Haemophilus influenzae Invasive Disease

Summary

Haemophilus influenzae are gram-negative coccobacilli that cause a broad range of infections. The organism is transmitted person to person by respiratory droplets. The most common manifestations of invasive disease are bacteremia, meningitis, and pneumonia. Signs and symptoms may include fever, headache, meningismus, cough, respiratory distress, or general ill appearance. Diagnosis is made by bacterial culture or polymerase chain reaction (PCR). Antimicrobial treatment is indicted for invasive *H. influenzae* infections to prevent poor patient outcomes and sequelae. The epidemiology of invasive *H. influenzae* disease has shifted in the post-Hib vaccination era (Hib = *H. influenzae* type b). Nontypeable *H. influenzae* is now the most common, while *H. influenzae* type a (Hia) is the most common encapsulated serotype.

Agent

General: *Haemophilus influenzae* is classified into six capsular types (a through f) and nonencapsulated (nontypable) strains.

Transmission

Reservoir**:**

Humans.

Mode of transmission:

- General**:** The organism resides in the human upper respiratory tract. Person-to-person transmission occurs through inhalation of respiratory tract droplets or through direct contact with respiratory tract secretions from infected or colonized individuals. In neonates, infection is acquired intrapartum by aspiration of amniotic fluid or by contact with genital tract secretions. Pharyngeal colonization is common, especially with non-type b strains.
- Type b**:** Widespread use of Hib conjugate vaccine has markedly reduced colonization rates for type b. Colonization rates increase following recent exposure in closed populations (such as family or childcare contacts of a person with disease).

Period of communicability:

- General**:** Undefined as the organism can be transmitted as long as it is present in the nasopharynx.
- Type b**:** For patients with invasive Hib disease, the patient is considered noninfectious 24 hours after initiation of appropriate antimicrobial therapy.

Clinical Disease

Incubation period:

Unknown.

Illness:

When bacteria disseminate from the mucosal surfaces of the upper respiratory tract into the bloodstream and elsewhere in the body, clinical illness occurs. Common manifestations of

invasive disease are bacteremia, meningitis, pneumonia, epiglottitis, cellulitis, otitis media, purulent pericarditis, septic arthritis or other musculoskeletal disease. Signs and symptoms may include fever, headache, meningismus, cough, respiratory distress, bone or joint pain, or general ill appearance. Non-encapsulated or nontypeable strains of *H. influenzae* usually cause noninvasive infections including otitis media, sinusitis, conjunctivitis, pneumonia, and bronchitis.

Laboratory Diagnosis

H. influenzae can be cultured from blood, cerebrospinal fluid (CSF), joint fluid, sputum, pleural fluid, and other body sites. A gram stain of infected body fluid can demonstrate the organism and allow a presumptive diagnosis to be made. Because occult meningitis is known to occur in young children with invasive Hib disease, a lumbar puncture should be strongly considered in the presence of invasive disease, even in the absence of central nervous system signs and symptoms. Isolation of the bacterium is needed to confirm *H. Influenzae* invasive disease, determine the serotype, and test for antimicrobial susceptibility. **All *H. influenzae* isolates associated with invasive disease must be serotyped** (which is performed at New Mexico Department of Health Scientific Laboratory Division).

Antigen detection methods, which have been historically used on CSF, blood, and urine specimens, are not recommended because they lack sensitivity and specificity. Slide agglutination is used to detect Hib capsular polysaccharide antigen in CSF, but a negative test does not exclude the diagnosis, and false positives have been reported. Positive antigen test results can occur from circulation of Hib antigen in urine or serum; this circulation can be caused by asymptomatic Hib carriage, recent vaccination, or fecal contamination of urine specimens. Cases identified exclusively by these methods should be considered suspect cases only.

Nucleic acid amplification (NAATs) available in multiplexed assays to detect *H. Influenzae* DNA directly in blood, CSF, or other clinical specimens also has the advantage of detecting *H. Influenzae* in the absence of a clinical sample. Real-time PCR detects DNA of all *H. Influenzae* in blood, CSF, or other clinical specimens, and may be particularly useful in patients in patients whose specimens are obtained after the initiation of antibiotics. Even when the organisms are nonviable following antimicrobial treatment, PCR can still detect *H. Influenzae* DNA.

Treatment

Patients with invasive *H. influenzae* must receive antimicrobial therapy. The choice of specific therapy should consider local antibiotic susceptibility patterns of invasive isolates. Treatment decisions are made by the patient's health care provider; consultation with infectious disease specialists can be beneficial in treating invasive infections.

Surveillance

Case Definition:

Confirmed

Isolation of *Haemophilus influenzae* from a normally sterile body site (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 (e.g., cerebrospinal fluid [CSF], blood, joint fluid, pleural fluid, pericardial fluid), using a validated polymerase chain reaction (PCR) assay

Probable

Meningitis WITH detection of *Haemophilus influenzae* type b antigen in cerebrospinal fluid (CSF)

Reporting:

Report all suspected, probable or confirmed cases of invasive *H. influenzae* immediately to the Epidemiology and Response Division (ERD) at 505-827-0006. Information needed includes: patient's name, age, sex, race, ethnicity, home address, home phone number, occupation and health care provider.

Case Investigation:

Use the Bacterial Meningitis Invasive Respiratory Disease (BMIRD) Form to complete the investigation. Information should also be entered into NM-EDSS per established procedures.

Control Measures (type b only)

1. Case management
    1.1. Isolation: For hospitalized patients with invasive Hib disease, droplet precautions should be used for 24 hours after initiation of antimicrobial therapy.
    1.2. Prophylaxis: Treatment of Hib disease with cefotaxime or ceftriaxone eradicates Hib colonization. Chloramphenicol in combination with ampicillin could be used as an alternative. The treatment course is usually 10 days. As ampicillin-resistant strains of Hib are now common throughout the United States, an index case who has been treated with a regimen other than the cefotaxime or ceftriaxone, are younger than 2 years old, and/or a member of a household with a susceptible contact should receive rifampin chemoprophylaxis at the end of therapy for invasive infection.
2. Contact management
    2.1. Isolation: Not applicable.
    2.2. Indications and Guidelines for Rifampin Chemoprophylaxis for Contacts of Index Cases of Invasive *Haemophilus influenzae*, type b (Hib) disease[1].

Type b: Chemoprophylaxis with rifampin is indicated for close contacts of patients with invasive *Haemophilus influenzae* type b (Hib) disease. Two Hib conjugate vaccines are currently licensed for routine immunization in infants. Prior to introduction of *H. influenzae* type b (Hib) conjugate vaccine, the majority of invasive disease in children was caused by type b. The epidemiology of invasive H. influenzae infection has changed in the post-Hib vaccination era, with the majority of the disease now caused by nontypeable *H. influenzae* in all age groups. Rifampin should be given orally once a day for four days, in a dose of 20 mg/kg (maximum daily dose 600 mg). For infants aged less than one month, the dose is not well established; 10 mg/kg has been recommended by some experts. The adult dose is 600 mg.

Prophylaxis Recommended:

1. For all household contacts[2] (except pregnant women) in the following circumstances:

a. Household with at least 1 child younger than 5 years of age who is unimmunized or incompletely immunized[3]

b. Household with a child younger than 12 months of age who has not completed the primary Hib series

c. Household with an immunocompromised child, regardless of that child's Hib immunization status or age

2. For preschool and childcare center contacts when two or more cases of Hib invasive disease have occurred within 60 days.

3. For index patient, if younger than 2 years old or a 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 the hospital

Prophylaxis NOT Recommended:

1. For occupants of households with no children younger than 4 years old other than the index patient

2. 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.

3. Not routinely recommended for preschool and childcare contacts of one index case. Consult with a medical epidemiologist for specific guidance.

4. For pregnant women

Prophylaxis is not recommended for contacts of cases with non-type b invasive infection.

1. It is unknown whether persons (particularly young children) in contact with a person with invasive non-type b *H. influenzae* disease are at increased risk for disease. Also unknown is whether chemoprophylaxis is efficacious under these circumstances. There have been very few documented cases of secondary disease in close contacts of invasive non-type b *H. influenzae* disease. Therefore, currently, ERD does not recommend chemoprophylaxis for contacts of non-type b H. influenzae cases.

2. Testing of asymptomatic contacts is not recommended

[1] Similar criteria may be used for Hia; except Hib immunization criteria is not applicable

[2] Defined as people residing with the index patient or nonresidents who spent four or more hours with the index case for at least 5 of the 7 days preceding the day of hospital admission of the index case.

[3] Complete immunization is defined as having had at least one dose of conjugate vaccine at 15 months of age or older; two doses between 12 and 14 months of age; or 2 or 3 dose primary series depending on vaccine type (see below Vaccine Section).

2.3. Surveillance

Careful observation of exposed unimmunized or incompletely immunized household, childcare, or nursery contacts is essential. Exposed children who develop a febrile illness should be evaluated immediately.

Vaccination

The Advisory Committee on Immunization Practices (ACIP) is a group of medical and public health experts that develop recommendations on use of vaccines in the US, recommendations for the use of Hib vaccine in children and adolescents aged 18 years or younger can be found at: https://www.cdc.gov/vaccines/schedules/hcp/imz/child-adolescent.html

Management of Invasive *H. influenzae*, type b (Hib) Disease in Childcare Centers (from: http://www.cdc.gov/vaccines/pubs/surv-manual/chpt02-hib.html#vaccination)

When two or more cases of invasive Hib disease have occurred within 60 days and unimmunized or incompletely immunized children attend the childcare facility or preschool, rifampin prophylaxis of all attendees (irrespective of their age and vaccine status) and child care providers should be considered. In addition to these recommendations for chemoprophylaxis, unimmunized or incompletely immunized children should receive a dose of vaccine and should be scheduled for completion of the recommended age-specific immunization schedule. Data are insufficient regarding the risk of secondary transmission to recommend chemoprophylaxis for attendees and childcare providers when a single case of invasive Hib disease occurs. The decision to provide chemoprophylaxis in this situation is at the discretion of the ERD medical epidemiologists.

The Advisory Committee on Immunization Practices recommends that because children who attend childcare are at increased risk for Hib disease, efforts should be made to ensure that all childcare attendees younger than 5 years old are fully vaccinated. Children < 24 months of age who develop invasive Hib disease should repeat the Hib vaccine series because they can remain at risk of a second episode of disease; children >24 months of age who develop invasive Hib disease usually develop a protective immune response and do not need immunization. The risk of Hib invasive disease for childcare center contacts of a patient with Hib invasive disease case is thought to be lower than that for a susceptible household contact. Public health officials should refer to the most recent edition of American Academy of Pediatrics (AAP) Red Book for information on chemoprophylaxis of childcare center contacts.

References

American Academy of Pediatrics. Kimberlin, DW ed. 2021-2024 Red Book: Report of the Committee on Infectious Diseases. 32nd ed. Elk Grove Village, IL: American Academy of Pediatrics; 2021.

Advisory Committee on Immunization Practices (ACIP). Epidemiology and Prevention of Vaccine-Preventable Diseases: *Haemophilus influenzae*. 14th ed. https://www.cdc.gov/vaccines/schedules/hcp/index.html. (Accessed 9 May 2023).

Centers for Disease Control and Prevention. *Haemophilus influenzae* Disease (including Hib). https://www.cdc.gov/hi-disease/index.html (Accessed 9 May 2023).

See *Haemophilus influenzae* Invasive Disease Fact Sheets (English) (Spanish)