Meningococcal Disease, Invasive (IMD)

Case Definition

**Confirmed Case**
Clinical evidence of invasive disease\(^{(A)}\) with laboratory confirmation of infection:
- Isolation of *Neisseria (N.) meningitidis* from a normally sterile site (blood, cerebrospinal fluid [CSF], synovial, pleural or pericardial fluid)
  OR
- Demonstration of *N. meningitidis* nucleic acid (e.g., PCR) from a normally sterile site.

**Probable Case**
Clinical evidence of invasive disease\(^{(A)}\) with purpura fulminans or petechiae and no other apparent cause and with non-confirmatory laboratory evidence:
- With detection of *N. meningitidis* antigen in the CSF
  OR
- In the absence of isolation of *N. meningitidis* for a normally sterile site or in the absence of demonstration of *N. meningitidis* nucleic acid from a normally sterile site.

*The following cases require prophylaxis of contacts but should not be reported to Alberta Health.*

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

**Meningococcal Pneumonia Case**
Clinical or radiological evidence of pneumonia with laboratory confirmation of infection:
- Presence of gram-negative diplococci on a Gram stain and a polymorphonuclear cell response from sputum or respiratory aspirate
  AND
- Isolation with heavy growth of *N. meningitidis* from an appropriate respiratory specimen (e.g., sputum or respiratory aspirate).

\(^{(A)}\) Clinical evidence of invasive disease includes meningitis and/or septicemia, orbital cellulitis, septic arthritis, pericarditis and pneumonia. Invasive disease may progress rapidly to purpura fulminans, shock and death.
Reporting Requirements

1. Physicians/Health Practitioners and Others
   Physicians, health practitioners and others shall notify the Medical Officer of Health (MOH) (or designate) of the zone, of all confirmed and probable cases in the prescribed form by the Fastest Means Possible (FMP).

2. Laboratories
   All laboratories shall report all positive laboratory results:
   • by FMP to the MOH (or designate) of the zone, and
   • by mail, fax or electronic transfer within 48 hours (two business days) to the Chief Medical Officer of Health (CMOH) (or designate).

3. Alberta Health Services and First Nations and Inuit Health Branch
   • The MOH (or designate) of the zone where the case currently resides shall notify the CMOH (or designate) by FMP of all confirmed and probable cases.
   • The MOH (or designate) of the zone where the case currently resides shall forward the initial Notifiable Disease Report (NDR) of all confirmed and probable cases to the CMOH (or designate) within one week of notification and the final NDR (amendment) within two weeks of notification.
   • For out-of-province and out-of-country cases, the following information should be forwarded to the CMOH (or designate) by FMP:
     o name,
     o date of birth,
     o out-of-province health care number,
     o out-of-province address and phone number,
     o positive laboratory report, and
     o other relevant clinical / epidemiological information.
   • For out-of-province and out-of-country susceptible contacts, the following information should be forwarded to the CMOH (or designate) as soon as possible:
     o name,
     o date of birth, and
     o out-of-province / country contact information.
Etiology

*N. meningitidis* is a gram-negative diplococcus. There are 13 different serogroups (A, B, C, D, 29E, H, I, K, L, W-135, X, Y, Z). Strains belonging to groups A, B, C, Y, and W-135 are most frequently implicated in systemic disease. Serogroup distribution may vary by location and time.

*N. meningitidis* does not survive well outside of the host. It is susceptible to many disinfectants including 70% ethanol, iodine, glutaraldehyde, and formaldehyde as well as temperature changes and desiccation. The bacteria may be inactivated by moist heat (121°F for at least 15 minutes) and dry heat (160°F–170°F for at least one hour).(1)

Clinical Presentation (2–5)

The term invasive meningococcal disease includes different clinical manifestations caused by *N. meningitidis*. All the manifestations are a result of events triggered by the bacterial endotoxin and its succeeding inflammatory response.

Invasive meningococcal disease generally presents itself either as sepsis (meningococcemia) or meningitis.

Meningitis occurs in approximately 50% of persons with invasive disease and is characterized by headache, fever, nuchal rigidity, impaired consciousness and photophobia. Symptoms in infants and toddlers may be subtle and non-specific such as lethargy, poor appetite and irritability. Meningococcemia occurs in 5–20% of cases and is typically more severe and manifests abruptly with fever, hemorrhagic rash (purpura fulminans) and rapid circulatory collapse. Early symptoms of sepsis include petechial rash, cold hands and feet, leg pains and pallorous or mottled skin color.

Meningococcemia may occur without extension to the meninges and should be suspected in cases of otherwise unexplained febrile illness associated with petechial rash and leukocytosis. In fulminating meningococcemia, the case fatality rate remains high ranging from 20–80%.

Pharyngitis, transient meningococcemia, pericarditis, arthritis and conjunctivitis are not commonly diagnosed and as such may not be confirmed due to rapid recovery following empiric antibiotic therapy. These extrameningeal or systemic manifestations most commonly involve the joints, eyes, lungs and heart.(5)

Up to 10% of populations in countries with endemic disease may be asymptomatic carriers with the *N. meningitidis* colonized in the nasopharynx. A small minority of individuals (less than 1%) who acquire the organism will progress to invasive disease that is characterized by one or more clinical syndromes such as:

**N. meningitidis pneumonia:**
Diagnosis based on a compatible clinical syndrome; chest x-ray and laboratory confirmation of infection (as noted in case definition section).

**Primary N. meningitidis pericarditis:**
The most common presenting symptoms are: stabbing substernal chest pain, fever, and dyspnea. Heart sounds are muffled and a pericardial friction rub is usually heard (though never in children under 18 months of age). Cardiomegaly is common especially in children.

**Primary N. meningitidis conjunctivitis:**
Usually presents as acute or hyperacute mucopurulent conjunctivitis that is indistinguishable clinically from gonococcal conjunctivitis. It is frequently catarrhal and more commonly unilateral. Also observed: painful, swollen, red eyelids with injected erythematous bulbar conjunctiva. Corneal erosions have also been reported.
Primary *N. meningitidis* arthritis:
This is a rare type of acute septic arthritis as the joint symptoms dominate the clinical picture and there is no preceding or ongoing meningitis or meningococcemia. The large joints are affected almost exclusively; more than one joint is involved and males are affected more than females. These cases will often be preceded by upper respiratory tract symptoms. There are two other clinical scenarios associated with *N. meningitidis* arthritis. One presents as a complication of acute meningitis/meningococcemia with septic joint(s) due to bacterial invasion or aseptic invasion of the joint and is the most common. The second is in the setting of chronic meningococcal infection (migratory and associated with arthralgias). In this scenario, the synovial fluid is usually sterile.

Diagnosis
Diagnosis is made when there are positive cultures from a normally sterile site (i.e., CSF, blood, joint, pleural or pericardial fluid). Gram staining of synovial fluid, CSF or buffy coat of blood may also be used. Bacterial antigen detection test of CSF can be used but it is primarily reserved for outbreak situations.

*N. meningitidis* can cause conjunctivitis, pneumonia, pericarditis and septic arthritis and are usually seen as systemic manifestations of the course of meningococcal disease. However, these presentations may be caused by invasive strains and subsequent invasive illness in close contacts has been documented.(6) In addition to previous clinical signs and symptoms, the following criteria have been developed to assist with diagnosis:

- Primary meningococcal conjunctivitis case (see Case definition)
- Meningococcal pneumonia case (see Case definition)
- Septic arthritis usually presents with swollen, warm, tender and erythematous joint(s). Evidence of gram-negative diplococci may be seen on Gram stain, and synovial fluid cultures will be positive 90% of the time.(7)
- Pericarditis can be identified when the client presents with stabbing substernal chest pain, fever and dyspnea. There are also ECG changes, heart sound changes and a pericardial friction rub. Cardiomegaly may also be seen in children AND preceded by bacteremia.(3)

*N. meningitidis* isolates are serogrouped at the PLPH by PCR. This assay requires approval by the Microbiologist on call. For serotyping and further bacteriologic studies, the specimen is sent to the National Microbiology Laboratory (NML).(8) Please see Appendix A for information regarding the handling of *N. meningitidis* isolates at the ProvLab.

Epidemiology (9–11)
Reservoir
Humans.

Transmission
Transmission is by direct contact with the secretions of the nose and throat of infected or colonized individuals, or by respiratory droplets. Bacteria transmitted through respiratory droplets can be propelled short distances (< one metre) during coughing and sneezing. The likelihood of person-to-person transmission is related to the nature and the duration of the contact. Persons in close contact are at increased risk but usually only colonization occurs. Fomite transmission is insignificant.

Effects of Vaccine on Disease Transmission
Effects on nasal or pharyngeal carriage of meningococci on induction of herd immunity by meningococcal conjugate vaccine have been established. The comparisons done in one large study provide evidence of a decrease (in carriage rates) of serogroup C meningococci. This same
study also showed that induced immunity (i.e., herd immunity) from conjugate vaccine interrupted the transmission of meningococcal serogroup C.(9)

During 1999–2000, carriage rates of group C meningococci in the United Kingdom declined 66%. In addition, incidence of meningococcal serogroup C disease declined 67% among unvaccinated persons aged 1–17 years and a decrease of 35% among persons aged >25 years who were not targeted for vaccination, indicating the additional vaccine benefit of eliciting herd immunity.

**Incubation Period**
The incubation period varies from two to ten days, but is most commonly three to four days.

**Period of Communicability**
IMD is communicable from seven days prior to the onset of clinical symptoms until meningococci are no longer present in discharges from the nose and mouth. This generally occurs within 24 hours of beginning treatment. Penicillin will temporarily suppress the organism but it does not usually eradicate it from the oronasopharynx.

**Host Susceptibility** (8;12)
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. Asplenis and individuals who have received cochlear implants are susceptible to bacteremic illness. Group-specific immunity of unknown duration follows even in sub-clinical infections.

People living in the same household as an IMD case are at 500 to1200-fold greater risk of developing IMD than the general population. The risk of secondary disease among close contacts is highest during the first few days after the onset of disease in the index case.

**Occurrence**

**General** (13–15)
Endemic meningococcal disease occurs worldwide with an estimate of 500,000 cases occurring annually. The greatest incidence is during winter and spring. Epidemics are irregular. Disease occurs commonly in children and young adults, more males than females, and more commonly, among newly aggregated adults under crowded living conditions. For many years the incidence of serogroup A has been high in the sub-Saharan region of Africa with epidemics occurring every five to ten years in the “meningitis belt”. Cyclic epidemics caused by serogroup A have occurred in China every 10 years for much of the past century. Serogroup A epidemics have occurred in Nepal, India, Ethiopia, Sudan, and other African countries. During the 1990s, serogroup B was the most common cause of disease in the Americas. Epidemics associated with serogroup B have also been reported in Cuba, Brazil, Chile, Argentina, Columbia, and others. Serogroups A and W-135 have affected pilgrims to Mecca in three separate outbreaks from 1986 to 2001. Secondary cases have been associated with pilgrims returning to their homes.

**Canada** (8;15;16)
Invasive meningococcal disease has been nationally reportable since 1924. It is endemic in Canada with periods of increased activity that occur about every 10 to 15 years, with no consistent pattern. The incidence of IMD varies with different serogroups, age groups, locations and time.
The last major outbreak of serogroup A was in 1940 to 1943. The peak incidence was approximately 13/100,000 annually. Since that time, the incidence of disease caused by serogroup A has remained < 2/100,000 per year.

From 1971 to 1974, serogroups A and C were most frequently identified. From 1975 to 1989, serogroup B was most prominent. In 1986, a new clone of serogroup C was identified in Canada. Between 1995–2006, serogroups B (38%) and C (32%) have been responsible for most of the cases of endemic disease.


From 1985 to 2001, there was an average of 303 cases of IMD reported per year in Canada with the incidence ranging from 1.6/100,000 to 0.7/100,000. In 2000 and 2001, there was a period of elevated activity across the country caused by serogroup C. Localized outbreaks, predominantly affecting adolescents and young adults, were reported by five provinces: Alberta, British Columbia, Manitoba, Quebec and Ontario. There were 101 confirmed cases of IMD caused by serogroup C in 2000 (241 total cases) and in 2001, 182 cases were reported (350 total cases). The rate of all cases in 2000 was 0.77/100,000 and in 2001 the rate was 1.18/100,000.

From 2002 to 2008 the rate of IMD in Canada has remained fairly steady at an average of 0.6/100,000 population.

Chart B: Incidence rates of IMD by Serogroup and year, Canada, 1995–2006:

IMD cases and rates in Canada by age group, 1995-2008

Chart C: IMD cases and rates in Canada by age group 1995–2008.
Alberta (8, 16, 17, 18)

*N. meningitidis* has been responsible for both sporadic case occurrence and disease outbreaks. In Alberta, IMD normally occurs at a rate of approximately one per 100,000 population annually. From 1997 to 2000, the rate of IMD was highest among children less than one year of age. In 2000 and 2001, the province experienced a higher incidence than expected (2.6 and 2.0/100,000 population respectively), occurring predominately in the 14 to 19 year age group. A mass immunization campaign with meningococcal polysaccharide vaccine for individuals two to 24 years was undertaken to prevent secondary infections.

Compared to 1997–2002, where serogroup C was the dominant serotype identified in 67% of the 241 cases, 2003–2009, showed that Serogroup B was the dominant serogroup identified in 47% of the 105 cases reported.

Group Y was typed in 25 cases (23.8%) group C in 13 cases (12.4%), eight cases were unknown (7.6%) and seven cases were identified as W135 serogroup (6.7%). The top three age groups affected during this time were; the 40–59 year olds with an average of 2.7 cases per year, the less than one year olds were reporting an average of 2.4 cases per year, followed closely by the 1–4 year olds who averaged two cases per year. Meningitis and septicemia/bacteremia were equally the most common manifestation reported in all cases.
Chart E: Most common serogroup Alberta 1990–2008

Key Investigation (19)

**Single Case/Household Cluster**

- Assess immunization history.
- Identify underlying medical conditions.
- Determine possible site of exposure including recent history of travel.
- Identify contacts that have had contact with the case within the seven days prior to the onset of symptoms and up to 24 hours after the case commences appropriate antibiotic therapy.
  - **Household contacts** include:
    - individuals living in the same household, and/ OR
    - individuals who share sleeping arrangements.
  - **Close contacts** are considered:
    - childcare and nursery school contacts, and/ OR
    - other individuals who have had direct contamination of the nose or mouth with oral and/or nasal secretions of the case (e.g., kissing on the mouth, shared cigarettes, shared drinking bottles)
- In health care settings, only persons who have had intensive, unprotected contact with the nasopharyngeal secretions (i.e., used no barrier protection such as a mask) of the case such as during intubation, suctioning, and/or resuscitation are considered contacts.
- In situations involving IMD during travel, decisions regarding tracing, contacting, and offering chemoprophylaxis to the contacts should be based on the type of travel, the length of time of exposure, and the type of exposure.
  - **Airline contacts** include:
    - those individuals sitting on either side of the index case (but not across the aisle) or other passengers or flight staff who have had direct contact with the respiratory secretions of the index case, and
    - the flight occurred within the previous 10 days (although flight manifests are rarely kept longer than 48 hours), and
    - the total time spent aboard the aircraft was at least eight hours, including ground time. (12,20) (See Management of Contacts)

Control

**Management of a Case** (19;21)

- Hospitalized individuals should be placed under droplet precautions for 24 hours after initiation of appropriate antibiotic therapy in addition to routine practices.
- Immunization should be offered once the case is well and out of hospital if they meet the eligibility criteria for vaccine. Refer to the current Alberta Immunization Manual. (17;22)

**Treatment of a Case** (19;23)

- Treatment should begin immediately after the presumptive diagnosis has been made.
- In children, the therapy should also be effective against *H. influenzae* type B and *S. pneumoniae* until the etiologic agent is known.
- Penicillin G (IV) is the drug of choice once microbiologic diagnosis is established. Cefotaxime, ceftriaxone, and ampicillin are also effective and may be used as alternatives. Chloramphenicol is recommended for individuals with severe penicillin allergies (anaphylaxis). The course of treatment is generally five to seven days.
- Ensure rifampin has been given to all cases following completion of treatment for invasive disease to ensure elimination of the organism (except if the individual was treated with ceftriaxone or cefotaxime).
Management of Contacts (8;15;17;19;22)

- Identify contacts as soon as possible.
- Counsel contacts about the increased risk of disease. The risk for household contacts is estimated to be 500 to 1200 times greater than the general population.
- Educate contacts about the need to seek immediate medical attention if they develop a febrile illness or other signs or symptoms of meningococcal infection within 10 days following their last exposure to the case during the infectious period.
- As the course of disease in many cases is variable it is prudent to err on the side of caution when offering chemoprophylaxis to contacts. In order to determine the infectious period (which is 7 days before onset of symptoms in the case to 24 hours after initiation of effective treatment), use the date the symptoms began as Day 1. If uncertain, consult the MOH.
- Chemoprophylaxis: Household and close contacts of all cases of IMD should be considered for chemoprophylaxis and counseled about the risks and benefits of chemoprophylaxis. (See Table 1)
  - Contacts of individuals with PMC, pneumonia, pericarditis and/or septic arthritis, where *N. meningitidis* is isolated, shall be offered chemoprophylaxis as well as serogroup-specific immunoprophylaxis. Both interventions have been shown to reduce nasopharyngeal carriage of *N. meningitidis*. (24;25)
    - Optimally, chemoprophylaxis should be given within 24 hours of case identification but may be offered up to 10 days after the most recent exposure to a case regardless of immunization status. (For the purposes of determining the 10 days, count the day of most recent exposure as day zero).
- Chemoprophylaxis should also be considered for contacts of cases strongly suspected to be IMD even if lab confirmation cannot be obtained within 24 hours.
- Chemoprophylaxis is unlikely to be of benefit if given more than 10 days after the most recent exposure.
- Rifampin is the drug of choice for contacts of IMD. It is provided free of charge to eligible contacts by Alberta Health and Wellness (AHW).
- In some circumstances, ciprofloxacin or ceftriaxone may be used with prior approval of the CMOH (or designate). Alberta Health Services may utilize local drug stock and have the medication replaced by AHW. In situations where exposure occurred during air travel, contacts, as defined under Key Investigation, should be offered chemoprophylaxis as indicated.
- In general, increased risk of disease has not been shown in casual contacts of sporadic cases, including contacts in the classroom. Chemoprophylaxis is generally not recommended for school contacts, transportation and workplace contacts, or social contacts that are not household or other contacts.
- HCW that do not have risk of ongoing exposure are also not considered to be at increased risk.
- Immunoprophylaxis: Household and close contacts of IMD cases who are eligible for chemoprophylaxis and have not been adequately immunized, should be offered meningococcal vaccine to further reduce the risk of secondary cases. The risk of disease in household and close contacts may persist for one year after disease in the case. (26)
  - The natural immunity from IMD has not been adequately studied, therefore, immunization is recommended regardless of past history of disease.
  - The vaccine chosen is dependent upon the serogroup that has caused disease in the index case and the age of the contact(s). The serogroup should be known before proceeding with immunization. This is generally known within two to five days. Refer to the current *Alberta Immunization Policy* for selection of vaccine(s) to offer (including as of
August 2014 serogroup B) and for schedule information about previously immunized individuals.
Table 1
Chemoprophylaxis for Invasive Meningococcal Disease (19,21,27,28)

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<th>Age Group</th>
<th>Dosage</th>
<th>Comments</th>
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| **RIFAMPIN** Provided by AHW for cases and contacts | | - Contraindicated in pregnancy and persons with liver disease.  
- Interferes with oral contraceptives, some anticonvulsants and anticoagulants.  
- Stains soft contact lenses. |
| Adults (18 years of age and older) | 600 mg po q12h for 2 days (4 doses) | | |
| Children ≥ 1 month     | Maximum of 10 mg/kg (maximum 600 mg) po q12h for 2 days (4 doses) | |
| Infants <1 month       | 5 mg/kg per dose po q12h for 2 days (4 doses) | | |

**CEFTRIAXONE** Provided by AHW for cases and contacts

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| ≥12 years          | 250 mg IM in a single dose    | - Alternative for pregnant women, persons with liver disease or allergy to rifampin.  
- Dilute in 1% lidocaine to reduce pain at injection site. |
| <12 years          | 125 mg IM in a single dose    | | |

**CIPROFLOXACIN** Provided by AHW for cases and contacts

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| ≥18 years              | 500 mg po in a single dose  | - Alternative for persons allergic to rifampin or ceftriaxone or unable to give IM injection.  
- Contraindicated in pregnancy and lactation.  
- A single dose medication regimen may improve compliance in some populations.  
- Safe in liver disease. |

Preventive Measures (17;20;22;29)

- Educate the public about the risks associated with sharing saliva-contaminated items (e.g., lipstick, food, drinks, cigarettes, etc.)
- Reduce overcrowding in living quarters and workplaces.
- Immunize with appropriate meningococcal vaccine. Refer to the current Alberta Immunization Manual.(29)
- Alberta has a routine immunization program for all infants and adolescents. Also for high risk groups including (but not limited to):  
  - persons with anatomical or functional asplenia (at least 14 days before splenectomy if possible),  
  - candidates and recipients of solid organ transplant,  
  - recipients of haematopoietic stem cell transplant,
• Refer to Alberta Immunization Manual for selection of vaccine(s) to offer and for schedule information as specific risk groups.

• Immunization may be recommended for travelers to parts of the world where meningococcal infection is endemic or epidemic. www.phac-aspc.gc.ca/publicat/ccdr-rmtc/09vol35/acs-dcc-4/index-eng.php
Appendix A:

Referral of *Neisseria meningitidis* Isolates to ProvLab
Effective July 7, 2011

1. **N. meningitidis Isolated**
   - **Is Isolate from Normally Sterile Site? (Invasive)**
     - Yes: Clinical Lab Notifies MOH & Attending Ordering Physician (FMP)
     - No: Continue
   - **Is Isolate from Primary Conjunctivitis (pure/predominant growth)**
     - Yes: Refer to Jan, 2011 AHW Meningococcal Conjunctivitis/Meningococcal pneumonia case definition
     - No: Continue
   - **Is Growth from a Respiratory Specimen with Gram-negative Diplococci and PMN Response in Gram Stain and HEAVY Growth in Culture?**
     - Yes: Clinical Lab Notifies MOH & Asks if Serogrouping is Required
       - MOH or Designate Notifies MOC at ProvLab
       - MOH or Designate Notifies MOC at ProvLab
     - No: Isolate Forwarded to ProvLab
   - **Does MOH/Public Health Require Serogrouping of Respiratory Isolate to Support Prophylaxis?**
     - Yes: Serogrouping Performed if Required (all invasive isolates, all eye isolates and/or MOH approved respiratory isolates)
       - Result Reported to MOC/MOH
     - No: Isolate Archived at ProvLab
   - **End**

Referral of *Neisseria meningitidis* Isolates to ProvLab Effective July 7, 2011

Is Isolate from Primary Conjunctivitis (pure/predominant growth)

Is Growth from a Respiratory Specimen with Gram-negative Diplococci and PMN Response in Gram Stain and HEAVY Growth in Culture?

Does MOH/Public Health Require Serogrouping of Respiratory Isolate to Support Prophylaxis?
References


(4) Bigham JM, Hutcheon ME, Patrick DM, Pollard AJ. Death From Invasive Meningococcal Disease Following Close Contact with a Case of Primary Meningococcal Conjunctivitis-Langley BC, 1999. CCDR 2001; 27-02.


(7) McCulloch M; Brooks H; Kalantarinia K. Isolated polyarticular septic arthritis: an atypical presentation of meningococcal infection. The American Journal of the Medical Sciences 2008 Apr;Vol. 335 (4): 323-6


Grimsrud K. Letter to all MOHs and CD Contacts Re: Rifampin alternatives in the chemoprophylaxis of invasive meningococcal disease (IMD). (B-036-05). Deputy Provincial Health Officer, Disease Control and Prevention. April 25, 2000.
