

# Invasive *Haemophilus influenzae* Quicksheet

June 2024



## Infectious agent

*Haemophilus influenzae*, a bacterium, can be isolated in six encapsulated forms (types a-f) and in unencapsulated forms. The polysaccharide capsule is an important virulence factor; unencapsulated or “nontypeable” strains can also cause invasive disease but more commonly cause mucosal infections. Pharyngeal colonization with *H. influenzae* is relatively common, especially with unencapsulated strains and non-b encapsulated strains.

Young children do not have the ability to make antibodies to polysaccharide and are more susceptible to infection with encapsulated bacteria. Children between six months and one year of age, who no longer have maternal antibody protection, are particularly susceptible. People with functional or anatomic asplenia and certain immunodeficiency syndromes 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. Sixty percent of these children had meningitis; 3%-6% died. Virtually all invasive *H. influenzae* disease in the pre-vaccine era (<1988) was due to Hib and Hib was the most common cause of bacterial meningitis. Since introduction of Hib conjugate vaccines in the United States, the incidence of invasive Hib disease has decreased by more than 99% in children younger than 5 years. 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-b and nontypeable strains.

*H. influenzae* type a (Hia) has emerged as the most common encapsulated serotype causing invasive disease, with a clinical presentation similar to Hib. In some American Indian and Alaska Native populations the rate of invasive Hia infection has been increasing and there is evidence of secondary cases having occurred. Among the general population of US children, the incidence of invasive Hia is low but has been increasing in recent years, with a nearly 300% increase over the last 10 years among children younger than 1 year. Invasive disease may also be caused by other encapsulated non-type b strains.

## Clinical symptoms

- Invasive *H. influenzae* diseases include meningitis, bacteremia or sepsis, epiglottitis, pneumonia, septic arthritis, osteomyelitis, pericarditis, and cellulitis. In contrast, mucosal infections such as bronchitis, sinusitis, and otitis media are considered noninvasive disease.
- Nontypeable 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.

### 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 (e.g., cerebrospinal fluid (CSF), blood, joint fluid, pleural fluid, pericardial fluid, 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

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 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 PCR, 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.

### ***H. influenzae* reporting and case definition**

All probable and confirmed cases of invasive *H. influenzae* in **children <5 years of age**, regardless of serotype, should be reported to CDPH within one working day of identification. Meningitis due to *H. influenzae* in persons  $\geq 5$  years of age should be reported as bacterial meningitis cases. Invasive *H. influenzae* in persons  $\geq 5$  years who do not have bacterial meningitis **is not reportable**; local health jurisdictions may pursue contact management for these cases as desired.

**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.

### **Surveillance and public health management**

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

1. Confirm that reported 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. Determine whether case's household has un- or undervaccinated children <4 years of age or an immunocompromised child regardless of his/her immunization status (see chemoprophylaxis section).
6. 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. It is reasonable to initiate prophylaxis for at-risk contacts of an invasive *H. influenzae* case while serotyping is in process (before the case is known to be due to Hib).
7. Vaccinate children who are not up-to-date for Hib.
8. Identify exposed un- or undervaccinated household, childcare, or preschool contacts of Hib cases who may have symptoms consistent with invasive Hib disease. Exposed children in whom a febrile illness occurs should receive prompt medical evaluation.

### **Recommended case management**

Initial therapy for children with meningitis possibly caused by Hib is cefotaxime or ceftriaxone. Treatment of other invasive *H. influenzae* infections is similar. Therapy is continued for 7 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 do not receive at least 1 dose of cefotaxime or ceftriaxone and who are younger than 2 years of age should receive rifampin prophylaxis at the end of therapy for invasive infection.

For additional treatment recommendations, see the [AAP Red Book](#).

### Isolation of patients with invasive Hib disease

Droplet precautions are recommended for 24 hours after initiation of appropriate antimicrobial therapy. Additional *H. influenzae* information and case report forms can be found on the [CDPH - \*Haemophilus Influenzae\* type B webpage](#).

### 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 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  $\geq 7$  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 or non-Hia strains. Clinicians may consider chemoprophylaxis of contacts of index cases of invasive Hia disease, using the same criteria as for Hib disease. Contact the CDPH Immunization Branch at (510) 620-3737 or Microbial Diseases Laboratory at (510) 412-3903 if urgent serotyping is needed.

Serotyping may not be available quickly enough to allow for prompt decision-making regarding chemoprophylaxis. Chemoprophylaxis should be considered for high-risk contacts when the serotype is unable to be determined or cannot be determined promptly. Although meningitis due to *H. influenzae* in persons  $\geq 5$  years is reportable as bacterial meningitis rather than as invasive *H. influenzae* disease, it is also reasonable to pursue serotyping and contact management for these cases.

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

### Chemoprophylaxis recommended in these limited situations

- For **ALL** household contacts<sup>a</sup> in any of the following circumstances:
  - Household with at least 1 child younger than 4 years of age who is unimmunized or incompletely immunized<sup>b</sup> **OR**
  - Household with a child younger than 12 months of age who has not completed the primary Hib series **OR**
  - Household with an immunocompromised child, regardless of that child's Hib immunization status or age
- 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 at the end of therapy for invasive infection.

### 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 are immunocompetent **AND** all 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 Hib immunization series.
- For preschool and childcare contacts of 1 index case.
- For pregnant people.

\*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.

<sup>a</sup>Defined 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.

<sup>b</sup>Complete 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.

From 2021-2024 AAP Red Book

Algorithm. *Haemophilus influenzae* reporting and contact management

