

Invasive Disease caused by *Haemophilus influenzae*

1. DISEASE REPORTING

1.1 Purpose of Reporting and Surveillance

1. To identify preschool-age children who may have been significantly exposed to *Haemophilus influenzae* type b (Hib) cases.
2. To establish close observation of such exposed children for signs of illness.
3. To recommend antibiotic prophylaxis and/or immunization to appropriate contacts of Hib cases.
4. To identify additional cases and establish risk factors for non-Hib cases.

1.2 Laboratory And Physician Reporting Requirements

Physicians are required to report suspected or confirmed cases of *Haemophilus influenzae*-related invasive disease, including bacteremia, meningitis, pneumonia, and epiglottitis, within 24 hours — **regardless of serotype**. Laboratories must report isolations of *H. influenzae* from normally sterile sites within one working day; by law, such isolates must be forwarded to the OSPHL.

1.3 Local Health Department Reporting and Follow-Up Responsibilities

1. Report all confirmed and presumptive (but *not* suspect) cases to Oregon Public Health Division (PHD) (see definitions below) by the end of the calendar week of initial physician/lab report. Use the case investigation form (download at <http://oregon.gov/DHS/ph/acd/reporting/forms/forms.shtml>). **Note that all cases of *H. influenzae* are reportable, regardless of serotype**; we just get more excited about type b's.
2. Begin follow-up investigation within 24 hours. Use the *Haemophilus influenzae* case investigation form. Send a copy of the completed form to PHD within seven days of initial report.
3. Identify significant contacts and recommend prophylaxis within 24 hours for Hib cases.

2. THE DISEASE AND ITS EPIDEMIOLOGY

2.1 Etiologic Agent

Haemophilus influenzae (Hi) is a small, Gram-negative bacillus. There are at least six serotypes of *H. influenzae* (designated a-f) distinguished by their capsular antigens, as well as unencapsulated (nontypeable) strains. Despite its name, this bacterium has nothing to do with the influenza viruses. (Note also that it is spelled differently too.)

2.2 Description of Illness

Disease can take many forms, including meningitis, bacteremia, periorbital or other cellulitis, septic arthritis, osteomyelitis, pericarditis, or pneumonia. Onset of symptoms is usually abrupt, and may include fever, headache, lethargy, anorexia, nausea, vomiting, and irritability. Progressive stupor or coma is common with meningitis.

Infections spread via the bloodstream after penetration of the mucous membranes of the nasopharynx. The exact mechanism allowing the penetration is unknown, but a recent upper respiratory tract infection may facilitate invasion. Recently, having a cochlear implant procedure has been identified as a possible risk factor for invasive disease.

Prior to routine vaccination, *H. influenzae* type b was the most common cause of bacterial meningitis and is a major cause of other invasive disease (including epiglottitis) in young American children. Prior to the introduction of effective conjugate vaccines in 1990, one child in 200 developed *Haemophilus* disease by the age of five.

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Asymptomatic carriage of Hib is not uncommon; in the pre-vaccine era the organism was recovered from the upper respiratory tract of 2–5% of healthy children. Thus, isolates from sputum or other not-normally-sterile sites are *not* indicative of invasive disease.

Neonatal sepsis and non invasive upper respiratory tract disease, including otitis media, sinusitis, and bronchitis are often caused by other, nonencapsulated strains of *H. influenzae*. These organisms are extremely common and can be recovered from the nasopharynx of 40% to 80% of healthy children.

The majority of *H. influenzae* cases in Oregon are nontypeable. In 2014 there were 80 cases of invasive *H. influenzae*, 63% were nontypeable, 5% were type b, 18% were type f, and 14% were of another serotype. Since 1995 there have been 55 cases of serotype b infection, sixteen of which occurred in children under age 4. There have been 4 cases in this young age group since 2010.

2.3 Reservoirs — Human cases and carriers.

2.4. Modes of Transmission

Hi organisms are transmitted by direct contact with respiratory droplets and discharges from the nose and throat of infected/colonized persons. With Hib, children <4 years of age who have had prolonged household, day care, or other close contact with a case are at increased risk of disease. The risk of secondary disease among household contacts is age dependent and estimated to be 4% for children <2 years of age, 2% for children 2–3 years of age, 0.1% for children 4–5 years of age, and 0% among immunocompetent contacts over the age of 6. The overall risk of secondary disease in the day care setting seems to be less than in households and is estimated at 1–2% for children <2 years of age and less than 1% in children age 2 or older.

2.5 Incubation Period

The incubation period is hard to define, because most persons who acquire Hi infections are asymptotically colonized. Those who become ill following exposure to a case usually do so within 10 days, although the risk may be slightly elevated for up to 60 days.

2.6 Period of Communicability

As long as the organism is present in discharges from the nose or throat. Communicability ends within 24 hours of initiation of appropriate chemoprophylaxis. Note, however, that treatment of invasive disease does not necessarily eradicate the organism from the nasopharynx. Those exposed \pm 7 days before onset of illness in the case are not at significantly increased risk. Hib cases are probably most infectious during the 3 days prior to onset of symptoms.

2.7 Treatment

Initial therapy for children with meningitis potentially caused by Hib includes cefotaxime or ceftriaxone. Meropenem or ampicillin and chloramphenicol administered intravenously are alternatives. Duration of therapy is usually a minimum of 10 days; more days may be indicated in complicated cases. As many as 40% of Hib isolates may be resistant to ampicillin.

3. CASE DEFINITIONS, DIAGNOSIS, AND LABORATORY SERVICES

3.1 Confirmed Case Definition

- Isolation of *Haemophilus influenzae* from a normally sterile body site (e.g., cerebrospinal fluid [CSF], blood, joint fluid, pleural fluid, pericardial fluid); or
- Detection of *Haemophilus influenzae*-specific nucleic acid in a specimen obtained from a normally sterile body site, using a validated polymerase chain reaction (PCR) assay

3.2 Presumptive Case Definition

- Meningitis with detection of *Haemophilus influenzae* type b antigen in cerebrospinal fluid [CSF]
- Patients with compatible illness who are epi-linked to a confirmed case, and from whom small, pleomorphic Gram-negative bacilli are detected in a specimen from a normally sterile site (e.g., blood, CSF, or synovial fluid)

3.3 Suspect Case (*not reportable to OHA*)

Non-epi-linked patients with compatible illness and the laboratory findings listed for presumptive cases.

3.4. Services Available at the Center for Public Health Laboratories

The OSPHL will confirm the identification and serotype isolates of *H. influenzae*. Isolates should be sent on media that support the growth of the organism (e.g., chocolate agar). All specimens must be properly packaged in double containers with absorbent material around them. Use the Bacteriology/Parasitology form. These specimens should not be sent with cold packs.

4. ROUTINE CASE INVESTIGATION

In general, further action is NOT recommended until a case has received a confirmation of serotype b (Hib). **However, if there is at least one completely unimmunized child <4 years of age in the case's household, do not wait for serotype confirmation; begin prophylaxis of all household members within 24 hours.**

4.1 Identify Source of Infection

Usually, this is not possible because the organism is carried asymptotically by a high percentage of people. Follow-up for serotypes other than b (i.e., non-Hib) is generally not indicated beyond completion of case identification, demographic, clinical and laboratory sections on page 1 of the Case Investigation report form. Although a long shot, with Hib cases it is worth checking if any household or day care contacts have had any illness suggestive of *H. influenzae*-caused invasive disease within the previous 60 days.

4.2 Identify Potentially Exposed Persons

While awaiting serotype report:

1. Determine whether any other members of the immediate household are <4 years of age, and if so, their Hib immunization status. If there is at least one completely unimmunized child <4 years of age, begin prophylaxis of all household members within 24 hours.¹ If no household members <4 years of age are identified, no further action is recommended until the case has received a confirmation of serotype b.
2. Determine whether the case had prolonged contact (4 or more hours in a day) with other children under age 2 in a day care facility in the week prior to onset of illness. If so, refer to §6. **We do NOT recommend taking further action in a daycare setting unless a case of serotype b has been confirmed.**²
3. Culturing of exposed persons to identify carriers is not useful.

4.3 Environmental Evaluation — None.

5. CONTROLLING FURTHER SPREAD (HIB ONLY)

5.1 Education

Parents or guardians of potentially exposed children <4 years of age should be instructed to monitor these contacts for 14 days for fever, lethargy, irritability, loss of appetite, vomiting, or other signs of illness, and to seek medical care immediately should any illness occur. If the exposed child is a day care contact, this observation should continue for 60 days. (See §6.)

5.2 Isolation

Droplet precautions should be implemented until 24 hours have passed following initiation of antibiotic therapy.

5.3 Follow up of Hib Cases

Therapy for invasive Hib disease might not eradicate respiratory carriage of the organism. Therefore, convalescing children—especially those having contact with children <4 years of age in households or <2 years of age in daycare settings—should receive appropriate chemoprophylaxis for at least 24 hours before resuming contact with any unimmunized or incompletely immunized children. Treatment of Hib disease with ceftriaxone or cefotaxime will eradicate nasal carriage. Treatment with meropenem, ampicillin or chloramphenicol does not eradicate carriage, and should be treated with rifampin prophylaxis.

5.4 Immunization and Prophylaxis

1. **Passive Immunization** — Generally, none (except for maternal antibodies, if any).
2. **Active Immunization**

Hib vaccine is available for use in children 6 weeks of age or older (See ACIP guidelines). Because of the length of time necessary to develop antibodies, vaccination does not play a major role in the management of patients with Hib disease or their contacts. The effects of Hib vaccination on asymptomatic carriage of Hib are uncertain. Thus, although immunized children may be protected from invasive disease, they may acquire and pass the or-

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ganism on to other, susceptible children. Children developing Hib invasive disease before the age of two are at high risk of recurrent Hib disease. They should be immunized according to the age-appropriate schedule ASAP during convalescence. Any earlier doses of Hib vaccine received by such children should be discounted.

3. Antibiotic Prophylaxis

Appropriate chemoprophylaxis should be recommended for all household contacts of Hib cases in the following circumstances:

- Household with at least 1 contact <4 years of age who is unimmunized or incompletely immunized¹
- Household with a child <12 months of age who has not received the primary series
- Household with a contact who is an immunocompromised child, regardless of that child's Hib immunization status

(In general, further action is NOT recommended until a case has received a confirmation of serotype b. However, if there is at least one completely unimmunized child <4 years of age in the case's household, do not wait for serotype confirmation; begin appropriate chemoprophylaxis of all household members within 24 hours.)

Chemoprophylaxis should also be considered for day care contacts when 2 or more cases of Hib invasive disease have occurred within 60 days and unimmunized or incompletely immunized children attend the facility. Recommendations for prophylaxis should be communicated to the case's physician and at least one responsible adult in the household.

The rifampin dosage is 20 mg/kg (maximum 600 mg) once daily for 4 days. For neonates (<1 month of age) the dose is 10 mg/kg once daily for 4 days. Rifampin is available in 150 mg and 300 mg capsules. It can be mixed with several teaspoons of applesauce or jelly, or suspended in a simple syrup (Syrup NF, Wild Cherry Syrup, etc.), following the manufacturer's instructions. 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. Note that the rifampin schedule for eradication of *Haemophilus influenzae* carriage is efficacious against *N. meningitidis* carriage as well, but not vice versa.

Antibiotic prophylaxis should begin as soon as possible, and is of less value if >14 days have passed since the last contact with the case. An elevated risk of disease may exist for up to 60 days following exposure.

If contacts meeting prophylaxis guidelines have been advised by the LHD to take rifampin but are unable to obtain rifampin by any other means due to financial circumstances, the LHD may dispense rifampin out of its TB stock *after* consulting with the TB Coordinator or Communicable Disease epidemiologist on call at the Health Division. 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.

6. WHEN THE CASE IS IN DAY CARE (HIB ONLY)

Ascertain if the case was in any day care facility or baby-sitting situation for least 4 hours in at least one day of the week prior to onset. If so, determine if any children <2 years of age were in the same room. If so:

1. The operator of the facility should be asked about other cases of meningitis or other suspect invasive disease occurring among other children during the past 2 months.
2. The parents of children in the same classroom as the case should be notified (preferably in writing) of the occurrence of Hib disease in the facility. The notice should advise parents to:
 - monitor their children carefully for a 60-day period for signs of illness such as fever, irritability, lethargy, and loss of appetite; and
 - seek medical care immediately should such symptoms occur.
3. Instruct the day care operator to notify the LHD immediately if another child becomes ill within the next 60 days. When 2 or more cases of Hib have occurred within 60 days and unimmunized or incompletely immunized children attend the child care facility, rifampin prophylaxis for workers and attendees should be considered in consultation with Public Health.

¹ Complete immunization is defined as having had at least 1 dose of conjugate vaccine at ≥ 15 months of age; 2 doses between 12 and 14 months of age; or a 2- or 3-dose primary series when <12 months with a booster dose at ≥ 12 months of age

7. REFERENCES

1. Osterholm MT, Pierson LM, White KE, Libby TA, Kuritsky JN, McCullough JG. The risk of subsequent transmission of *Haemophilus influenzae* type b disease among children in day care: results of a two-year statewide prospective surveillance and contact survey. *N Engl J Med* 1987; 316:1–5.]
2. Broome CV, Mortimer EA, Katz SL, Fleming DW, Hightower AW. Special Report – Use of chemoprophylaxis to prevent the spread of *Haemophilus influenzae* b in day-care facilities. *N Engl J Med* 1987; 316:1226–8.

8. UPDATE LOG

January 2007. Updated chemoprophylaxis regimens and practices associated with the daycare settings. Addressed the use of cefotaxime and ceftriaxone in treatment of invasive disease and eradication of nasal carriage.

December 2010. Clarified recommendations for prophylaxis while awaiting serotype report. Updated epidemiological data. (Jamie Thompson).

January 2015. Section 2.2: Updated serotype distribution with 2014 data. (Poissant)

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