

Meningococcal Invasive Disease

NOTE: The main difference between this and previous protocols is reporting and management of meningococcal conjunctivitis.

Criteria for case referral by Communicable Disease Control Unit, Manitoba Health to regional health authorities for investigation:

- verbal or written report from a member of the public or health care professional that a case of invasive or non-invasive meningococcal disease may have occurred;
- **or**
- positive laboratory report (see *Case Definitions* below).

Case Definitions

Invasive Meningococcal Disease (IMD)

Confirmed Case: Invasive disease¹ with laboratory confirmation of infection by isolation of *Neisseria meningitidis* from a normally sterile site (blood, cerebrospinal fluid, joint, pleural, pericardial fluid, petechial or purpuric lesion, etc.).

Probable Case: Invasive disease¹ with:

- demonstration of *N. meningitidis* antigen² in CSF or *N. meningitidis* DNA by PCR in a specimen obtained from a normally sterile site,
- **or**
- purpura fulminans³ or petechiae⁴ in the absence of laboratory confirmation and no other apparent cause.

1 Invasive meningococcal disease usually manifests itself as meningitis and/or septicemia, although other manifestations may be observed. Invasive disease may progress rapidly to purpura fulminans, shock and death.

2 Not urine or serum.

3 Purpura associated with symmetric peripheral gangrene (Mandell).

4 Lesion less than 3 mm in diameter containing extravasated red blood cells or hemoglobin; purpura represent larger lesions (Mandell).

Presumptive Case: Gram-negative diplococci in any sterile fluid with clinically compatible illness.

Noninvasive Meningococcal Disease

Conjunctivitis: Isolation of *N. meningitidis* from the eye or the conjunctival sac in association with purulent conjunctivitis.

Pneumonia: A gram stain showing gram-negative diplococci and a polymorphonuclear cell response from sputum or respiratory aspirate and isolation with heavy growth of *N. meningitidis* from sputum or respiratory aspirate and clinical or radiological evidence of pneumonia.

Reporting Requirements

- All positive specimens noted above are reportable by laboratory.
- All invasive and non-invasive disease as described above are reportable by the attending health care professional.

Clinical Presentation/Natural History

An acute bacterial disease characterized by sudden onset with fever, intense headache, nausea and often vomiting; stiff neck and frequently, a petechial rash with pink macules or, very rarely, vesicles. Similar rashes can be caused by organisms other than *Neisseria meningitidis*. Delirium and coma are common; occasional fulminating cases exhibit sudden prostration, ecchymoses and shock at onset. Case-fatality rates used to exceed 50%, but with early diagnosis, modern therapy and supportive measures, the case-fatality rate is usually less than 15%. Up to 10% of populations in countries with endemic disease may be asymptomatic carriers with the nasopharynx colonized with *N. meningitidis*.

A small minority of persons who acquire the organism will progress to invasive disease. One or more clinical syndromes characterize invasive disease, including bacteremia, sepsis or meningitis. Many patients with sepsis develop a petechial rash,

sometimes with joint involvement. Meningococemia may occur without extension to the meninges and should be suspected in cases of otherwise unexplained acute febrile illness associated with petechial rash and leukocytosis. In fulminating meningococemia, the death rate remains high despite prompt antibacterial treatment.

Etiology

Neisseria meningitidis, (meningococcus). In the 1970s in Canada, Groups A and C predominated. This was followed by Group B predominance until 1986 when there was a resurgence of Group C infections. Recent outbreaks in Manitoba have been associated with Group C organisms. Additional serogroups have been recognized as pathogens (e.g., Groups W-135, X, Y and Z). Organisms belonging to some of these serogroups may be less virulent, but fatal infections and secondary cases have occurred with all. Respiratory *Neisseria meningitidis* may be non-typeable and non-pathogenic.

Epidemiology

Reservoir and Source: Humans

Transmission: By direct contact, including respiratory droplets from nose and throat of infected or colonized persons. Usually only colonization occurs; invasion sufficient to cause systemic disease is comparatively rare. Carrier prevalence of 25% may exist without cases of meningitis. During epidemics, over half the men in a military unit may be healthy carriers of pathogenic meningococci. Fomite transmission is insignificant.

Occurrence:

General: Worldwide. Greatest incidence occurs during winter and spring; epidemics are irregular. Meningococcal disease, while primarily a disease of very small children, occurs commonly in older children and young adults; in males more than in females; and more commonly among newly aggregated adults in crowded living conditions, such as in barracks and institutions. An area of high incidence has existed for many years in the

sub-Saharan region of mid-Africa, where the disease is usually caused by Group A organisms. More recently, there have been Group A epidemics in Nepal and India, as well as in Ethiopia, Sudan and other African countries.

During the 1990s, Group B was the most common cause of disease in the Americas. Epidemics have been reported from Cuba, Brazil, Chile, Argentina, Colombia and other countries. In 1994, incidence of Group B disease doubled in Oregon with the appearance of the same enzyme-type involved in the recent South American outbreaks. Community outbreaks of Group C disease have been observed with increasing frequency in the United States and Canada since 1990. These outbreaks have particularly affected school- and college-aged persons.

Manitoba: A large outbreak occurred in First Nations communities in 1993 due to Group C, which prompted an immunization campaign on reserves. Five Group C cases in teens in spring 2001 resulted in a mass immunization program for teens aged 13-19 years, living in or attending school in Winnipeg.

Incubation Period: Varies from two to 10 days, commonly three to four days.

Susceptibility and Resistance: Susceptibility to clinical disease is low and decreases with age; a high ratio of carriers to cases prevails. Persons who are deficient in certain complement components are especially prone to recurrent disease. Splenectomized persons are susceptible to bacteremic illness. Group-specific immunity of unknown duration follows even subclinical infections.

Period of Communicability: From seven days prior to the onset of clinical symptoms until meningococci are no longer present in discharges from nose and mouth, which occurs within 24 hours after beginning treatment. Penicillin will temporarily suppress the organisms, but it does not usually eradicate them from the oronasopharynx.

Diagnosis

Positive culture from CSF, blood, petechial scrapings, joint fluid or appropriate respiratory specimen; demonstration of meningococcal DNA in CSF or plasma by PCR; gram stain of petechial scraping, synovial fluid, CSF or buffy coat of blood; or bacterial antigen detection test of CSF.

Key Investigations

- Contact history
- Chemoprophylaxis history
- Immunization history

Control

Management of Cases:

Treatment

- Penicillin given parenterally in adequate doses is the preferred drug for proven meningococcal disease. Ampicillin and chloramphenicol are also effective.
- Strains resistant to penicillin have been reported in Africa and Spain.
- Treatment should begin immediately after the presumptive clinical diagnosis is made, even before meningococci have been identified.
- In children, until the specific etiologic agent has been identified, the therapy must be effective against *H. influenzae* type B (HIB) as well as *S. pneumoniae*. While ampicillin is the preferred drug for both, as long as the organisms are ampicillin-sensitive, it should be combined with a third-generation cephalosporin or chloramphenicol in the many places where ampicillin-resistant *H. influenzae* B strains are known to occur.
- **Patients with meningococcal disease should be given rifampin or ciprofloxacin before discharge from hospital** (unless they received ceftriaxone) to assure elimination of the organism.

Public Health Measures:

- Hospitalized patients should be placed under Droplet precautions for 24 hours after appropriate antibiotic therapy is administered.

Management of Contacts:

- Public health nurses will trace *close contacts* and, with the assistance of the local Medical Officer of Health, determine who should receive chemoprophylaxis.
- *Close contacts* are household contacts of the case; contacts who share sleeping arrangements; child care and nursery school contacts; and all people with direct contamination of their nose or mouth with oral or nasal secretions from a case (e.g., through intimate contact; sharing food, eating utensils, food or cigarettes; being directly coughed upon). Close contacts should be identified as soon as possible and counseled as to their increased risk of disease (500 to 800 times above the general population for household contacts) and the need to seek immediate attention if they develop a febrile illness or other signs or symptoms of meningococcal infection within the 10 days following their **last** exposure to the case during the infectious period (see *Period of Communicability*). In addition, they should be considered for chemoprophylaxis (see below).
- In general, increased risk of disease has not been shown in casual contacts of sporadic cases, including contacts in the classroom. Chemoprophylaxis and counseling are therefore **not** recommended for school contacts, transportation and workplace contacts or social contacts who are not close contacts as defined above.

- In health care settings, only those health care workers whose nose or mouth has been contaminated with oral or nasal secretions from a case (as might occur during intubation or suctioning or if the worker was directly coughed upon) require prophylaxis.
- When a case occurs in a traveller who was within the infectious period during the journey, any decision on the need for prophylaxis should be based on the type of travel, the length of time fellow travellers could have been exposed to the case and the type of exposure. Any decision should be based on consultation with the provincial or territorial epidemiologist. When international travel is involved, the case should also be reported to the Duty Officer of Health Canada (1-800-545-7661) or the Centre of Emergency Preparedness and Response (613-957-0316), Division of Quarantine, Travel and Migration Health, Bureau of Health Security. To date, there have been no reported cases of IMD resulting from transmission while aboard aircraft. However, current surveillance systems may not find secondary cases resulting specifically from air travel. The theoretical risk of transmission during air travel should be considered. It is recommended that contact tracing should be initiated if:
 - the diagnosis of invasive/noninvasive disease occurred no more than 48 hours after air travel AND
 - the total time spent aboard the aircraft was at least eight hours, including ground time.
 - An attempt should be made to trace, contact and offer chemoprophylaxis to the passengers who were sitting immediately on either side of the index case (but not across the aisle).

These individuals may be at an increased risk as bacteria transmitted through respiratory droplets can be propelled short distances (<1m) during coughing and sneezing. For the purposes of contact tracing after a case has been identified on an international flight, the On-Call Duty Officer for Health Canada or the Centre of Emergency Preparedness and Response, Office of Public Health Security, Quarantine, Travel and Migration Health Program, should be contacted.

- Manitoba Health provides chemoprophylaxis at no charge to contacts only.
- Chemoprophylaxis medications are available through several hospital depots (see attached letter on rifampin depots). Health care providers who are approached by contacts requesting chemoprophylaxis should refer them to their local public health nurse or the hospital infection control or occupational health nurse if they are hospital employees.
- Chemoprophylaxis should be administered regardless of immunization status.
- Chemoprophylaxis is unlikely to be of benefit if given more than 10 days after the most recent exposure to a case.
- The chemoprophylactic regimen varies by age:
 - For persons younger than 18 years of age, because of limited safety data on ciprofloxacin, the preferred drug is rifampin.
 - Newborns up to one month of age, 5 mg/kg p.o. b.i.d. for two days.
 - Children one month to 12 years or 56.4 kg: 10 mg/kg p.o. b.i.d. for two days.
 - Persons 12 years and older or 56.4 kg: 600 mg p.o. b.i.d. for two days.

- Persons 18 years of age and older should receive a single 500 mg dose of ciprofloxacin. Ciprofloxacin has demonstrated safety in this age group and has the advantages of lower cost, single dosing and absence of red discoloration of body fluids.
- Since **rifampin** and **ciprofloxacin** are contraindicated in pregnancy, ceftriaxone 250 mg I.M. diluted in 1% lidocaine should be used. Contraindications and cautions are outlined in the attached fact sheets for patients on rifampin, ciprofloxacin and ceftriaxone (not yet available).
- *Immunization* of close contacts, in addition to provision of chemoprophylaxis, is recommended by the National Advisory Committee on Immunization (NACI) for disease due to serogroups contained in available vaccines (A, C, Y, W-135). This is because of data indicating that despite chemoprophylaxis, from 0.3%-3% of cases of meningococcal disease occur in close contacts. The median interval in one study between disease in the index case and contacts was seven weeks. Some of these secondary cases can be attributed to failure of chemoprophylaxis (e.g., failure of administration, poor compliance, presence of antibiotic resistance). The situation in Canada is unknown. For contacts of serogroup C disease, the conjugate vaccine should be used in preference to the polysaccharide vaccine. Vaccine is not recommended for contacts of serogroup B disease or disease of unknown serogroup. *Manitoba Health*

currently does not provide vaccine at no charge for use in this circumstance. When a routine conjugate meningococcal C program is approved for the general population, this decision will be reviewed.

Management of Outbreaks:

- Immunization with conjugate or polysaccharide vaccines may be useful in certain circumstances. Guidelines for the use of meningococcal polysaccharide vaccine are available in the U.S. Advisory Committee on Immunization Practices statement on the Control and Prevention of Serogroup C Meningococcal Disease (MMWR Recommendations and Reports June 30, 2000/Vol. 49/No. RR-7). Brief recommendations are also available in the Canadian Immunization Guide. The local medical officer of health and/or public health branch will co-ordinate decisions about the need for focal or widespread immunization.
- For Group B outbreaks and other non-vaccine preventable strains, measures to reduce crowding should be instituted when possible.

Preventive Measures:

- Provide universal immunization programs with conjugate C vaccine.
- Reduce overcrowding in living quarters and workplaces, such as barracks, schools, camps and ships.
- Immunize travellers to parts of the world where meningococcal infection is endemic or epidemic.
- Immunize anatomic or functional asplenic individuals two years of age or older, as well as persons with terminal complement component deficiencies and military recruits.

Additional Resources

For the Public:

- CDC Unit fact sheet on Meningococcal Disease
- Important notes on Rifampin
- Important notes on Ciprofloxacin
- Important notes on Ceftriaxone (not yet developed)

For Health Care Professionals:

- Letter explaining operation of rifampin/ciprofloxacin depot system
- Meningococcal rifampin dosage table
- Meningococcal Contact Form
- Recommendations of the Advisory Committee on Immunization Practices on Control and Prevention of Serogroup C Meningococcal Disease