Invasive *Haemophilus influenzae*, including type b

Disease Plan

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Last updated: December 3, 2018, by Bree Barbeau

Questions about this disease plan?

Contact the Utah Department of Health Bureau of Epidemiology at 801-538-6191.
# CRITICAL CLINICIAN INFORMATION

## Clinical Evidence

<table>
<thead>
<tr>
<th>Signs/Symptoms</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumonia</td>
<td>Fever, chills, shortness of breath, sweating, chest pain, headache, muscle pain, excessive tiredness</td>
</tr>
<tr>
<td>Bacteremia</td>
<td>Fever, chills, pain in the belly, nausea, diarrhea, anxiety, shortness of breath, confusion</td>
</tr>
<tr>
<td>Meningitis</td>
<td>Fever, headache, stiff neck, nausea, increased sensitivity to light, confusion</td>
</tr>
</tbody>
</table>

## Period of Communicability

- Communicable until 24 hours after initiation of appropriate antibiotic therapy

## Incubation Period

- Unknown, but may be as short as 2–4 days

## Mode of Transmission

- Person-to-person either by droplet or direct contact with nasopharyngeal secretion

## Laboratory Testing

<table>
<thead>
<tr>
<th>Type of Lab Test</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Culture</td>
<td>Serotyping by slide agglutination</td>
</tr>
<tr>
<td></td>
<td>Polymerase Chain Reaction Testing (especially useful for capsular typing)</td>
</tr>
<tr>
<td></td>
<td>Nucleic acid amplification tests</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Type of Specimens</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood</td>
<td>Cerebrospinal fluid</td>
</tr>
<tr>
<td></td>
<td>Other sterile body fluids</td>
</tr>
</tbody>
</table>

## Treatment Recommendations

### Type of Treatment

- **Haemophilus influenzae**
  - Ampicillin OR chloramphenicol PLUS rifampin prophylaxis
  - Cephalosporins PLUS Quinolones
  - Cefotaxime and Ceftriaxone – known to eradicate Hib from nasopharynx

- Pneumonia caused by *H. influenzae*
  - Ceftriaxone OR cefotaxime OR ceftaroline OR ertapenem OR ampicillin-sulbactam PLUS macrolide OR clarithromycin OR clarithromycin XL OR doxycycline

- Meningitis caused by *H. influenzae*
  - Children – ceftriaxone or cefotaxime intravenously for 7-10 days; ampicillin can be substituted if the organism is sensitive to this antibiotic.
  - Adults – cefotaxime or ceftriaxone intravenously for 7 days

### Time Period to Treat

- Infected individuals should be treated immediately; highly contagious until 24 hours post antibiotic treatment.

### Prophylaxis (Type B Only)

- Prophylactic vaccines – variety of vaccines most are administered before 18 months
- Prophylaxis (rifampin) should be initiated within two weeks of the onset of disease of the index case (see below for who should receive prophylaxis).
### Contact Management

<table>
<thead>
<tr>
<th>Isolation of Case</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Cases of <em>H. influenzae</em> type B should be isolated until 24 hours after antibiotic treatment starts.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Quarantine of Contacts (Type B Only)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Observe for signs of illness (<em>H. influenzae</em>); treat with appropriate antimicrobial when indicated.</td>
</tr>
</tbody>
</table>

### Infection Control Procedures

| • Standard Precautions |
WHY IS *HAEMOPHILUS INFLUENZAE* IMPORTANT TO PUBLIC HEALTH?

*Haemophilus influenzae (H. influenzae)* is a cause of bacterial infection that is often severe, particularly among infants. Since the introduction of Hib polysaccharide and conjugate vaccines in 1985 and 1990, the incidence of invasive Hib disease in children less than five years of age has decreased by 99%, to less than 1 case per 100,000 children younger than five years of age. Continued monitoring of invasive *H. influenzae* disease through Active Bacterial Core surveillance (ABCs), which includes serotype information on all invasive *H. influenzae* isolates, has demonstrated low rates of invasive Hib in children younger than five years of age; between 2010 and 2014, the average incidence was 0.15 cases per 100,000, which is below the Healthy People 2020 goal of 0.27/100,000.

In the post–Hib vaccine era, the epidemiology of invasive *H. influenzae* disease in the United States has changed. The majority of invasive *H. influenzae* disease in all age groups is now caused by non-typeable *H. influenzae*.

**Figure 1. Incidence of Hib disease in relation to licensing of Hib vaccines**
DISEASE AND EPIDEMIOLOGY

Clinical Description

Invasive disease due to *H. influenzae* may produce various clinical syndromes including meningitis, bacteremia or sepsis, epiglottitis, pneumonia, septic arthritis, empyema, cellulitis, or, pericarditis; less common infections include endocarditis and osteomyelitis. Mucosal infections, such as bronchitis, sinusitis and conjunctivitis, and otitis media, can also be caused by *H. influenzae*, but they are considered to be noninvasive disease.

Causative Agent

*H. influenzae* is a small gram-negative coccobacillus that may be either encapsulated (types a–f) or unencapsulated (non-typeable). Non-typeable strains are thought to be less virulent than encapsulated strains. *H. influenzae* type b (Hib) is the serotype that requires control measures.

Beta-lactamase-negative, ampicillin-resistant (BLNAR) *H. influenzae* is an emerging pathogen. The prevalence of BLNAR *H. influenzae* strains have increased in some countries (Japan and Spain), although their prevalence in the United States and elsewhere remains low (approximately 3%). Possible explanations for this observation include inadequate vaccination against *H. influenzae* type b in some regions, increasingly frequent use of cephalosporins, and under-dosing of oral ampicillin. There are no significant differences in clinical presentation of pneumonia due to BLNAR *H. influenzae* compared to pneumonia due to ampicillin-susceptible *H. influenzae* strains. These pathogens appear to have in vitro susceptibility to ceftriaxone. Depending on local susceptibility findings, ceftriaxone may be an appropriate choice for treatment of clinical infections due to BLNAR *H. influenzae* pending further study of clinical infections with this pathogen.

Differential Diagnosis

Invasive *H. influenzae* can cause pneumonia, bacteremia, or meningitis. The presentation of these diseases is similar to other invasive bacterial diseases such as *Streptococcal pneumoniae* or *Streptococcal pyogenes*. As with other causes of bacterial meningitis, characteristic symptoms of *H. influenzae* meningitis are fever, decreased mental status, and stiff neck.

Laboratory Identification

Microscopy of gram stained infected body fluid may identify gram-negative coccobacilli. *H. influenzae* identified via culture of infected body fluid, such as CSF, blood, pleural fluid amniotic fluid, or joint fluid, All *H. influenzae* isolates from normally sterile sites (e.g., blood, CSF, pleural fluid, peritoneal fluid, pericardial fluid, bone, joint fluid) are required to be sent to the Utah Public Health Laboratory (UPHL) for serotyping. Laboratories occasionally use antigen detection methods, but these are not considered confirmatory in the absence of culture positivity. Primary Children’s Medical Center (PCMC) can test for type b. However, the test done by PCMC is a send-out performed by ARUP that is an IgG antibody test. The isolate is still required to be sent to UPHL for serotyping.
UPHL: The UPHL serotypes all isolates of *H. influenzae* from clinical laboratories.

Treatment

Typical treatment regimens for Hib include cephalosporins and quinolones. Once identified, the patient should be isolated until 24 hours after initiating appropriate antimicrobial treatment that eliminates carriage. Currently, only cefotaxime and ceftriaxone are known to eradicate Hib from the nasopharynx when they are used to treat active infection. Therefore, if the patient is treated with ampicillin or chloramphenicol instead, he/she must receive rifampin prophylaxis. The treatment course is usually 10 days. Also, note that Hib disease does not necessarily confer immunity to subsequent disease. For additional guidelines on treatment and chemoprophylaxis for invasive Hib disease, see the Red Book.

Immunize as follows:

a. Children with invasive Hib disease at <24 months of age: Immunize according to the age-appropriate schedule for unvaccinated children and as if they had received no prior doses, as disease in this age group does not reliably result in a protective immune response. Begin one month after onset of disease or as soon as possible thereafter.

b. Children with invasive Hib disease at ≥24 months of age: No Hib immunization is necessary, regardless of previous immunization status, because the disease probably induces a protective immune response and second episodes in children this age are rare. However, Hib vaccination is not contraindicated and can be given as a single antigen or as part of a combination vaccine.

Morbidity/Mortality

Invasive infections due to *H. influenzae* are serious and can be rapidly fatal. Hearing impairment or other neurologic sequelae occur in 15–30% of Hib meningitis survivors, and the case-fatality rate is 3–6%, despite appropriate antimicrobial therapy.

Reservoir

Humans (asymptomatic and symptomatic carriers) are the only known host as the bacterium does not survive in the environment on inanimate surfaces.

Transmission

*H. influenzae* infection is transmitted from person-to-person by droplet or direct contact with nasopharyngeal secretions of an infected person. The most common portal of entry is the nasopharynx. Newborns can become infected by inhaling amniotic fluid or genital tract secretions containing the organism.

Susceptibility

The vaccine only confers immunity to one strain: type b. Disease before the age of two years does not confer immunity; vaccine is still required. The genetic constitution of the host may be important
in susceptibility to infection with Hib. Risk for Hib disease has been associated with a number of genetic markers, but the mechanism of these associations is unknown. No single genetic relationship regulating susceptibility or immune responses to polysaccharide antigens has yet been convincingly demonstrated.

**Incubation Period**

The incubation period is unknown, but for invasive disease, may be as short as 2–4 days.

**Period of Communicability**

If the person is not on antibiotic therapy, disease is communicable as long as organisms are present in the upper respiratory tract, which may be for a prolonged period, even without nasal discharge. *H. influenzae* is communicable until 24 hours after initiation of appropriate antibiotic therapy.

The contagious potential of invasive *H. influenzae* disease is considered to be limited. However, certain circumstances, particularly close contact with a case (e.g., in a household, childcare center, or institutional setting), can lead to outbreaks of Hib or direct secondary transmission of the disease. Asymptomatic carriage is known to occur.

**Epidemiology**

*H. influenzae* type b (Hib) is the only type for which there is a vaccine and for which control measures are considered necessary.

Before the widespread use of Hib conjugate vaccines, Hib was a leading cause of bacterial meningitis in the United States among children younger than five years of age and a major cause of other life-threatening invasive bacterial disease in this age group. The introduction of Hib vaccine in 1988 resulted in a 99% decrease in invasive Hib disease in children younger than five years of age. During 2010-2011, 33% of children younger than five years of age with confirmed invasive Hib disease were younger than six months of age and too young to have completed a three-dose primary vaccination series. Of these age-eligible children, 64% were either unvaccinated, incompletely vaccinated (received fewer than three doses), or their vaccination status was unknown.

Since the introduction of Hib vaccine, the incidence of all infection due to the encapsulated and non-typeable strains of *H. influenza* combined has decreased. However, *H. influenzae* type f has become the most common serotype causing invasive infections in the United States. With the reduction of invasive disease due to Hib, the remaining disease is now distributed among age groups. In Utah, invasive disease due to non-typeable strains predominates, and is seen in all age groups.

Unimmunized children, particularly those younger than four years of age, who are in prolonged close contact (such as in a household setting) with a child with invasive Hib disease, are at increased risk for invasive Hib disease. Other factors causing predisposition to invasive disease include sickle cell disease, asplenia, HIV infection, certain immunodeficiency syndromes, and malignant neoplasms. In adults, underlying conditions such as chronic pulmonary disease, smoking, HIV, alcoholism, pregnancy, and older age increase the risk of *H. influenzae* disease.
Risk factors for Hib disease include exposure factors and host factors that increase the likelihood of exposure to Hib, including being unvaccinated against Hib, household crowding, large household size, childcare attendance, low socioeconomic status, low parental education levels, and school-aged siblings. Historically, invasive Hib was more common in boys; African American, Alaska Native, Apache and Navajo children; childcare attendees; children living in crowded conditions; and children who were not breastfed.

**PUBLIC HEALTH CONTROL MEASURES**

**Public Health Responsibility**

- Investigate all suspect cases of disease; complete and submit appropriate disease investigation forms.
- **Ensure isolate submission to UPHL for serotyping.**
- Provide education to the general public, clinicians, and first responders regarding disease transmission and prevention.
- Identify clusters or outbreaks of this disease.
- Identify sources of exposure to minimize further transmission.
- Ensure surveillance is maintained to identify the emergence of other *H. influenzae* types as causes of invasive disease, and to monitor Hib vaccine effectiveness and assess progress toward disease elimination.

**Prevention**

Routine childhood vaccination is the best preventive measure against Hib disease. Good personal hygiene (proper hand washing, disposal of used tissues, not sharing eating utensils, etc.) is also important.

**Chemoprophylaxis**

The following are chemoprophylaxis recommendations. They may be used at the discretion of the local health jurisdiction as deemed necessary. Chemoprophylaxis is ONLY indicated for contacts to *H. influenzae* type b (Hib) disease. Identification of young children who are household or childcare contacts of patients with Hib invasive disease and assessment of their vaccination status may help identify persons who should receive antimicrobial prophylaxis or who need to be immunized.
Figure 2. Indications and guidelines for Rifampin chemoprophylaxis for contacts of index cases of invasive *Haemophilus influenza* type b (Hib) disease

<table>
<thead>
<tr>
<th>Recommended Chemoprophylaxis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemoprophylaxis may be indicated for household (or close) contacts of a child with invasive Hib disease, childcare or preschool contacts, and the index patient, depending upon individual circumstances as described below.</td>
</tr>
</tbody>
</table>

**Chemoprophylaxis for index patient**

If the index patient was treated with an agent other than cefotaxime or ceftriaxone, antimicrobial therapy to eradicate nasopharyngeal carriage is recommended if either of the following is also true for the index patient:

- If the index patient is younger than two years of age, or
- The index patient lives in a household with a child younger than four years of age who has not received an age-appropriate number of doses of Hib conjugate vaccine or an immunocompromised child.

**Chemoprophylaxis for household contacts**

Chemoprophylaxis is recommended for all household contacts (including the index case) in the following circumstances:

- Household with at least one contact younger than four years who has not received an age-appropriate number of doses of Hib conjugate vaccine.\(^2\)
- The susceptible child(ren) should receive a dose of Hib conjugate vaccine and be scheduled for completion of Hib immunization if additional doses are necessary to complete immunization.
- Household with a contact who is an immunocompromised child, regardless of that child’s Hib immunization status.

In addition to receiving antimicrobial prophylaxis, exposed unimmunized or incompletely immunized children who are household contacts of patients with invasive Hib disease must be carefully observed for signs of illness. Exposed children in whom febrile illness develops should receive prompt medical attention.

**Chemoprophylaxis for childcare or preschool contacts**

Chemoprophylaxis is recommended for childcare or preschool contacts when unimmunized or incompletely immunized children attend the facility and two or more cases of Hib invasive disease have occurred among attendees within 60 days.\(^3,4\)
Exposed unimmunized or incompletely immunized children who are child care or preschool contacts of patients with invasive Hib disease must be carefully observed for signs of illness. Exposed children in whom febrile illness develops should receive prompt medical attention.

Recommended regimen

Prophylaxis should be initiated as soon as possible in contacts. In the index case, it should be initiated within two weeks of the onset of disease, and may be initiated in conjunction with treatment.

- **Rifampin** is the drug of choice for chemoprophylaxis. The regimen is as follows – Rifampin 20mg/kg (maximum dose 600 mg) once per day for four days.
- The dose of rifampin for infants younger than one month of age has not been established. Some experts recommend lowering the dose to 10mg/kg.
- Consultation with an expert in infectious disease is recommended for contacts in whom rifampin is contraindicated.

Chemoprophylaxis not recommended

- Chemoprophylaxis is not indicated for contacts of people with invasive disease caused by non-type b strains of *H. influenzae*.
- Occupants of households with no children younger than four years of age other than the index patient.
- Occupants of households when all household contacts 12 to 48 months of age have completed their Hib immunization series⁵ and when all household contacts younger than 12 months of age have completed their primary series of Hib immunizations.
- For nursery school and child care contacts of one index case, especially people older than two years of age.
- For pregnant women.

¹Close (household) contact is defined as a person who resides with the index patient or who spent ≥4 hours with the index patient for at least five of the seven days before the day of hospital admission of the index case.
²The primary series of Hib conjugate vaccine consists of 2–3 doses, depending on the Hib vaccine formulation. See the Table 2 for more details.
³Only children who are age-appropriately immunized and on Rifampin should be permitted to enter the childcare group during the time prophylaxis is given. Children enrolling in a childcare center or other setting during the time prophylaxis is given should also receive rifampin, as should supervisory personnel.
⁴When a single case has occurred, the advisability of rifampin prophylaxis in exposed childcare groups with unimmunized or incompletely immunized children is controversial, but many experts recommend no prophylaxis.
Complete immunization is defined as having had ≥1 dose of conjugate vaccine at ≥15 months of age; 2 doses between 12 and 14 months of age; or a 2- or 3-dose primary series (number of doses required depends on vaccine type and age at initiation) when <12 months with a booster dose at ≥12 months of age.

**Vaccine**

Table 1 lists the Hib conjugate vaccines that are currently available in the United States. The combination vaccines that include the Hib conjugate vaccine have been licensed by the FDA following immunogenicity and safety studies. These combination vaccines decrease the number of injections needed for protection against vaccine-preventable diseases. HbOC (HibTiter) is no longer available in the United States.

**TABLE 1. Haemophilus influenzae type b (Hib) conjugate vaccines licensed and available in the United States**

<table>
<thead>
<tr>
<th>Vaccine product</th>
<th>Manufacturer</th>
<th>Trade Name</th>
<th>Components</th>
<th>Primary series</th>
<th>Booster dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Monovalent vaccine</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PRP-OMP*†</td>
<td>Merck &amp; Co, Inc</td>
<td>PedvaxHIB</td>
<td>PRP conjugated to OMP</td>
<td>2, 4 months</td>
<td>12–15 months</td>
</tr>
<tr>
<td>PRP-T</td>
<td>sanofi pasteur</td>
<td>ActHIB</td>
<td>PRP conjugated to tetanus toxoid</td>
<td>2, 4, 6 months</td>
<td>12–15 months</td>
</tr>
<tr>
<td>PRP-T</td>
<td>GlaxoSmithKline</td>
<td>Hiberix</td>
<td>PRP conjugated to tetanus toxoid</td>
<td>Not licensed for primary series</td>
<td>12–15 months§</td>
</tr>
<tr>
<td><strong>Combination vaccine</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PRP-OMP-HepB*†</td>
<td>Merck &amp; Co, Inc</td>
<td>Comvax</td>
<td>PRP-OMP + hepatitis B vaccine</td>
<td>2, 4 months</td>
<td>12–15 months</td>
</tr>
<tr>
<td>DTaP-IPV/PRP-T</td>
<td>sanofi pasteur</td>
<td>Pentacel</td>
<td>DTaP-IPV + PRP-T</td>
<td>2, 4, 6 months</td>
<td>15–18 months¶</td>
</tr>
<tr>
<td>MenCY/PRP-T**</td>
<td>GlaxoSmithKline</td>
<td>MenHibRix</td>
<td>MenCY + PRP-T</td>
<td>2, 4, 6 months</td>
<td>12–15 months</td>
</tr>
</tbody>
</table>

*If a PRP-OMP vaccine is not administered as both doses in the primary series, or if there is uncertainty about which products were administered previously, a third dose of Hib conjugate vaccine is needed to complete the primary series.
†Preferred vaccine for American Indian/Alaska Native children.
‡To facilitate timely booster vaccination, Hiberix can be administered as early as age 12 months, in accordance with Hib vaccination schedules for routine and catch-up immunization (CDC. Licensure of a Haemophilus influenzae type b [Hib] vaccine [Hiberix] and updated recommendations for use of Hib vaccine. MMWR 2009;58:1008–9).
¶The booster dose may be administered as early as age 12 months, provided that at least 6 months have elapsed since the third dose.
**Recommendations for the MenCY component of MenCY/PRP-T have been published previously (CDC. Infant meningococcal vaccination: Advisory Committee on Immunization Practices (ACIP) recommendations and rationale.
Hib Conjugate Vaccine Schedules (Table 2 below)
In the United States, the primary series of Hib conjugate vaccine, which is administered before seven months of age, requires two or three doses, depending upon the vaccine preparation. The minimum age for the first dose is six weeks. Hib conjugate vaccines can be administered at the same visit as other routine immunizations.

It is ideal to use the same Hib conjugate vaccine to complete the primary series. However, if it is unknown which vaccine was previously administered, or if the same vaccine is not available, the vaccines can be interchanged. If two different preparations are used, a three-dose primary series is required.

In the United States, a booster dose is required at 12–15 months of age (or as soon thereafter as possible); 12 months is the minimum age for the final dose. Any of the Hib conjugate vaccines may be used for the booster dose; the vaccine need not be the same as the one used for the primary series.

Table 2: *Haemophilus influenzae* type b vaccine detailed schedule for unvaccinated children

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Age at 1st Dose (months)</th>
<th>Primary series</th>
<th>Booster</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRP-T*</td>
<td>2-6</td>
<td>3 doses, 8 weeks apart</td>
<td>12–15 months</td>
</tr>
<tr>
<td></td>
<td>7-11</td>
<td>2 doses, 4 weeks apart</td>
<td>12–15 months</td>
</tr>
<tr>
<td></td>
<td>12-14</td>
<td>1 dose</td>
<td>2 months later</td>
</tr>
<tr>
<td></td>
<td>15-59†</td>
<td>1 dose</td>
<td>--</td>
</tr>
<tr>
<td>PRP-OMP</td>
<td>2-6</td>
<td>2 doses, 8 weeks apart</td>
<td>12–15 months</td>
</tr>
<tr>
<td></td>
<td>7-11</td>
<td>2 doses, 4 weeks apart</td>
<td>12–15 months</td>
</tr>
<tr>
<td></td>
<td>12-14</td>
<td>1 dose</td>
<td>2 months later</td>
</tr>
<tr>
<td></td>
<td>15-59</td>
<td>1 dose</td>
<td>--</td>
</tr>
</tbody>
</table>

*Hiberix brand PRP-T vaccine is approved only for the last dose of the Hib series among children 12 months of age and older.
†MenHibrix brand PRP-T vaccine is not recommended for children 19 months of age or older.

Hib Conjugate Vaccine Recommendations for Children Not Up-To-Date

“Catch-up Schedule” The catch up schedule for Hib conjugate vaccine depends upon the age at which the series is initiated and the number of doses previously received:

- Children younger than six months of age at initiation of vaccination should receive three doses of the Hib conjugate vaccine at four to eight week intervals, and a booster (single dose) eight weeks from the last dose for children 12–15 months of age.
- Children who are 7–11 months of age at initiation of vaccination should receive two doses of Hib conjugate vaccine at four to eight week intervals up to 12 months of age, and a booster (single dose) eight weeks from the last dose for children 12 months of age to five years.
• Children who have received ≤1 dose of Hib conjugate vaccine before one year of age and are now 12–14 months of age should receive two doses of Hib conjugate vaccine eight weeks apart, up to five years of age.
• Children with an incomplete series of Hib conjugate vaccination who are now 15–59 months old should receive a single dose of Hib conjugate vaccine.

Impaired Host Defense

Certain children may be at increased risk of invasive Hib disease because of immune deficiency, or other host defense abnormalities (e.g., sickle cell disease, functional or anatomic asplenia). These children should receive Hib conjugate vaccine as recommended for all infants. Any children younger than 59 months of age with these risk factors who have an incomplete vaccination history should be vaccinated according to the catch-up schedule. For unimmunized children at increased risk of Hib disease who are older than 59 months of age, the following is recommended:

• Unimmunized children older than 59 months who have sickle cell disease or asplenia should receive a single dose of Hib conjugate vaccine.
• Unimmunized children older than 59 months who have human immunodeficiency virus, IgG2 subclass deficiency, bone marrow transplant, or malignancy should receive two doses of Hib conjugate vaccine, separated by four to eight weeks.

Consult the chapter on *H. influenzae* in the *Red Book* of the American Academy of Pediatrics (AAP) for a full discussion of vaccines, immunization schedules, and special circumstances. For example, children, including those older than five years of age, with underlying conditions predisposing them to Hib disease may need additional doses.

Isolation and Quarantine Requirements

**Isolation:** *H. influenzae* is communicable until 24 hours after initiation of appropriate antibiotic therapy. Cases of invasive *H. influenzae* type B disease should be isolated until 24 hours after initiating appropriate antimicrobial treatment.

**Hospital:** Standard body substance precautions.

**Quarantine:** Personal surveillance and prophylaxis with an appropriate antimicrobial when indicated by clinical situation of the contact, or potential for future transmission. Otherwise, there are no restrictions.
CASE INVESTIGATION

Reporting

All cases of *H. influenzae* recovered from a normally sterile site (e.g., CSF, blood, joint fluid, pleural effusion, pericardial fluid, peritoneal fluid, subcutaneous tissue fluid, placenta, amniotic fluid) should be reported to public health.

Table 3. Criteria to determine whether a case should be reported (CSTE)

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Reporting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical evidence</td>
<td></td>
</tr>
<tr>
<td>Meningitis</td>
<td>N</td>
</tr>
<tr>
<td>Epiglottitis</td>
<td>S</td>
</tr>
<tr>
<td>Healthcare record indicates a diagnosis of disease caused by <em>H. influenzae</em></td>
<td>S</td>
</tr>
<tr>
<td>Death certificate indicates disease caused by <em>H. influenzae</em> as a cause of death or a significant condition contributing to death.</td>
<td>S</td>
</tr>
<tr>
<td>Laboratory evidence</td>
<td></td>
</tr>
<tr>
<td>Isolation of <em>H. influenzae</em> (any type) from a normally sterile site</td>
<td>S</td>
</tr>
<tr>
<td>Detection of <em>H. influenzae</em>-specific nucleic acid in a normally sterile body site using a validated polymerase chain reaction (PCR) assay</td>
<td>S</td>
</tr>
<tr>
<td>Detection of <em>H. influenzae</em> type b (Hib) antigen in CSF</td>
<td>N</td>
</tr>
</tbody>
</table>

Notes:
- S = This criterion alone is sufficient to identify a case for reporting.
- N = All "N" criteria in the same column are necessary to identify a case for reporting.

Case Definition

*Haemophilus influenzae* (2015)

The following case definition for invasive *H. influenzae* disease has been approved by the Council of State and Territorial Epidemiologists (CSTE) and was published in 2015.

Description of criteria to determine how a case should be classified

**Probable:**
- Meningitis WITH detection of *H. influenzae* type b antigen in cerebrospinal fluid (CSF).
Confirmed:

- Isolation 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, or amniotic fluid).

  **OR**

- Detection of *H. influenzae*-specific nucleic acid in a specimen obtained from a normally sterile body (e.g., cerebrospinal fluid [CSF], blood, joint fluid, pleural fluid, pericardial fluid, peritoneal fluid, subcutaneous tissue fluid, placenta, or amniotic fluid), using a validated polymerase chain reaction (PCR) assay.

Comment(s): Positive antigen test results from urine or serum samples are unreliable for diagnosis of *H. influenzae* disease and should not be used as a basis for case classification. Isolates of *H. influenzae* are important for antimicrobial susceptibility testing.

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

- Detection of *H. influenzae* type b antigen in cerebrospinal fluid (CSF)
- Detection of *H. 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, peritoneal fluid, subcutaneous tissue fluid, placenta, or amniotic fluid), using a validated polymerase chain reaction (PCR) assay; or
- Isolation 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, or amniotic fluid)

Epidemiologic Linkage

Not applicable for case classification.

Table 4. Criteria to determine whether a case is classified (CSTE)

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Case Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical evidence</strong></td>
<td></td>
</tr>
<tr>
<td>Meningitis</td>
<td>Probable Confirmed</td>
</tr>
<tr>
<td><strong>Laboratory evidence</strong></td>
<td></td>
</tr>
<tr>
<td>Isolation of <em>H. influenzae</em> (any type) from a normally sterile site</td>
<td>S</td>
</tr>
<tr>
<td>Detection of <em>H. influenzae</em>-specific nucleic acid in a normally sterile</td>
<td>S</td>
</tr>
<tr>
<td>body site using a validated polymerase chain reaction (PCR) assay</td>
<td></td>
</tr>
<tr>
<td>Detection of <em>H. influenzae</em> type b (Hib) antigen in CSF</td>
<td>N</td>
</tr>
</tbody>
</table>
Case Investigation Process

- Public health should immediately determine whether the reported case is due to serotype b. To do this, public health should:
  - Identify the laboratory where the initial testing occurred, and
  - Call them to ensure that the isolate is immediately sent to UPHL for serotyping, and
  - Call UPHL to notify them that an *H. influenzae* strain is coming and that serotyping needs to occur as soon as possible.

- Cases due to *H. influenzae* type b should be immediately investigated:
  - Identify all close contacts (view chemoprophylaxis section for details).
  - Assure that they are provided chemoprophylaxis and vaccine within SEVEN days of hospitalization of the index case.

Outbreaks

An outbreak is defined as:

- Two or more cases in a closed population in a 30-day period; or
- Two or more cases with direct epidemiological linkage.

Identifying Case Contacts

See [Chemoprophylaxis](#) for definition of case contacts.

Case Contact Management (Hib only)

- Assure that contacts receive chemoprophylaxis. See [Chemoprophylaxis](#) for specifics.
- Ensure appropriate immunization of contacts. The number of doses required is determined by the current age of the child and the number, timing, and type of Hib vaccine doses previously received.
  - Unvaccinated and incompletely vaccinated children younger than five years of age should be scheduled for completion of the recommended age-specific immunization schedule.
  - Infants should be placed on an accelerated schedule using minimum intervals between doses.
  - Unvaccinated high-risk individuals older than five years of age should receive one dose.
- Conduct surveillance. Careful observation of exposed contacts, especially children younger than four years of age, is essential. Those in whom a febrile illness develops should receive prompt medical attention, regardless of Hib vaccination status.
REFERENCES


ARUP Labs; Physician’s Guide to Laboratory Test Selection and Interpretation.

Centers for Disease Control, Case Definitions for Infectious Conditions Under Public Health Surveillance. MMWR 46 (RR-10), 1997.l.


Johns Hopkins Point of Care Information Technology.


✅ VERSION CONTROL


Updated March 7, 2017: Added Critical Clinician Information section. Updated cased definition and references section.

Update October 2017: Updated normally sterile-site definition to include peritoneal fluid, subcutaneous tissue fluid, placenta, and amniotic fluid as outlined in the CDC Manual for the Surveillance of Vaccine-Preventable Diseases; updated references.

Update September 2018: Added Rules for Entering Laboratory Test Results section.

Update December 2018: Updated Critical Clinician Information, Disease and Epidemiology, Public Health Control Measures, and Case Investigation sections to reflect changes from EAG.
✅ UT-NEDSS MINIMUM/REQUIRED FIELDS BY TAB

<table>
<thead>
<tr>
<th>Demographic</th>
<th>Laboratory</th>
</tr>
</thead>
<tbody>
<tr>
<td>First Name</td>
<td>• Organism</td>
</tr>
<tr>
<td>Birth Gender</td>
<td>• Specimen Source</td>
</tr>
<tr>
<td>Race</td>
<td>• Test Result</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>• Test Status</td>
</tr>
<tr>
<td>State</td>
<td>• Test Type</td>
</tr>
<tr>
<td>County</td>
<td>• Organism Serotype</td>
</tr>
<tr>
<td>Date of Birth</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Clinical</th>
<th>Epidemiological</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease</td>
<td>• Childcare Associated</td>
</tr>
<tr>
<td>Date Diagnosed</td>
<td></td>
</tr>
<tr>
<td>Imported From</td>
<td></td>
</tr>
<tr>
<td>Onset Date</td>
<td></td>
</tr>
<tr>
<td>Syndrome:</td>
<td></td>
</tr>
<tr>
<td>• Please specify:</td>
<td></td>
</tr>
<tr>
<td>Syndrome:</td>
<td></td>
</tr>
<tr>
<td>Died</td>
<td></td>
</tr>
<tr>
<td>Date of Death</td>
<td></td>
</tr>
<tr>
<td>List dose number, date, manufacturer and lot number of all doses given:</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Reporting</th>
<th>Administrative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date first reported to public health</td>
<td>• Outbreak name</td>
</tr>
<tr>
<td></td>
<td>• State case Status</td>
</tr>
<tr>
<td></td>
<td>• Outbreak Associated</td>
</tr>
</tbody>
</table>
RULES FOR ENTERING LABORATORY TEST RESULTS

The following rules describe how laboratory results reported to public health should be added to new or existing events in UT-NEDSS. These rules have been developed for the automated processing of electronic laboratory reports, although they apply to manual data entry, as well.

Test-Specific Rules
Test specific rules describe what test type and test result combinations are allowed to create new morbidity events in UT-NEDSS, and what test type and test result combinations are allowed to update existing events (morbidity or contact) in UT-NEDSS.

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Test Result</th>
<th>Create a New Event</th>
<th>Update an Existing Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCR/amplification</td>
<td>Positive</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Negative</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Equivocal/Other</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Culture</td>
<td>Positive</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Negative</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Equivocal/Other</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Typing/Identification</td>
<td>Positive</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Negative</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Equivocal/Other</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Whitelist Rules
Whitelist rules describe how long an existing event can have new laboratory data appended to it. If a laboratory result falls outside the whitelist rules for an existing event, it should not be added to that event, and should be evaluated to determine if a new event (CMR) should be created.

**Haemophilus influenzae Morbidity Whitelist Rule:** If the specimen collection date of the laboratory result 60 days or less after the event date of the last positive laboratory result, the laboratory result should be added to the morbidity event.

**Haemophilus influenzae Contact Whitelist Rule:** If the specimen collection date of the laboratory result is 21 days or less after the event date of the contact event, the laboratory result should be added to the contact event.

Graylist Rule
We often receive laboratory results through ELR that cannot create cases, but can be useful if a case is created in the future. These laboratory results go to the graylist. The graylist rule describes how long an existing event can have an old laboratory result appended to it.
**Haemophilus influenzae**

**Graylist Rule:** If the specimen collection date of the laboratory result is 30 days before to 7 days after the event date of the morbidity event, the laboratory result should be added to the morbidity event.

**Other Electronic Laboratory Processing Rules**
- If an existing event has a state case status of “not a case,” ELR will never add additional test results to that case. New labs will be evaluated to determine if a new CMR should be created.