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.

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. 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 child care 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. The most common manifestations of invasive disease are bacteremia, meningitis, pneumonia, epiglottitis, 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

Culture: *H. influenzae* can be cultured from blood, cerebrospinal fluid (CSF), synovial fluid, sputum, and pleural fluid. A gram stain of infected body fluid can demonstrate the organism and allow a presumptive diagnosis to be made. 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: Because the type b capsular antigen can be detected in body fluids, including urine, blood, and CSF of patients, clinicians often request a rapid antigen detection test for diagnosis of Hib disease. 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. The method for antigen detection is latex agglutination (LA). LA is a rapid and sensitive method used to detect Hib capsular polysaccharide antigen in CSF, serum, urine, pleural fluid, or joint fluid but false negative and false positive reactions can occur.

If the Hib antigen is detected in CSF but a positive result is not obtained from culture of sterile site, the patient should be considered as having a probable case of Hib disease 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. Real-time PCR detects DNA of all *H. influenzae* 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. Even when the organisms are nonviable following antimicrobial treatment, PCR can still detect *H. influenzae* DNA. Isolation of the bacterium is needed to confirm *H. influenzae* invasive disease, determine the serotype, and test for antimicrobial susceptibility.

Treatment

Patients with invasive *H. influenzae* must receive antimicrobial therapy. The choice of specific therapy should take into account 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 – A clinically compatible case associated with isolation of *H. influenzae* by culture from a normally sterile site.

Probable – A clinically compatible case with detection of *H. influenzae* antigen in 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. Therefore, there is no need for prophylaxis of an index case that has been adequately treated with those medications. However, an index case who has been treated with meropenem, ampicillin or chloramphenicol, and who is younger than 2 years old or who have a susceptible household contact, should receive rifampin prophylaxis 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.

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[1] (except pregnant women) in the following circumstances:

a. Household with at least one contact younger than 4 years of age who is unimmunized or incompletely immunized[2]

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

c. Household with a contact who is an immunocompromised child, regardless of that child's Hib immunization status

2. For preschool and child care 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 child care 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] 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.

[2] 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, child care, 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/child-adolescent.html.

Management of Invasive *H. influenzae*, type b (Hib) Disease in Child Care 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 child care 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 child care 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 child care are at increased risk for Hib disease, efforts should be made to ensure that all child care 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 child care 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 child care center contacts.

References

American Academy of Pediatrics. Kimberlin, DW ed. 2018-2021 Red Book: Report of the Committee on Infectious Diseases.31st ed. Elk Grove Village, IL: American Academy of Pediatrics; 2018.

Heymann, DL, ed. Control of Communicable Diseases Manual. 20th edition. Washington, DC: American Public Health Association; 2014.

Surveillance Manual's Chapter on Haemophilus influenzae type b. Manual from the Surveillance of Vaccine-Preventable Diseases textbook. From: Published 18 May 2018 http://www.cdc.gov/vaccines/pubs/surv-manual/chpt02-hib.html Accessed 14 December 2018.

Advisory Committee on Immunization Practices (ACIP) - https://www.cdc.gov/vaccines/schedules/hcp/index.html. (accessed December 14, 2018).

Centers for Disease Control and Prevention. *Haemophilus influenzae* Disease (including Hib) Published 13 February 2018. https://www.cdc.gov/hi-disease/index.html Accessed 14 December 2018.

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