



Invasive *Haemophilus influenzae* Public Health Investigation Quicksheet

Infectious agent

Haemophilus influenzae, a bacterium, can be isolated in six encapsulated forms (types a-f) and also in unencapsulated forms. The polysaccharide capsule is an important virulence factor; unencapsulated or “nontypable” strains typically do not cause invasive disease. Pharyngeal colonization with *H. influenzae* is relatively common, especially with unencapsulated strains and non-b capsular strains.

Young children do not have the ability to make antibodies to polysaccharide and are more susceptible to infection with encapsulated bacteria. This is especially true for children between six months and one year of age who no longer have maternal antibody protection. People with functional or anatomic asplenia and other conditions are also at higher risk of infection with encapsulated bacteria.

Epidemiology

Before effective *H. influenzae* type b (Hib) vaccines were introduced, one in 200 children developed invasive Hib disease by the age of 5 years. 60% of these children had meningitis; 3%-6% died. Virtually all invasive disease in the prevaccine era (<1988) was due to Hib and Hib was the most common cause of bacterial meningitis. Since the introduction of Hib conjugate vaccines in the U.S., the incidence of invasive Hib disease has declined by 99%. Invasive Hib disease in the U.S. today is uncommon and occurs primarily in underimmunized children and among infants too young to have completed the primary vaccination series. The majority of invasive *H. influenzae* cases reported in children in recent years have been caused by non-type b and nontypeable strains.

Clinical symptoms

- Invasive Hib disease can produce a number of clinical syndromes including pneumonia, bacteremia, meningitis, epiglottitis, septic arthritis and cellulitis. Other encapsulated strains (a-f) can cause disease similar to type b infections.
- Nontypable strains generally cause noninvasive respiratory tract infections such as conjunctivitis and otitis, but can occasionally cause invasive disease.

Mode of transmission

H. influenzae is transmitted person-to-person by inhalation of respiratory aerosols or by direct contact with respiratory tract secretions.

Neonates can become infected by aspiration of amniotic fluid or by contact with genital tract secretions containing the organism.

Communicability

The contagious potential of invasive *H. influenzae* disease is considered to be limited. However, close contact with a case (e.g., in a household, daycare center, or institutional setting), can lead to outbreaks of Hib or secondary transmission of the disease.

Period of communicability

Likely to be as long as *H. influenzae* is present in the upper respiratory tract, which may be a prolonged period.

Incubation period

The incubation period is unknown

Laboratory testing

Culture and sensitivities

The diagnosis of invasive disease is established by the growth of *H. influenzae* from a normally sterile body site, i.e., cerebrospinal fluid (CSF), blood, joint fluid, pleural effusion, pericardial effusion, peritoneal fluid, subcutaneous tissue fluid, placenta, and amniotic fluid. Gram stain can facilitate presumptive diagnosis. All isolates should be tested for antimicrobial susceptibility.

Polymerase chain reaction (PCR) detection

Although culture is the gold standard for confirming *H. influenzae*, real-time PCR is an accepted alternative. Real-time PCR assays are available to detect DNA of all six *H. influenzae* serotypes in blood, CSF, or other clinical specimens. A major advantage of PCR is that it allows for detection of *H. influenzae* from clinical samples in which the organism could not be detected by culture methods, such as when a patient has been treated with antibiotics before a clinical specimen is obtained for culture.

Serotyping

All *H. influenzae* isolates associated with invasive disease in children <5 years of age should be serotyped in order to identify the strain, monitor epidemiologic trends, and differentiate between type b and other serotypes for which control measures are not required. The six encapsulated types have distinct capsular polysaccharides that can be differentiated by slide agglutination with type-specific antisera.

The CDPH Microbial Diseases Laboratory (MDL) can perform *H. influenzae* serotyping on isolates from sterile sites if the hospital or local health department laboratory cannot perform such typing. Please contact the MDL Special Pathogens Unit at (510) 412-3903 before sending isolates or for further information regarding laboratory testing for *H. influenzae*.

Antigen detection

The type b capsular antigen can be detected in body fluids, including urine, blood, and CSF of patients.

Antigen detection may be used as an adjunct to culture, particularly in the diagnosis of patients who have received antimicrobial agents before specimens are obtained for culture. Methods for antigen detection include latex agglutination and counterimmunoelectrophoresis.

If Hib antigen is detected in CSF but a positive result is not obtained from culture or sterile site, the patient should be considered as a probable Hib case and reported as such. Because antigen detection tests can be positive in urine and serum of persons without invasive Hib disease, persons who are identified exclusively by positive antigen tests in urine or serum should not be reported as cases.

CDC *H. influenzae* case classification

Clinical description: Invasive disease may manifest as pneumonia, bacteremia, meningitis, epiglottitis, septic arthritis, cellulitis, or purulent pericarditis; less common infections include endocarditis and osteomyelitis.

Probable: Meningitis with detection of *Haemophilus influenzae* type b antigen in cerebrospinal fluid (CSF).

Confirmed:

- 1) Isolation of *Haemophilus influenzae* from a normally sterile body site (e.g., blood or CSF, or less commonly, joint, pleural, or pericardial fluid). OR
- 2) 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

All probable and confirmed cases of invasive *H. influenzae* <5 years of age, regardless of serotype, should be reported to CDPH. Cases occurring in persons ≥ 5 years of age resulting in meningitis should be reported as 'Bacterial Meningitis'.

Disease reporting and case investigation

The purpose of surveillance is to monitor the *H. influenzae* disease burden and the long-term efficacy of Hib vaccine.

1. Confirm that suspected case meets case definition and/or is highly suspected.

2. Ensure that case is receiving appropriate antibiotic treatment.
3. Request serotyping of the isolate at the hospital, if feasible.
4. Forward isolates associated with invasive disease to the CDPH Microbial Diseases Lab.
5. For Hib cases: Determine whether case household has un- or undervaccinated children <4 years of age or an immunocompromised child regardless of his/her immunization status (see chemoprophylaxis section).
6. Notify CDPH immediately of any Hib case <5 years.
7. When indicated, prophylaxis of contacts should be initiated as soon as possible given that most secondary cases in households occur during the first week after hospitalization of the index case.
8. It may be necessary to consider prophylaxis for at-risk contacts of an invasive *H. influenzae* case when type is unknown.
9. Vaccinate children who are not up-to-date for Hib.
10. Perform active surveillance of exposed unimmunized or incompletely immunized household, childcare or preschool contacts of Hib cases. Exposed children in whom a febrile illness occurs should receive prompt medical evaluation.
11. Report confirmed and probable invasive *H. influenzae* cases <5 years of age to CDPH.

Recommended case management

Initial therapy for children with meningitis possibly caused by Hib is cefotaxime or ceftriaxone. Meropenem is an alternative empiric agent. Ampicillin can be substituted if the Hib isolate is susceptible to ampicillin. Treatment of other invasive *H. influenzae* infections is similar. Therapy is continued at least 10 days by the IV route and longer in complicated infections.

Treatment with cefotaxime or ceftriaxone eradicates Hib colonization, eliminating the need for prophylaxis of the index patient. Patients who are treated with ampicillin, meropenem, or another antibiotic regimen and who are younger than 2 years of age should receive rifampin prophylaxis at the end of therapy for invasive infection. Dexamethasone may be beneficial for infants and children with Hib meningitis to decrease the risk of hearing loss.

For additional treatment recommendations, see the 2015 AAP Red Book.

Isolation of patients with invasive Hib disease

Droplet precautions are recommended for 24 hours after initiation of appropriate parenteral antimicrobial therapy.

Additional *H. influenzae* information and case report forms can be found on the CDPH website at:

[http://www.cdph.ca.gov/HealthInfo/discond/Pages/HaemophilusInfluenzaetypeb\(Hib\).aspx](http://www.cdph.ca.gov/HealthInfo/discond/Pages/HaemophilusInfluenzaetypeb(Hib).aspx)

Chemoprophylaxis for close contacts

The risk of invasive Hib disease is increased among un- or under-immunized household contacts <4 years of age. Factors that predispose to invasive disease include sickle cell disease, asplenia, HIV infection, certain immunodeficiency syndromes, and malignant neoplasms.

Rifampin eradicates Hib from the pharynx in approximately 95% of carriers and decreases the risk of secondary invasive disease in exposed household contacts.

Indications and guidelines for chemoprophylaxis in different circumstances are described in the 2015 AAP Red Book and summarized in the table below.

When indicated, prophylaxis should be initiated as soon as possible. Because some secondary cases occur later, initiation of prophylaxis ≥ 7 days after hospitalization of the index patient may still be of some benefit.

Chemoprophylaxis is not recommended for contacts of people with invasive disease caused by non-Hib strains. However, chemoprophylaxis should be considered for high-risk contacts when the serotype is unknown or cannot be determined promptly.

Contact the CDPH Immunization Branch at (510) 620-3737 or Microbial Diseases Laboratory at (510) 412-3903 if urgent serotyping is needed.

Rifampin* chemoprophylaxis for contacts of index cases of invasive Hib disease

Chemoprophylaxis recommended

- For all household contacts^a in the following circumstances:
 - Household with at least 1 contact younger than 4 years of age who is unimmunized or incompletely immunized^b
 - Household with a child younger than 12 months of age who has not completed the primary Hib series
 - Household with a contact who is an immunocompromised child, regardless of that child's Hib immunization status
- For preschool and childcare center contacts when 2 or more cases of Hib invasive disease have occurred within 60 days, administer chemoprophylaxis to all contacts irrespective of age and vaccination status.
- For index patient, if younger than 2 years of age or member of a household with a susceptible contact and treated with a regimen other than cefotaxime or ceftriaxone, chemoprophylaxis usually is provided just before discharge from hospital.

Chemoprophylaxis Not Recommended

- For occupants of households with no children younger than 4 years of age other than the index patient.
- For occupants of households when all household contacts 12 through 48 months of age have completed their Hib immunization series and when household contacts younger than 12 months of age have completed their primary series of Hib immunizations.
- For preschool and child care contacts of 1 index case.
- For pregnant women.

*Rifampin should be given orally, once a day for 4 days (20 mg/kg; maximum dose, 600 mg). The dose for infants <1 month of age is not established; some experts recommend lowering the dose to 10 mg/kg. For adults, each dose is 600 mg.

^aDefined as people residing with the index patient or nonresidents who spent 4 or more hours with the index patient for at least 5 of the 7 days preceding the day of hospital admission of the index case.

^bComplete immunization is defined as having had at least 1 dose of conjugate vaccine at 15 months of age or older; 2 doses between 12 and 14 months of age; or the 2- or 3-dose primary series (depending on vaccine used) when younger than 12 months with a booster dose at 12 months of age or older.