Meningococcal Disease

1. DISEASE REPORTING

1.1 Purpose of Reporting and Surveillance

1. To identify persons who have been significantly exposed to a person with meningococcal infection, in order to recommend antibiotic prophylaxis and to inform them about signs and symptoms of illness.

2. Under very rare circumstances, to recommend prophylactic immunization in a defined population or community.

1.2 Laboratory and Physician Reporting Requirements

Physicians and others providing health care must report confirmed or suspected cases to the LHD by telephone within 24 hours. If LHD staff are unreachable, they must contact Oregon Public Health Division (PHD). Laboratories are required to report within 1 working day, and to submit all isolates from normally sterile sites to the OSPHL.

1.3 Local Health Department Reporting and Follow-Up Responsibilities

1. Report all confirmed and presumptive (but not suspect) cases (see definitions below) to PHD within 24 hours of initial physician/lab report.

2. Begin follow-up investigation within 24 hours.

3. Identify significant contacts and recommend prophylaxis within 24 hours of report.

4. If the case is lab-confirmed, make sure that the isolate is forwarded to the OSPHL.

2. THE DISEASE AND ITS EPIDEMIOLOGY

2.1 Etiologic Agent

*Neisseria meningitidis*—a Gram-negative diplococcal bacterium with nine serogroups that have been frequently associated with systemic disease: A, B, C, D, X, Y, Z, 29E, and W135. Four other serogroups (H, I, K, and L) rarely cause invasive disease. Groups B and C are the most common causes of disease in Oregon and the United States, respectively.

2.2 Description of Illness

Disease is characterized by acute onset of fever, headache, weakness, low blood pressure, and rash. The rash may be initially urticarial, maculopapular, or petechial, and often appears in areas where elastic in underwear or socks applies pressure to the skin, or in the fingernail beds. Invasive disease may occur without signs of meningitis. In infants and small children, fever and vomiting are often the only symptoms. All clinical illnesses associated with *N. meningitidis* are significant and warrant investigation. In the absence of associated invasive disease, finding *N. meningitidis* in sputum is not considered a remarkable event, and is not reportable. In addition to the more common presentations of bacteremia and meningitis, *N. meningitidis* can cause pneumonia or primary meningococcal conjunctivitis.

The exact mechanism allowing the penetration of meningococci from the nasopharyngeal membranes is unknown, but a recent upper respiratory tract infection may facilitate invasion. Factors that increase carriage and
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disease risk include crowded living conditions (like army barracks) and either primary or secondary tobacco smoke exposure. Recently, having a cochlear implant procedure has been identified as a possible risk factor for invasive disease.

2.3 Reservoirs

Humans are the sole reservoir.

2.4 Modes of Transmission

Transmission is by direct exposure to droplets or direct contact with discharges from the nose or throat of a colonized person—symptomatic or otherwise. It is important to distinguish colonization from disease. Colonization is common, but invasive disease is very rare. Surveys of household or other contacts of cases reveal that 5% – 25% of these persons may carry *N. meningitidis* in the nasopharynx. Most individuals are carriers at some point in their lives; that carriage can be chronic, intermittent, or transient. Disease incidence is highest in late winter to early spring. The burden of invasive meningococcal disease is typically highest in the very young (those 0–4 years of age), with a second, lower peak in incidence in young adults. Close contacts of cases (e.g. household members or day-care contacts) are at increased risk of becoming colonized/infected and developing illness. The attack rate for household contacts of cases is 0.3–1% (some 300–1,000 times the rate for the general population). For persons exposed to a case during the case’s period of communicability (see below), the risk of developing symptomatic illness is highest during the 10-day period following onset of illness of the first case. (An elevated risk may extend for up to 60 days.)

2.5 Incubation Period

Usually 3 to 4 days, but may range from 2 to 10 days

2.6 Period of Communicability

Persons are infectious as long as meningococci are present in discharges from the nose or pharynx. Cases are probably most infectious during the 3 days prior to onset of symptoms, and are considered no longer communicable 24 hours after initiation of treatment or chemoprophylaxis with appropriate antibiotics. Those exposed 7 or more days before onset of illness in the case are not at significantly increased risk. Depending on the antimicrobials used, therapy for invasive disease may not eradicate the organism from the nasopharynx, and chemoprophylaxis may also be required (see §5.4.3).

2.7 Treatment

Penicillin G, administered intravenously in high doses every 4 to 6 hours, is the therapy of choice for invasive disease. Cefotaxime, ceftriaxone, and ampicillin are acceptable alternatives. Five to seven days of antimicrobial therapy is adequate.

3. CASE DEFINITIONS, DIAGNOSIS AND LABORATORY SERVICES

3.1 Confirmed Case Definition

- Isolation of *N. meningitidis* from a normally sterile body site (e.g., blood or CSF, or less commonly, synovial, pleural, or pericardial fluid) or from purpuric lesions; or
- Detection of *N. meningitidis*-specific nucleic acid in a specimen obtained from a normally sterile body site (e.g., blood or CSF), using a validated polymerase chain reaction (PCR) assay.

3.2 Presumptive Case Definitions

- Detection of *N. meningitidis* antigen in formalin-fixed tissue by immunohistochemistry (IHC), or in CSF by latex agglutination; or
- Detection of Gram-negative diplococci, not yet identified, from CSF
- Consistent signs and symptoms occurring within 2–10 days of contact with a confirmed case during the period of communicability.

3.3 Suspect Case (not reportable to Oregon PHD)

Any person with an undiagnosed compatible illness, with or without signs or symptoms of meningeal irritation (see §2.2).

3.4 Services Available at the State Public Health Laboratories

OSPHL will confirm the identification and serogroup of *N. meningitidis* isolates. Pure isolates should be sent on appropriate media that support the growth of the organism (e.g., chocolate agar). All specimens must be
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properly packaged in double containers with absorbent material around them and the Bacteriology/Parasitology form. These specimens should not be sent with cold packs. All isolates of *N. meningitidis* obtained from a normally sterile site must be sent to the OSPHL.

4. ROUTINE CASE INVESTIGATION

4.1 Case Interview

Interview the case (or parents) and others who may be able to provide pertinent information.

1. Identify Source of Infection

Often not possible, because of the high percentage of people who carry the organism. However, it is useful to ask whether any household, day-care, or other close contacts have recently had an illness suggestive of meningococcal disease.

2. Identify Potentially Exposed Persons

Obtain the name, address, and telephone number of all persons who have had significant exposure to the case during the communicable period. These include:

- all persons who have spent at least 4 hours (cumulatively, within one week of index patient’s onset) in close, face-to-face association with the case, thereby increasing the risk of droplet transmission (e.g. household members, day-care contacts, cellmates); or
- anyone directly exposed to the patient’s nasopharyngeal secretions (e.g., via kissing, mouth-to-mouth resuscitation, intubation, or nasotracheal suctioning). Health care workers who have not had direct contact with the case’s nasopharyngeal secretions are not at increased risk, and prophylaxis is not indicated.

4.2 Culturing of exposed persons

While sometimes suggested by well-meaning persons as a means to identify carriers, this is not a useful exercise.

4.3 Environmental Evaluation

Generally, none, although in outbreak settings an investigation may be warranted to identify environmental factors (disinfection practices, ventilation patterns, etc.) that may favor droplet transmission.

5. CONTROLLING FURTHER SPREAD

5.1 Education

Potentially exposed persons should be instructed to watch for fever, rash, lethargy, irritability, headache, loss of appetite, or vomiting. Should signs or symptoms develop within the next two weeks, they should seek medical care immediately. They should be advised that an elevated risk may persist for 60 days.

5.2 Isolation

In addition to standard precautions, hospitalized cases should be placed under droplet precautions until at least 24 hours after initiation of antibiotic treatment or prophylaxis.

5.3 Case Follow-up

Some of the antibiotics commonly used for treatment do not reliably eradicate nasopharyngeal colonization. Unless rifampin, ceftriaxone or ciprofloxacin (which are effective against colonization) were used, the patient should also be chemoprophylaxed with an effective antibiotic before hospital discharge.

5.4 Protection of Contacts

1. Passive Immunization

   None.

2. Active Immunization

   ACIP recommends routine vaccination with quadrivalent (contains antigens from serogroups A, C, Y, and W-135) meningococcal conjugate vaccine (MenACWY-D (Menactra®) licensed in 2005; or MenACWY-CRM (Menevo®) licensed in February 2010) for all persons 11–18 years of age. Meningococcal vaccine is also recommended for persons 9 months–55 years of age who are at increased risk for the disease due to complement deficiency, travel to or residence in a country where meningococcal disease is hyperendemic or epidemic, or inclusion in a defined risk group during a community or institutional outbreak.
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The conjugate vaccines are preferred to the quadrivalent meningococcal polysaccharide vaccine (MPSV4) in persons 9 months–55 years of age. Only Menactra® is approved for children 9–23 months of age. High-risk persons 2–10 years of age should receive Menactra® or Menveo®. Neither of the two meningococcal conjugate vaccines are approved for use in persons >55 years of age; high-risk persons >55 years old may receive MPSV4. None of the quadrivalent vaccines protect against serogroup B disease. Vaccination may be useful when a significant outbreak of disease due to serogroup A, C, Y, or W135 is continuing in a defined population, e.g., school, institution, or community.

For up-to-date vaccination recommendations, visit: [www.cdc.gov/vaccines/pubs/ACIP-list.htm#mening](http://www.cdc.gov/vaccines/pubs/ACIP-list.htm#mening)

Table 1. Summary of meningococcal conjugate vaccine recommendations by risk group, ACIP (2011)2,3

<table>
<thead>
<tr>
<th>Risk group</th>
<th>Primary series</th>
<th>Booster dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persons aged 11 through 18 years</td>
<td>1 dose, preferably at age 11 or 12 years</td>
<td>At age 16 years if primary dose at age 11 or 12 years At age 16 through 18 years if primary dose at age 13 through 15 years</td>
</tr>
<tr>
<td>HIV-infected persons aged 11 through 18 years</td>
<td>2 doses, 2 months apart</td>
<td>No booster needed if primary dose on or after age 16 years</td>
</tr>
<tr>
<td>Persons aged 2 through 55 years with persistent complement component deficiency* or functional or anatomic asplenia</td>
<td>2 doses, 2 months apart</td>
<td>Every 5 years At the earliest opportunity if a 1-dose primary series administered, then every 5 years</td>
</tr>
<tr>
<td>Persons aged 2 through 55 years with prolonged increased risk for exposure†</td>
<td>1 dose</td>
<td>Persons aged 2 through 6 years: after 3 years Persons aged 7 years or older: after 5 years</td>
</tr>
<tr>
<td>Children aged 9 through 23 months at high risk for invasive meningococcal disease (except children with functional or anatomic asplenia)‡</td>
<td>2 doses, 3 months apart</td>
<td>Initial booster 3 years after completing the primary series§</td>
</tr>
<tr>
<td>Children at high risk for invasive meningococcal disease with functional or anatomic asplenia</td>
<td>2 doses, 2 months apart, beginning at age 2 years and ≥4 weeks after completion of PCV13 vaccine series</td>
<td>Initial booster 3 years after completing the primary series§</td>
</tr>
</tbody>
</table>

* Such as C5-C9, properdin, or factor D.
† Microbiologists routinely working with *Neisseria meningitidis* and travelers to or residents of countries where meningococcal disease is hyperendemic or epidemic.
‡ Children who have persistent complement component deficiencies (e.g., C5-C9, properdin, factor H, or factor D), children who are traveling to or residents of countries where meningococcal disease is hyperendemic or epidemic, and children who are in a defined risk group during a community or institutional meningococcal outbreak.
§ If person remains at increased risk.

**Antibiotic Prophylaxis**

Chemoprophylaxis should be recommended for all household members of confirmed or presumptive cases and other exposed persons, as defined in §4.1. Chemoprophylaxis should be initiated as soon as possible, ideally <24 hours after index patient identification.† If >14 days have passed since the last contact with the index patient, chemoprophylaxis is likely to be of little benefit. Chemoprophylaxis should also be recommended to day-care contacts under certain circumstances (see §6). It should not be recommended to persons who have had only brief or casual contact with the case. If such persons are anxious about their exposure, they should be advised that their risk of disease is extremely low. They should be further advised to be alert to signs and symptoms of illness, especially fever, and to seek medical care immediately should illness develop.
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Prophylaxis of close contacts of culture positive patients with pneumonia or primary meningococcal conjunctivitis without accompanying bacteremia is not recommended in the U.S. due to a lack of evidence of transmission.5

**Rifampin** is the drug of choice in most instances. The rifampin dosage for those <1 month of age is 5 mg/kg twice daily for two days; for children ≥1 month of age, 10 mg/kg twice daily for two days; and for those ≥18 years of age, 600 mg twice daily for two days. **Rifampin chemoprophylaxis is not recommended for pregnant women.** Those taking rifampin should be informed that gastrointestinal upset, orange discoloration of urine, discoloration of soft contact lenses, and decreased effectiveness of oral contraceptives can occur. Rifampin is ~90% effective in eradicating the carrier state. Note that the rifampin schedule for eradication of *Haemophilus influenzae* carriage is efficacious against *N. meningitidis* carriage as well, but not vice versa.

**Ceftriaxone** can be used for children and adults (including pregnant women) to eradicate nasopharyngeal carriage if rifampin is contraindicated. It is given as a single IM dose of 125 mg for children <15 years of age and 250 mg for older persons.

**Ciprofloxacin** is not routinely recommended for people <18 years of age. However, it can be used for chemoprophylaxis of persons ≥18 years old. It is administered orally in a single 500 mg dose for those ≥18 years. **Cipro is not recommended for pregnant women.**

**Azithromycin** is considered the least preferable option and is not routinely recommended.

Table 2. Recommended Chemoprophylaxis Regimens for High-Risk Contacts and People with Invasive Meningococcal Disease6

<table>
<thead>
<tr>
<th>Age</th>
<th>Dose</th>
<th>Duration</th>
<th>Formulation</th>
<th>Efficacy (%)</th>
<th>Cautions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Rifampin</strong></td>
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<tr>
<td>&lt;1 month</td>
<td>5 mg/kg, orally, every 12 hours</td>
<td>2 days</td>
<td>150mg or 300mg capsules; can be sprinkled on applesauce or mixed with simple syrup or compounded by a pharmacy into suspension</td>
<td>90–95</td>
<td>Can interfere with efficacy of oral contraceptives and some seizure and anticoagulant medications; can stain soft contact lenses</td>
</tr>
<tr>
<td>≥1 month</td>
<td>10 mg/kg (maximum 600 mg), orally, every 12 hours</td>
<td>2 days</td>
<td></td>
<td>90–95</td>
<td></td>
</tr>
<tr>
<td><strong>Ceftriaxone</strong></td>
<td></td>
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<tr>
<td>&lt;15 years</td>
<td>125 mg, intramuscularly</td>
<td>Single dose</td>
<td>Sterile suspension for intravenous or intramuscular injection only</td>
<td>90–95</td>
<td>To decrease pain at infection site, dilute with 1% lidocaine</td>
</tr>
<tr>
<td>≥15 years</td>
<td>250 mg, intramuscularly</td>
<td>Single dose</td>
<td></td>
<td>90–95</td>
<td>To decrease pain at infection site, dilute with 1% lidocaine</td>
</tr>
<tr>
<td><strong>Ciprofloxacin</strong></td>
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<td></td>
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<tr>
<td>≥1 month</td>
<td>20 mg/kg (maximum 500 mg), orally</td>
<td>Single dose</td>
<td>Tablets: 250mg, 500mg, 750mg; Suspension: 50mg/1mL or 100mg/1mL</td>
<td>90–95</td>
<td>Not recommended routinely for people younger than 18 years of age; use may be justified after assessment of risks and benefits for the individual patient</td>
</tr>
<tr>
<td><strong>Azithromycin</strong></td>
<td></td>
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<tr>
<td></td>
<td>10 mg/kg (maximum 500 mg)</td>
<td>Single dose</td>
<td>Tablets: 600mg; Suspension: 1 gram packet diluted in 100mL = 10mg/1mL</td>
<td>90</td>
<td>Not recommended routinely (equivalent to rifampin for eradication of Neisseria meningitidis from nasopharynx in only one study)</td>
</tr>
</tbody>
</table>

* Not recommended for use in pregnant women

† Use only if fluoroquinolone-resistant strains of *N. meningitidis* have not been identified in the community; Centers for Disease Control and Prevention. Emergence of fluoroquinolone-resistant *Neisseria meningitidis* – Minnesota and North Dakota, 2007–2008. *MMWR Morb Mortal Wkly Rep.* 2008;57(7):173–175.
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6. MANAGING SPECIAL SITUATIONS

6.1 Case Attends a Day-care Facility

If the child has attended any such facility for at least 4 hours (cumulatively) during the week before onset, then within 24 hours of the initial report:

1. The operator of the day-care facility should be interviewed to determine whether other cases of meningococcal disease occurred among attending children during the past 60 days.
2. The parents of children who are in the same classroom as the case should be notified (preferably in writing) of the occurrence of meningococcal disease in the facility. The notice should advise parents to:
   - seek chemoprophylaxis for their attending children without delay.
   - watch their children carefully for a two-week period for signs of illness, especially fever, and seek medical care immediately if illness should occur. Advise parents that an elevated risk may persist for up to two months following the occurrence of a case.
3. Instruct the day-care operator to notify the LHD immediately if another person becomes ill with signs and symptoms of meningococcal disease over the next two months.
4. Chemoprophylaxis should also be given to all staff in the ill child’s classroom.
5. Children and staff in other rooms are usually not at elevated risk, and do not need chemoprophylaxis.

6.2 Multiple Cases in a Defined Population within a 3-month Period

If three or more confirmed or probable cases of meningococcal disease of the same serogroup among persons who have a common affiliation but not close contact occur within a 3-month period, a primary attack rate should be calculated. Contact Oregon Public Health Division immediately for consultation.

6.3 Troubleshooting Prophylaxis Availability

What if the contact’s insurance refuses to cover the cost of prophylaxis?

Prophylaxis should be covered by all insurance policies in Oregon (e.g., Oregon Health Plan, etc.), though a copayment may be required. If the pharmacist cannot obtain authorization, the insurance company should be contacted directly for pre-approval.

Also, as prophylaxis requires only 1 to 4 doses and generics for the recommended antibiotics are available, inquire with the pharmacist what the out-of-pocket cost would be: the total cost of the medication might be less than a copayment.

What if contacts are still unable to obtain rifampin due to financial circumstances?

If contacts meeting prophylaxis guidelines have been advised by the LHD to take rifampin, and they are unable to obtain rifampin by any other means due to financial circumstances, then the LHD may dispense rifampin out of its TB stock after consulting with the TB Program or Public Health Division epidemiologist on call. The LHD must then send a memo to the state TB program describing the circumstances, accounting for the rifampin dispensed and requesting replacement of stock.

What if there is not a compounding pharmacy available to prepare rifampin suspension for pediatric contacts requiring prophylaxis?

Rifampin is formulated as 150mg or 300mg capsules, which can be opened and sprinkled on applesauce or jello, or mixed with simple syrup (e.g., Syrup NF, Wild Cherry Syrup, etc.), following the manufacturer’s instructions.

If neither of these rifampin formulations is readily available or the child cannot be dosed appropriately using capsules, ceftriaxone injection is recommended to eradicate nasopharyngeal carriage of \textit{N. meningitidis}. Ceftriaxone for injection may be acquired through emergency rooms, urgent care clinics, and some private clinics and pharmacies in either 125mg or 250mg doses.

Finally, if none of the above options is available, one dose of oral ciprofloxacin is an alternative for contacts aged 1 month and older. Oral azithromycin is considered the least preferable option, and is not routinely recommended.
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7. REFERENCES


5. Cohn A, personal communication. Meningitis and Vaccine Preventable Diseases Branch, Division of Bacterial Diseases, National Center for Immunization and Respiratory Diseases, Office of Infectious Diseases, CDC, September 20, 2011.


8. UPDATE LOG

May 2007. This is the corrected version of what was meant to be the July release. The confirmed case definition was modified to incorporate PCR results. Recommendations for the new conjugate vaccine MCV4 were incorporated into the active immunization section. Primary meningococcal conjunctivitis and pneumonia were added as uncommon but possible presentations of meningococcal disease. (June Bancroft)

December 2011. Updated vaccination recommendations and clarified time frame for chemoprophylaxis administration. (Jamie Thompson)

July 2012. Added information about how to troubleshoot prophylaxis availability to Managing Special Situations Section. Clarified prophylaxis recommendations. (Jamie Thompson)

February 2015. Updated case definitions to be in line with CSTE case definitions. Added latex agglutination as acceptable test results in CSF for a confirmed case. (Poissant)