSV who remain at increased risk for infection (e.g., persons residing in areas in which disease is epidemic), particularly for children who were first vaccinated when they were younger than 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 after receiving MPSV has not been determined, antibody levels rapidly decline in 2–3 years, and if indications still exist for vaccination, revaccination may be considered 5 years after receipt of the first dose. MCV is recommended for revaccination of persons 11–55 years of age. However, use of MPSV is acceptable.

The Advisory Committee on Immunization Practices (ACIP) expects that MCV will provide longer protection than MPSV. However, studies are needed to confirm this assumption. More data will likely become available within the next 5 years to guide recommendations on revaccination for persons who were previously vaccinated with MCV. At the present time, revaccination after receipt of MCV is not recommended.

## Adverse Reactions Following Vaccination

### Meningococcal Polysaccharide Vaccine

Adverse reactions to MPSV are generally mild. The most frequent are **local reactions**, such as pain and redness at the injection site. These reactions last for 1–2 days, and occur in up to 48% of recipients. Fever (100°–103°F) within 7 days of vaccination is reported for up to 3% of recipients. Systemic reactions, such as headache and malaise, within 7 days of vaccination are reported for up to 60% of recipients. Fewer than 3% of recipients reported these systemic reactions as severe.

### Meningococcal Conjugate Vaccine

Reported adverse reactions following MCV are similar to those reported after MPSV. The most frequent are local reactions, which are reported in up to 59% of recipients. Fever (100°–103°F) within 7 days of vaccination is reported for up to 5% of recipients. Systemic reactions, such as headache and malaise are reported in up to 60% of recipients

### Meningococcal Vaccine Recommendations

- Both MCV and MPSV recommended for control of outbreaks caused by vaccine-preventable serogroups
- Outbreak definition:
  - 3 or more confirmed or probable primary cases
  - period  $\leq 3$  months
  - primary attack rate  $\geq 10$  cases per 100,000 population\*

\*Population-based rates should be used rather than age-specific attack rates

### Meningococcal Vaccine Revaccination

- Revaccination may be indicated for persons at increased risk for infection\*
- Revaccination may be considered 5 years after receipt of the MPSV
- MCV is recommended for revaccination of persons 11–55 years of age although use of MPSV is acceptable
- Revaccination after receipt of MCV is not recommended at this time

\*e.g., asplenic persons and those who reside in areas in which disease is endemic (does not include college settings)

### Meningococcal Vaccines Adverse Reactions

	MPSV	MCV
• Local reactions for 1–2 days	4%–48%	11%–59%
• Fever $\geq 100^\circ\text{F}$	3%	5%
• Systemic reactions (headache, malaise fatigue)	3%–60%	4%–62%

## Meningococcal Vaccines Contraindications and Precautions

- Severe allergic reaction to vaccine component or following a prior dose of vaccine
- Moderate or severe acute illness

with 7 days of vaccination. Less than 3% of recipients reported these systemic reactions as severe.

All severe adverse events that occur after receipt of any vaccine should be reported to the Vaccine Adverse Events Reporting System (VAERS). For information on reporting, see the VAERS website at <http://www.vaers.hhs.gov>.

## Contraindications and Precautions to Vaccination

For both MCV and MPSV, a **severe allergic (anaphylactic) reaction** to a vaccine component or following a prior dose of either vaccine is a contraindication to receipt of further doses. A **moderate or severe acute illness** is reason to defer routine vaccination, but a minor illness is not. Breastfeeding and immunosuppression are not contraindications to vaccination. Studies of vaccination with MPSV during pregnancy have not documented adverse effects among either pregnant women or newborns. No data are available on the safety of MCV during pregnancy. However, pregnancy is not considered to be a contraindication to either MPSV or MCV.

## Vaccine Storage and Handling

Both MPSV and MCV should be shipped in insulated containers to prevent exposure to freezing temperature. Vaccine should be stored at refrigerator temperature (35°–46° F, [2°–8° C]). The vaccines must not be exposed to freezing temperature, and any vaccine exposed to freezing temperature should not be used.

Single-dose vials of MPSV must be used within 30 minutes of reconstitution, and multidose vials must be discarded 10 days after reconstitution. MCV should not be drawn into a syringe until immediately before use.

## Surveillance and Reporting of Meningococcal Disease

Invasive meningococcal disease is a reportable condition in most states. All healthcare workers should report any case of invasive meningococcal disease to local and state health departments.

## Antimicrobial Chemoprophylaxis

In the United States, the primary means for prevention of sporadic meningococcal disease is antimicrobial chemoprophylaxis of close contacts of infected persons. Close contacts include household members, child care center contacts, and anyone directly exposed to the patient's oral secretions (e.g., through kissing, mouth-to-mouth resuscitation, endotracheal intubation, or endotracheal tube management).

For travelers, antimicrobial chemoprophylaxis should be considered for any passenger who had direct contact with respiratory secretions from an index patient or for anyone seated directly next to an index patient on a prolonged flight (i.e., one lasting more than 8 hours). The attack rate for household contacts exposed to patients who have sporadic meningococcal disease was estimated to be four cases per 1,000 persons exposed, which is 500–800 times greater than the rate for the total population. In the United Kingdom, the attack rate among healthcare workers exposed to patients with meningococcal disease was determined to be 25 times higher than among the general population.

Because the rate of secondary disease for close contacts is highest immediately after onset of disease in the index patient, antimicrobial chemoprophylaxis should be administered as soon as possible, ideally less than 24 hours after identification of the index patient. Conversely, chemoprophylaxis administered more than 14 days after onset of illness in the index patient is probably of limited or no value. Oropharyngeal or nasopharyngeal cultures are not helpful in determining the need for chemoprophylaxis and might unnecessarily delay institution of this preventive measure.

Rifampin, ciprofloxacin, and ceftriaxone are 90%–95% effective in reducing nasopharyngeal carriage of *N. meningitidis* and are all acceptable antimicrobial agents for chemoprophylaxis. Systemic antimicrobial therapy for meningococcal disease with agents other than ceftriaxone or other third-generation cephalosporins might 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.

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