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Haemophilus Influenzae, Invasive Disease Surveillance and Investigation Protocol

Table of Contents

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I. ABOUT THE DISEASE

Haemophilus influenzae is a bacterium that can cause severe infections, particularly among infants. The bacterium strains are either encapsulated (type a, b, c, d, e, or f) or unencapsulated (nontypeable). Both encapsulated and unencapsulated strains can cause invasive disease; however, nontypeable strains more commonly cause less severe mucosal infections such as otitis media, conjunctivitis, and sinusitis. A vaccine is available to prevent *H. influenzae* type b (Hib) disease. However, the Hib vaccine does not prevent disease caused by the other types of *H. influenzae*.

Following the introduction of an effective Hib vaccine, the incidence of invasive Hib disease decreased by 99 percent in children younger than five years of age. In recent years, *H. influenzae* type a (Hia) has emerged as the most common encapsulated serotype responsible for invasive disease. A notable increase of Hia has occurred in some North American Indigenous populations, as well as in the general population of children in the United States. Invasive Hia has a clinical presentation similar to Hib.

A. Clinical Presentation

The most common types of invasive disease caused by *H. influenzae* are:

1) Pneumonia* (lung infection)
2) Bloodstream infection
3) Meningitis (swelling of the lining of the brain and spinal cord)
4) Epiglottitis (swelling in the throat)
5) Cellulitis (skin infection)
6) Infectious arthritis (inflammation of the joint)

*Doctors consider pneumonia an invasive infection when *H. influenzae* also infects the blood or fluid surrounding the lungs.

Symptoms of *H. influenzae* depends on the site of infection. Symptoms may include:

1) Fever
2) Chills
3) Nausea with or without vomiting
4) Stiff neck
5) Cough
6) Warm, red, swollen joints
7) Shortness of breath or difficulty breathing

B. Etiologic Agent

Haemophilus influenzae is a pleomorphic gram-negative coccobacillus. Encapsulated strains express one of six antigenically distinct capsular polysaccharides (a through f serotypes). Nonencapsulated strains lack capsule genes and are designated nontypable.

C. Reservoir
Humans, including asymptomatic carriers, are the only known reservoir. The natural habitat of the organism is the upper respiratory tract of humans.

D. Incubation Period
The incubation period is unknown but is thought to be two to four days.

E. Mode of Transmission
Haemophilus influenzae colonizes the upper respiratory tract and is transmitted person-to-person by inhalation of respiratory droplets or by direct contact with respiratory tract secretions. In neonates, infection is acquired intrapartum by aspiration of amniotic fluid or by contact with genital tract secretions containing the organism. Asymptomatic colonization by *H. influenza* is common, especially with nontypable and non-type b capsular type strains. The most common portal of entry is the nasopharynx.

F. Period of Communicability
A person infected with *H. influenzae* (including Hib) is contagious as long as there are bacteria present in the nose or throat. Communicability stops within 24 to 48 hours of starting effective antimicrobial therapy. The contagious potential of invasive Hib disease is considered to be limited. However, certain circumstances, particularly close contact with a case-patient (e.g., household, childcare, or institutional setting) can lead to outbreaks or direct, secondary transmission of the disease.

II. DISEASE CONTROL AND PREVENTION

A. Disease Control Objectives
Reduce the risk of secondary cases by:
1) Isolating the index case until 24 hours after initiation of effective antimicrobial therapy.
2) Providing prophylaxis when indicated to close contacts.

B. Disease Prevention Objectives
Prevent cases of Hib disease by encouraging full immunization of infants per the Advisory Committee on Immunization Practices (ACIP) approved schedule.

C. Disease Prevention and Control Intervention
Prevention
Transmission of *H. influenza* can be prevented by:
1) Immunization of all infants (protects against Hib)
2) Respiratory hygiene/cough etiquette

3) Hand hygiene

Control measures and chemoprophylaxis (for invasive Hib disease)

Haemophilus influenzae can spread to people who have close or lengthy contact with a person with *H. influenzae* disease. There are no guidelines for control measures around cases of invasive nontypeable or non-b *H. influenzae* disease. Rapid identification of invasive Hib cases is important to allow for early administration of chemoprophylaxis and Hib vaccine (if recommended) to household and childcare classroom contacts of case-patients. Chemoprophylaxis is not recommended for contacts of persons with invasive disease caused by nontypeable or non-b *H. influenzae* because cases of secondary transmission of disease have not been documented. However, clinicians may consider prophylaxis of contacts of index cases of invasive *H. influenzae* type a (Hia) disease.

The risk of invasive Hib disease is increased among unimmunized household contacts younger than four years. Rifampin eradicates Hib from the pharynx in approximately 95 percent of carriers and decreases risk of secondary invasive illness in exposed household contacts. A contact is defined as someone residing with the index case or nonresident who spends four or more hours with the index case for at least five of the seven days preceding the day of hospital admission of the index case. Child care center contacts also may be at increased risk of secondary disease, but secondary disease in childcare contacts is rare when all contacts are older than two years. See Table 1 below for Rifampin chemoprophylaxis dosage information.

Do not withhold chemoprophylaxis pending determination of serotype if that will result in significant delays. When indicated, chemoprophylaxis should be initiated as soon as possible. Most secondary cases in households occur during the first week after hospitalization of the index case. Chemoprophylaxis initiated seven or more days after hospitalization of the index patient may still be of some benefit. Indications and guidelines for chemoprophylaxis are as follows:

Chemoprophylaxis for Hib disease is recommended for the following:

1) All household contacts if there is at least one child younger than four years who is unimmunized or incompletely immunized.
2) All household contacts if there is a child in the household younger than 12 months of age who has not received the primary series of Hib conjugate vaccine.
3) All household contacts if there is an immunocompromised child in the household, regardless of the child's Hib immunization status or age.
4) For preschool and childcare center contacts when two or more cases of Hib invasive disease have occurred within 60 days.
5) For index patients, if younger than two years or a member of a household with a susceptible contact and treated with a regimen other than cefotaxime or ceftriaxone, chemoprophylaxis at the end of therapy for invasive infection.

6) Exposed children in whom febrile illness develops should receive prompt medical evaluation.

Chemoprophylaxis for Hib disease is *not* recommended for the following:

1) Occupants of households with no children younger than four years of age other than the index patient.
2) Occupants of households when all household contacts are immunocompetent, all household contacts 12 to 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) Preschool or childcare contacts of one index case.
4) Pregnant women.
5) Contacts of people with non-type b *H. influenza* strains of invasive disease.

Child Care Center or Preschool Contacts:

1) In addition to 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 (see Table 2).
2) When two or more cases of Hib invasive disease have occurred within 60 days, prophylaxis for all attendees and childcare providers should be considered regardless of their age and vaccine status.
3) When unimmunized or incompletely immunized children attend the childcare facility or preschool prophylaxis for all attendees and childcare providers should be considered regardless of their age and vaccine status.
4) If the index case is younger than two years of age or has a household member who is susceptible to contact and the index case was treated with an antibiotic regimen other than cefotaxime or ceftriaxone, the index case should receive rifampin prophylaxis at the end of therapy for invasive infection.

Invasive *H. influenza* type a (Hia)

1) Clinicians can consider chemoprophylaxis of household contacts of cases with invasive Hia disease in households with a child younger than four years or an immunocompromised child. For these individuals and contacts, chemoprophylaxis recommendations for Hib may be followed; however, because there is not a licensed vaccine for Hia, the criteria for vaccination do not apply.
2) A similar approach as Hib may also be considered for preschool and childcare contacts in consultation with local or state public health.

Table 1. Recommended Chemoprophylaxis Dosage for Contacts of an invasive *Haemophilus influenza* Type b (Hib) case (Source: American Academy of Pediatrics Red Book, 32nd Edition, 2021-2024)

Rifampin			
Age	Dose	Duration	Cautions
< 1 month of age	10 mg/kg orally once per day	4 days	
≥ 1 month of age	20 mg/kg orally once per day	4 days	Maximum dose, 600mg
Adults	600 mg orally once per day	4 days	Can interfere with effectiveness of: -oral contraceptives -some seizures prevention medications -anticoagulant medications May stain soft contact lenses

Table 2. Recommended Regimens for Routine *Haemophilus influenzae* Type b (Hib) Conjugate Immunization for Children immunized at 2 Months through 4 Years of Age (Source: American Academy of Pediatrics Red Book, 32nd Edition, 2021-2024)

Vaccine	Primary Series	Booster Dose	Catch Up Dose
PRP-T	2, 4, and 6 months of age	12 through 15 months of age	16 months through 4 years of age
PRP-OMP	2 and 4 months of age	12 through 15 months of age	16 months through 4 years of age
DTaP-IPV-Hib	2, 4, and 6 months of age	12 through 15 months of age	16 months through 4 years of age
DTaP-IPV-Hib-HepB	2, 4, and 6 months of age	Use other Hib containing vaccine for booster, at least 6 months after last priming dose	

D. Treatment

People diagnosed with H. influenzae disease take antibiotics to treat the infection. Depending on how serious the infection is, people with *H. influenzae* disease may need care in a hospital. Other treatments may include:

1) Breathing support
2) Medication to treat low blood pressure
3) Wound care for parts of the body with damaged skin

For complete treatment guidelines for invasive Hib disease, see the *H. influenzae* chapter of the Red Book (American Academy of Pediatrics, 2021 Report of the Committee on Infectious Diseases, Red Book®, 32nd Edition). A summary of treatment recommendations include:

1) Initial therapy for children with *H. influenzae* meningitis is cefotaxime or ceftriaxone. Intravenous ampicillin may be substituted if the isolate is found to be susceptible. Treatment of other invasive *H. influenzae* infections is similar. Therapy is continued for six days by the intravenous route and longer in complicated infections.
2) Dexamethasone is beneficial for treatment of infants and children with Hib meningitis to diminish the risk of hearing loss, if administered before or concurrently with the first dose of antimicrobial agent(s).
3) Epiglottis is a medical emergency. An airway must be established promptly via controlled intubation.
4) Infected pleural or pericardial fluid should be drained.
5) For acute suppurative otitis media (AOM), amoxicillin is recommended for infants younger than six months, for those six through 23 months of age with bilateral disease, and for those older than six months with severe signs and symptoms. A watch-and-wait option can be considered for older children and those with nonsevere disease.

III. DISEASE INVESTIGATION

A. Criteria for Case Ascertainment

Clinical Criteria

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

Laboratory Criteria for Diagnosis

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

3) Isolation of *Haemophilus influenzae* from a normally sterile body site (e.g., cerebrospinal fluid [CSF], blood, joint fluid, pleural fluid, pericardial fluid)

B. Case Definition and Case Classification

Case Classifications

Probable

1) 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., cerebrospinal fluid [CSF], blood, joint fluid, pleural fluid, pericardial fluid) **OR**
2) 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

Case Classification Comments

Positive antigen test results from urine or serum samples are unreliable for diagnosis of *Haemophilus influenzae* disease and should not be used as a basis for case classification.

Isolates of *Haemophilus influenzae* are important for antimicrobial susceptibility testing.

C. Reporting Timeframe to Public Health

Cases of *Haemophilus Influenzae* should be reported to the local health department within 24 hours.

D. Outbreak Recognition

Increased rates of *H. influenzae* that may or may not be linked epidemiologically are considered an outbreak. Outbreaks of *H. influenzae* occur in propagated form. Propagated outbreaks are those that involve person-to-person transmission and result in two or more generations of cases. *Haemophilus influenzae* outbreaks of this nature are generally recognized after larger than expected numbers of cases of *H. influenza*e are reported within a limited time period. Since the incubation period of *H. influenzae* is thought to be short, probably two to four days, and the infectious period can last until the patient is started on an effective antibiotic, the onset dates for cases with a common source are usually spread over several days to a week.

E. Healthcare Provider Responsibilities

1) Report all suspected cases of invasive *H. influenzae* disease by telephone **within 24 hours** to the local health department serving the patient's county of residence and follow up with a written report found at oeps.wv.gov/hflu/Documents/lhd/H_flu.pdf. Please be prepared to provide the patient's name, address, telephone number, date of birth, sex, race, ethnicity, physician's name, office address, office phone and fax numbers, and any other information requested by the local health department.
2) Submit paper copies of laboratory reports to the local health department serving the patient's county of residence via fax.
3) Immediately submit *H. influe*nzae isolates from sterile sites to the West Virginia Department of Health and Human Resources, Bureau for Public Health's West Virginia Office of Laboratory Services (WV OLS) for serotyping. The isolate should be accompanied by the Microbiology Laboratory Specimen Submission form. WV OLS can be reached by calling 304-558-3530.
4) If applicable, notify the infection preventionist immediately and institute control measures for invasive *H. influe*nzae type b disease immediately upon recognition, as follows (American Academy of Pediatrics, 2021 Report of the Committee on Infectious Diseases, Red Book®, 32nd Edition):
    a) Patients with invasive Hib disease must be placed on droplet precautions until 24 hours after initiation of effective antimicrobial therapy.
    b) Provide chemoprophylaxis for high-risk contacts of invasive Hib disease – see section II. C. Disease Prevention and Control for recommendations.

F. Laboratory Responsibilities

1) Immediately notify the physician and infection preventionist of a positive test result for invasive Hib.
2) Forward *H. influe*nzae isolates cultured from normally sterile sites to WV OLS for serotyping. The isolate should be accompanied by the Microbiology Laboratory Specimen Submission form. WV OLS may be contacted as follows:
3) Phone: 304-558-3530
4) Web: dhhr.wv.gov/ols/Pages/default.aspx
5) Mailing address: 167 11th Ave., South Charleston, WV 25303
6) Notify by telephone and fax a copy of a positive test result of invasive *H. influe*nzae to the local health department serving the patient's county of residence **within 24 hours** of diagnosis for public health investigation. A laboratory designated to be a validated submitter to the West Virginia Electronic Disease Surveillance System (WVEDSS) may substitute electronic reporting for the required paper-based reporting. Reports shall include the patient's name. For reference labs, please fax and notify the Bureau for Public Health's Division of Infectious Disease Epidemiology at (phone) 304-558-5358 and (fax) 304-558-8736.

G. Local Health Responsibilities

1) Educate the public about invasive Hib disease, including its transmission.
2) Educate providers and laboratories to report confirmed and probable cases of invasive *H. influenzae* disease **within 24 hours** of diagnosis to the local health department.
3) Educate laboratories to submit *all* invasive *H. influenza* isolates cultured from normally sterile sites to WV OLS for serotyping.
4) Educate providers about chemoprophylaxis for high-risk contacts (close contacts) of invasive Hib.
5) Upon receiving a report of invasive *H. influenzae* disease:
   a) Assure case is on respiratory droplet precautions until 24 hours after initiation of effective antimicrobial therapy.
   b) Investigate and report the case to WVEDSS by using the WVEDSS invasive *H. Influenzae* form: oeps.wv.gov/hflu/Documents/lhd/H_flu.pdf
   c) Identify **close contacts** of index cases for whom chemoprophylaxis is recommended. See section II. C. Disease Prevention and Control for chemoprophylaxis recommendations.

H. State Health Responsibilities

1) Educate the public about invasive Hib disease, especially its transmission.
2) Educate providers and laboratories to report confirmed and probable cases of invasive *H. influenzae* disease **within 24 hours** of diagnosis to the local health department.
3) Educate laboratories to submit *all* invasive *H. influenza* isolates cultured from normally sterile sites to the WV OLS for serotyping.
4) Educate providers about chemoprophylaxis for high-risk contacts (close contacts) of invasive Hib.
5) Provide consultation and guidance to providers, laboratories, and local health departments.
6) Provide assistance to local health departments in implementing control measures as needed.
7) Refer to section II. C. Disease Prevention and Control for chemoprophylaxis recommendations.

IV. DISEASE SURVEILLANCE

A. Public Health Significance

Before the introduction of effective vaccines, *H. influenzae* serotype b (Hib) caused more than 95 percent of cases of invasive *H. influenzae* disease among children younger than five years of age. In the pre-vaccine era, the most common type of invasive *H. influenzae* disease was meningitis with the peak incidence of invasive Hib infections occurring between six and 18 months of age. In contrast, the peak age for epiglottis was two to four years of age.

Unimmunized children younger than four years of age are at increased risk of invasive Hib disease, especially if they are in prolonged close contact (such as in a household setting) with a child with invasive Hib disease. Other factors that predispose individuals to invasive disease include sickle cell disease, asplenia, human immunodeficiency virus (HIV) infection, certain immunodeficiency syndromes, and malignant neoplasms. Historically, invasive Hib was more common in boys; black, Alaska Native, Apache, and Navajo children; childcare attendees; children living in crowded conditions; and children who were not breastfed.

Since the introduction of Hib conjugate vaccines in the United States, the incidence of invasive Hib disease has decreased by 99 percent to fewer than one case per 100,000 children younger than five years of age. In the United States, invasive Hib disease occurs primarily in under immunized children and among infants too young to have completed the primary immunization series. In the post-Hib vaccine era, nontypeable *H. influenzae* now causes the majority of invasive *H. influenzae* disease in all age groups.

B. Disease Surveillance Objectives

1) To determine demographic characteristics and risk factors of infected persons with *H. influenzae* invasive disease in West Virginia.
2) To identify the types of infections associated with invasive *H. influenzae* isolates.
3) To distinguish failure of the *H. influenzae* type b (Hib) vaccine from failure to vaccinate as the more significant risk factor for disease.

C. Surveillance Indicators

1) Proportion of *H. influenzae* cases reported to West Virginia Electronic Disease Surveillance System with complete information (clinical, demographic, clinical case definition-species, specimen type, vaccine history, and serotype testing).
2) Proportion of Hib cases among children younger than five years of age with complete vaccination history.
3) Proportion of Hib cases among children younger than five years of age with serotyped isolate.
4) Proportion of cases reported to public health within the required timeframe.

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V. REFERENCES

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