The Disease and Its Epidemiology

A. Etiologic Agent

*Haemophilus influenzae* invasive disease is caused by the bacterium *H. influenzae* (*H. flu*), which is a small pleomorphic gram-negative coccobacillus (short, thick rod) that may be encapsulated (typeable) or unencapsulated (nontypeable). There are six capsular polysaccharide serotypes, which are designated as types a through f. *Haemophilus influenzae* type b (Hib) caused more than 95% of invasive *H. flu* disease among children less than 5 years of age prior to the introduction of effective vaccines. In the post-vaccine era, nontypeable strains cause the majority of invasive disease in all age groups. Nontypeable strains are frequent inhabitants of the respiratory tract and a common cause of respiratory and ear infections.

B. Clinical Description

Invasive disease caused by *Haemophilus influenzae* may produce any of several clinical syndromes, including meningitis (infection of the tissue surrounding the brain and spinal cord), bacteremia (blood infection) or sepsis, epiglottitis (which may cause airway obstruction), pneumonia, septic arthritis (joint infection), and cellulitis (skin infection). Less common forms of invasive disease are osteomyelitis (bone infection) and pericarditis (infection of the sac covering the heart). In contrast, syndromes of mucosal infections such as bronchitis, sinusitis, and otitis media are considered noninvasive disease. The noninvasive syndromes are not nationally notifiable nor reportable in Colorado.

C. Reservoirs

Humans are the only known reservoir. *H. flu* organisms colonize the nasopharynx and may remain either transiently or for several months. Untreated *H. flu* is communicable as long as organisms are present, which may be for a prolonged period even without nasal discharge.

D. Modes of Transmission

The mode of transmission is person-to-person by inhalation of respiratory droplets or by direct contact with discharges from the nose or throat of an infected person. The portal of entry is the nasopharynx. In neonates, infection is acquired intrapartum by aspiration of amniotic fluid or contact with genital tract secretions containing the organism.

E. Incubation Period

The incubation period is unknown.

F. Period of Communicability or Infectious Period

*H. flu* is noninfectious within 24 to 48 hours of starting effective antibiotic treatment. Droplet precautions are recommended for hospitalized cases for 24 hours after initiation of parenteral (i.e., IV) antimicrobial
therapy. Untreated *H. flu* is communicable as long as organisms are present, which may be for a prolonged period even without nasal discharge.

### G. Epidemiology

Before the widespread use of Hib conjugate vaccines, Hib was the most common cause of bacterial meningitis in children less than 5 years of age; the peak incidence for most forms of invasive disease occurred in children less than 18 months of age. In the United States, however, the peak age for epiglottitis was 2 to 4 years; Hib was unusual beyond 5 years of age.

After the initiation of routine infant immunization in the 1990s, Hib meningitis virtually disappeared in the United States. Invasive Hib disease in infants and young children decreased by 99% to less than one case per 100,000 children younger than 5 years of age. Unimmunized children less than 4 years of age, however, are still at increased risk of invasive Hib disease, especially if they have prolonged close contact (such as a household setting) with a person with invasive Hib disease. The risk of secondary Hib cases is greatest during the first week after the onset of illness in the index case. Secondary cases in families and childcare centers, however, are rare.

In the post-vaccine era, the majority of invasive *H. flu* infections in the United States in all age groups are caused by nontypeable strains. Invasive *H. flu* occurs worldwide; in developing countries, *H. flu* (including all serotypes and nontypeable strains) causes an estimated 480,000 pneumonia deaths each year among children less than 5 years of age.

### Case Definition

#### Clinical Description

Invasive disease caused by *Haemophilus influenzae* may produce any of several clinical syndromes, including meningitis, bacteremia, epiglottitis, or pneumonia.

#### Laboratory Criteria for Diagnosis

Isolation of *H. influenzae* or detection of *H. influenzae* nucleic acid from a normally sterile site (e.g., positive culture or PCR from blood or cerebrospinal fluid [CSF] or, less commonly, joint, pleural, or pericardial fluid). Isolates from all invasive *H. influenzae* cases should be sent to the CDPHE Lab for serotyping.

#### Case Classification

<table>
<thead>
<tr>
<th>Confirmed: A clinically compatible case that is laboratory confirmed (positive culture or PCR from a normally sterile site)</th>
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<tr>
<td>Probable: A clinically compatible case with detection of <em>H. influenzae</em> type b antigen in CSF</td>
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Note: Positive antigen test results from urine or serum samples are unreliable for diagnosing *H. influenzae* disease.

### Reporting Criteria

What to Report to the Colorado Department of Public Health and Environment (CDPHE) or local health agency

- Confirmed, probable, and suspect invasive *H. influenzae* cases.
- *H. flu* cases should be reported within 1 working day of a presumptively positive laboratory test or diagnosis.
- Cases should be reported using telephone, fax or the Colorado Electronic Disease Reporting System (CEDRS) to CDPHE or local health departments. See below for phone and fax numbers.
- Only confirmed and probable invasive *H. flu* cases are reported to CDC.
• **Note:** Sputum and throat are not considered sterile sites; therefore, *H. influenzae* isolated from these sites does not need to be reported or investigated.

**Purpose of Surveillance and Reporting**

- To identify cases for investigation.
- To identify exposed persons, assure timely administration of antimicrobial prophylaxis, and prevent further spread of the disease.
- To monitor trends in disease incidence and serotype.
- To provide data about vaccine effectiveness.

**Important Telephone and Fax Numbers**

CDPHE Communicable Disease Epidemiology Branch
- Phone: 303-692-2700 or 800-866-2759
- Fax: 303-782-0338
- After hours: 303-370-9395

CDPHE Microbiology laboratory: 303-692-3480


The following documents are available on the CD Manual website:

- Summary of Invasive *Haemophilus influenzae* Investigation and Control Guidelines
- Flowchart to Determine Need for Prophylaxis and Hib Vaccination of *H. influenzae* serotype *b* (Hib) Close Contacts 6 Weeks to 47 Months of Age
- Detailed Vaccination Schedule for *Haemophilus influenzae* type *b* Conjugate Vaccine

**State Laboratory Services**

Laboratory Testing Services Available

- The CDPHE Microbiology Laboratory will confirm and serotype isolates of *Haemophilus influenzae*.
- Isolates from all invasive *H. flu* disease cases should be sent to the CDPHE Microbiology Laboratory for serotyping. Routine serotyping informs public health surveillance and is necessary to determine appropriate disease control.

**Case Investigation**

All reports of invasive Hib disease need to be investigated. Confirm that the specimen was collected from a normally sterile site (e.g. blood, CSF). The purpose of *H. flu* investigations is to prevent secondary cases of *H. flu* serotype *b* disease among unvaccinated young children who are close contacts of the index case.

**Invasive *H. flu* cases caused by non-*b* serotypes do not require a contact investigation or disease control.** There are no guidelines for control measures around cases of invasive nontypable or non-*b* *H. influenzae* disease. Chemoprophylaxis is not recommended for contacts of persons with invasive disease caused by nontypable or non-*b* *H. influenzae* because cases of secondary transmission of disease have not been documented.

If a delay of more than 3 working days is anticipated in obtaining the serotype information, consider evaluating the household contacts to determine if they meet the criteria for prophylaxis.

Hib cases should be investigated to:

- Identify close contacts of the case and if necessary provide recommendations for antibiotic chemoprophylaxis to prevent secondary cases.
- Provide information about the disease, its transmission, and methods of prevention.
• Promptly identify clusters or outbreaks of disease and initiate appropriate prevention and control measures.

If the \textit{H. flu} case is unable to be interviewed due to their age or medical condition, information may be obtained from the hospital infection control practitioner, healthcare provider, parents/relatives, friends and/or others involved with the case.

A. Identify and Evaluate Contacts (Contact Investigation)

\textit{H. flu} serotype b cases need to be investigated to prevent disease among young children who are close contacts of the index case. Identification of young children who are household or childcare contacts of invasive Hib disease cases and assessment of their vaccination status helps identify persons who may need antimicrobial prophylaxis and/or vaccination. Antibiotic prophylaxis is only recommended for household contacts and possibly childcare contacts of confirmed and probable \textit{H. flu} serotype b cases in certain circumstances (see Disease Control Measures, section C Prophylaxis). \textbf{If the serotype is determined to be non-b or nontypeable, no disease control is needed.}

◦ Obtain information about the case’s household contacts, including the ages of children in the household and whether any children in the household are immunocompromised.
◦ Household contacts are defined as persons residing with the index case or nonresidents who spent 4 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.
◦ Obtain the Hib vaccination records for any children < 5 years of age defined as household contacts.
◦ Determine whether the case attends childcare.
◦ If the case attends childcare, obtain the age range of the children in the childcare classroom or childcare home. Determine if any children in the classroom or home childcare are immunocompromised.

Symptomatic Contacts (Exposure during the 7 days prior to hospitalization of the case.)
◦ Invasive \textit{H. flu} symptoms include some of the following: fever, stiff neck, drowsiness, irritability, sudden vomiting, or an infection of a joint that is red, tender, or swollen.
◦ Contacts having symptoms of invasive \textit{H. flu} should contact their physician immediately.

Asymptomatic Contacts (Exposure during the 7 days prior to hospitalization of the case.)
◦ In certain situations, antibiotic prophylaxis is recommended for contacts of a Hib case (see Disease Control Measures, section C Prophylaxis).
◦ Provide information about Hib disease symptoms to parents of young children who are close contacts.
◦ Recommend Hib vaccination for unimmunized or underimmunized children < 5 years of age.
◦ Counsel contacts to seek medical care if symptoms develop.

B. Surveillance / Forms

◦ Local public health agencies have primary responsibility for investigating cases in their jurisdictions.
¬ • For all confirmed and probable \textit{H. flu} cases, complete the appropriate tabs on the events page (e.g. diagnosis details, hospitalization, etc.) in CEDRS and the applicable fields on the surveillance form (EIP county vs. non-EIP county).
¬ • The Active Bacterial Core Surveillance (ABCs) Case Report form is completed by CDPHE chart reviewers for cases in EIP counties. This form does not need to be completed by local public health.
¬ • Call the CDPHE Communicable Disease Program if there are a higher number of cases in your area than usual or an outbreak is suspected.
Disease Control Measures for Hib Cases

A. Treatment

- Antimicrobial therapy should begin immediately for confirmed and probable cases of Hib.
- Recommended treatment is cefotaxime or ceftriaxone.
- Acceptable alternative regimens are meropenem or the combination of chloramphenicol and ampicillin. If these alternative antibiotics are used and the case is <2 years of age or the case has a susceptible household contact, the case should receive rifampin prophylaxis at the end of therapy to eliminate carriage.
- Treatment course is usually 10 days, however, longer treatment may be indicated for complicated cases.

B. Vaccination

*Haemophilus influenzae* serotype b (Hib) vaccine is only effective against serotype b disease, and does not provide protection against other serotypes or nontypeable strains. All infants, including those born preterm, should receive a primary series of conjugate Hib vaccine (separate or in combination), beginning at 2 months of age. The number of doses in the primary series depends on the type of vaccine used. A primary series of PRP-OMP (PedvaxHIB or COMVAX) vaccine is two doses; PRP-T (ActHIB, Pentacel, or MenHibrix) requires a three-dose primary series (see table below). A booster is recommended at 12-15 months regardless of which vaccine is used for the primary series.

| ACIP-Recommended *Haemophilus influenzae* type b (Hib) Routine Vaccine Schedule |
|-----------------------------------------------|----------------|----------------|----------------|----------------|
| Type                          | Vaccine         | 2 months | 4 months | 6 months | 12-15 months |
| PRP-T                          | ActHIB          | X (1st)  | X (2nd)  | X (3rd)  | X |
|                                | Pentacel*       | X (1st)  | X (2nd)  | X (3rd)  | X |
|                                | Hiberix†        | —        | —        | —        | X |
|                                | MenHibrix§      | X (1st)  | X (2nd)  | X (3rd)  | X |
| PRP-OMP                        | PedvaxHIB       | X (1st)  | X (2nd)  | —        | X |
|                                | COMVAX          | X (1st)  | X (2nd)  | —        | X |

* The recommended age for the 4th dose of Pentacel is 15-18 months, but it can be given as early as 12 months, provided at least 6 months have elapsed since the 3rd dose.

† Hiberix is approved only for the last dose of the Hib series among children 12 months of age and older. The recommended age is 15 months, but to facilitate timely booster vaccination it may be given as early as 12 months.

§ The recommended age for the 4th dose of MenHibrix is 12-18 months.
Refer to the Flowchart to Determine Need for Prophylaxis and Hib Vaccination of H. influenzae serotype b (Hib) Close Contacts 6 Weeks - 47 Months of Age.

Children <2 years of age who have had Hib disease should be immunized according to the age-appropriate schedule for unimmunized children, as if they had not received previous Hib vaccinations. Immunization should begin 1 month after the onset of disease and is recommended because children <2 years of age having Hib disease can remain at risk of developing a second episode of disease.

Children ≥2 years of age who have had Hib disease do not need Hib vaccination, as disease almost always provides a protective immune response.

C. Prophylaxis

Antimicrobial prophylaxis

Antibiotic prophylaxis is only recommended for household contacts and possibly childcare contacts of confirmed and probable H. flu serotype b (Hib) cases in certain circumstances. **Prophylaxis is not recommended for contacts of nontypeable H. flu or nontype b strains.** Regardless of serotype, testing of contacts is not recommended. When indicated, prophylaxis should be started as soon as possible, since the risk of secondary cases is greatest during the first week after hospitalization of the index case.

- Household Contacts
  
  Household contacts are defined in Case Investigation, section A (Identify and Evaluate Contacts). If anyone in the household meets the following criteria, then antibiotic prophylaxis is recommended for all household contacts of the confirmed or probable H. flu serotype b case, except pregnant women:
  
  - Any household contact is <12 months of age and has not completed the Hib primary vaccine series.
  - Any household contact is an immunocompromised child, regardless of Hib immunization status.
  - Any household contact is <4 years of age and unimmunized or incompletely immunized for Hib.

Contacts needing prophylaxis should be referred to their family doctor. In rare situations, a local health department or CDPHE physician may call in a prescription to a pharmacy.

- Childcare Contacts
  
  There is controversy and conflicting data regarding antibiotic prophylaxis of childcare contacts of a single Hib case. Consult with the vaccine-preventable disease (VPD) unit at CDPHE for recommendations for a single case of Hib in a childcare or preschool setting.

  However, if two or more invasive Hib cases are reported within 60 days and incompletely or unimmunized children attend the school or childcare, discuss prophylaxis for all childcare or preschool contacts and staff, irrespective of immunization status with CDPHE VPD epidemiologists.

  See Section B Vaccination to determine if a household or childcare contact is up-to-date for Hib vaccine.

  Generally, prophylaxis of childcare contacts is not needed if all childcare classroom or home childcare contacts are ≥3 years of age. If there are immunocompromised children in the childcare classroom or home childcare, recommend antibiotic prophylaxis of the immunocompromised children, and contact your CDPHE Epidemiologist to discuss antibiotic prophylaxis of all the childcare classroom or home childcare contacts.

CDPHE Field Epidemiologists have sample letters that may be used to notify parents of the occurrence of a case of Hib disease in a childcare facility, to educate them about signs and symptoms of the disease, and recommend prophylaxis if necessary.

Antibiotic Prophylaxis

- Rifampin is the drug of choice for prophylaxis. Rifampin prophylaxis is not recommended for pregnant women.
Rifampin Prophylaxis for Hib Exposure

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Dosage / Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1 Month of Age</td>
<td>10 mg/kg orally once daily for 4 days</td>
</tr>
<tr>
<td>Children</td>
<td>20 mg/kg orally once daily for 4 days (maximum dose - 600 mg)</td>
</tr>
<tr>
<td>Adults</td>
<td>600 mg orally once daily for 4 days</td>
</tr>
</tbody>
</table>

Contacts needing prophylaxis should be referred to their family doctor. In rare situations, a local health department or CDPHE physician may call in a prescription to a pharmacy.

**D. Education**

- Advise parents of the signs and symptoms of Hib disease if children <4 years of age and/or immunocompromised children have been exposed.
- Recommend Hib vaccination for contacts <5 years of age, who are not up-to-date on their Hib vaccinations.
- CDPHE Field Epidemiologists have sample letters to notify parents.
- Information about Hib is available on CDC’s website: [http://www.cdc.gov/vaccines/vpd-vac/hib/default.htm](http://www.cdc.gov/vaccines/vpd-vac/hib/default.htm)

**E. Managing Special Situations**

**Childcare / Preschool**

Refer childcare providers to the Infectious Disease in Child Care and School Settings: Guidelines for Child Care Providers: [https://www.colorado.gov/pacific/cdphe/infectious-disease-guidelines-schools-and-childcare-settings](https://www.colorado.gov/pacific/cdphe/infectious-disease-guidelines-schools-and-childcare-settings) “Bacterial Meningitis” page for additional H. flu information. When two or more invasive Hib cases have been detected within 60 days in the same childcare facility and under or unimmunized children are in attendance, prophylaxis for all attendees (regardless of age and vaccine status) and childcare providers should be discussed with CDPHE VPD epidemiologists.

- Determine the age range of the children in the case’s childcare classroom or home childcare.
- If there are children <3 years of age in the case’s classroom or home childcare, evaluate their Hib immunization records to determine if antibiotic prophylaxis may be necessary. See Disease Control Measures, section B Vaccination for details about evaluating the children’s Hib immunization records and see section C Prophylaxis to determine the need for antibiotic prophylaxis.
- If there are children 3-5 years of age in the case’s classroom or home childcare who are unimmunized or incompletely immunized for Haemophilus influenzae type b (Hib), recommend vaccination. See Disease Control Measures, section B Vaccination for information about reviewing Hib vaccination records and recommending Hib vaccination.

**School**

Refer school personnel to the CDPHE the Infectious Disease in Child Care and School Settings: Guidelines for Child Care Providers: [https://www.colorado.gov/pacific/cdphe/infectious-disease-guidelines-schools-and-childcare-settings](https://www.colorado.gov/pacific/cdphe/infectious-disease-guidelines-schools-and-childcare-settings) “Bacterial Meningitis” page for additional information. The risk of secondary spread of Haemophilus influenzae type b (Hib) is a concern for unimmunized or incompletely immunized childcare contacts <3 years of age. Children <3 years of age are not typically in a school setting. Thus, the immunization records of school contacts do not routinely need to be reviewed and antibiotic prophylaxis is not routinely recommended for school contacts.

- Verify that the case is not in a classroom with children <3 years of age.
- If the case is in a classroom with children <3 years of age, consult your CDPHE VPD epidemiologist for guidance.
Patients and Staff in Health Care Facilities (Hospitals and Long Term Care Facilities)
Hospitals and long term care facilities generally have written infection control policies and procedures for handling cases of communicable disease among patients and staff members. If a facility does not have such policies in place, provide the following recommendations:

- Standard and droplet precautions (respiratory isolation) are recommended during the first 24 hours of antimicrobial therapy of the case.
- Health care workers caring for Hib cases do not need prophylaxis.
- If the case has Hib and had close contact while infectious with children <4 years of age, who are not household or childcare contacts, discuss the type and duration of contact with your CDPHE Field Epidemiologist.

F. Environmental Measures
No specific environmental measures are recommended. Hib does not survive in the environment on inanimate surfaces.

References

