Haemophilus influenzae, Invasive Disease

**BASIC EPIDEMIOLOGY**

**Infectious Agent**
Haemophilus influenzae (*H. influenzae*) is a small, Gram-negative bacillus, a bacterium capable of causing a range of diseases including ear infections, cellulitis (soft tissue infection), upper respiratory infections, pneumonia, and such serious invasive infections as meningitis with potential brain damage and epiglottitis with airway obstruction. There are at least 6 serotypes of *H. influenzae* (designated a-f) distinguished by their capsular antigens, as well as unencapsulated (nontypeable) strains. *Haemophilus influenzae*, type b (Hib), however, often causes the most severe disease and is the only type which is preventable by vaccine. Despite its name, this bacterium has nothing to do with the influenza viruses. (Note also that it is spelled differently.)

**Transmission**
*Haemophilus influenzae* bacteria are found in the nose and throat, usually without causing symptoms, and are spread mainly by breathing, coughing and sneezing. *H. influenzae* is transmitted by direct contact with respiratory droplets and discharges from the nose and throat of infected/colonized persons.

**Incubation Period**
The incubation period is hard to define, because most persons who acquire *Haemophilus influenzae* infections are asymptomatically colonized. Those who become ill following exposure to a case usually do so within 10 days, although the risk may be slightly elevated for up to 60 days.

**Communicability**
As long as the organism is present in discharges from the nose or throat. Communicability ends within 24 hours of initiation of appropriate chemoprophylaxis. Note, however, that treatment of invasive disease does not necessarily eradicate the organism from the nose/throat. Those exposed more than 7 days before onset of illness in the case are not at significantly increased risk. Hib cases are probably most infectious during the 3 days prior to onset of symptoms.

**Clinical Illness**
All types of *Haemophilus influenzae* can cause illness, although Hib is the most common cause of severe illness. Disease can take many forms, including:
- Meningitis- brain swelling
- Bacteremia- blood infection
- Periorbital or other cellulitis- skin lesions
- Septic arthritis- joint infection
- Osteomyelitis- bone infection
- Pericarditis- infection of the sac around the heart
- Pneumonia- lung infection
- Epiglottitis - Swelling of the windpipe
Onset of symptoms is usually abrupt, and may include:

- Fever
- Headache
- Lethargy
- Anorexia
- Nausea
- Vomiting
- Irritability

Progressive stupor or coma is common with meningitis. Infections spread via the bloodstream after penetration of the mucous membranes of the nasopharynx. The exact mechanism allowing the penetration is unknown, but a recent upper respiratory tract infection may facilitate invasion. Recently, having a cochlear implant procedure has been identified as a possible risk factor for invasive disease. Asymptomatic carriage of Hib is not uncommon; in the pre-vaccine era the organism was recovered from the upper respiratory tract of 2–5% of healthy children. Thus, isolates from sputum or other not-normally-sterile sites are not indicative of invasive disease. Neonatal sepsis and non-invasive upper respiratory tract disease, including otitis media, sinusitis, and bronchitis are often caused by other, non-encapsulated strains (non-type b) of H. influenzae. These organisms are extremely common and can be recovered from the nasopharynx of 40% to 80% of healthy children.

### DEFINITIONS

**Clinical Case Definition**

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

**Laboratory Criteria for Diagnosis**

- Detection of Haemophilus influenzae type b antigen in cerebrospinal fluid [CSF]
- 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
- Isolation of Haemophilus influenzae from a normally sterile body site (e.g., cerebrospinal fluid [CSF], blood, joint fluid, pleural fluid, pericardial fluid)

**Note:** Serotyping of isolates can be performed at the DSHS laboratory. Serotyping is recommended for all H. influenzae isolates from sterile sites and required on isolates from children under 5 years old.

**Case Classification**

- **Confirmed:** A case that is laboratory confirmed
- **Probable:** Meningitis with detection of Haemophilus influenzae type b antigen in cerebrospinal fluid (CSF). (Antigen test results in urine or serum are unreliable for diagnosis of H. influenzae disease).

**Note:** Conjunctivitis, otitis media, and bronchitis caused by H. influenzae are not invasive infections, and do not need to be reported.
SURVEILLANCE AND CASE INVESTIGATION

Case Investigation
Local and regional health departments should investigate any reported cases of invasive *H. influenzae*. Health departments should also facilitate the typing of untyped specimens (from sterile sites) as soon as possible. Submission to the DSHS laboratory for *H. influenzae* isolates from sterile sites on children under 5 for serotyping is mandated by the Texas Administrative Code regardless of typing at other facilities. Investigations of *H. influenzae* type b should include rapid identification and evaluation of close contacts.

Case Investigation Checklist
- Confirm laboratory results meet the case definition.
  - See the Sterile Site and Invasive Disease Determination Flowchart for confirming a specimen meets the criteria for sterile site.
- For those under 5 years old, if *Haemophilus influenzae* was isolated from a sterile site the TAC requires an isolate be forwarded to the DSHS laboratory for typing and molecular analysis.
  - TAC requires isolates for cases under 5 years of age from sterile sites be sent to the DSHS laboratory regardless of typing results at other facilities
  - If an isolate is not available but *Haemophilus influenzae* is suspected, forward any specimen from a sterile site that is available.
  - DSHS Austin lab will type the isolate and notify submitter of the results
  - Update serotype results in NEDSS case investigation.
- For those 5 years or older if *Haemophilus influenzae* was isolated from a sterile site but the type is unknown, request that the laboratory forward the isolate to the DSHS laboratory for typing and molecular analysis.
  - If an isolate is not available but *Haemophilus influenzae* is suspected, forward any specimen from a sterile site that is available.
  - If isolate is typed, update serotype in NEDSS case investigation.
- Review medical records or speak to an infection preventionist or physician to verify demographics, symptoms, underlying health conditions, and course of illness.
- Complete the *Haemophilus influenzae* Investigation Form by interviewing the case (or surrogate) to identify close contacts, risk factors, vaccination history, and other pertinent information.
  - All cases of *H. influenzae*, regardless of type should have a full investigation completed.
- Ensure appropriate control measures are implemented (see Control Measures below).
- Refer household or close contacts that meet the prophylaxis criteria to their healthcare provider for appropriate chemoprophylaxis (See Prophylaxis Criteria below).
- Send the completed *Haemophilus influenzae* Case Investigation Form to DSHS Eaidu via fax, secure email, or mail.
- In the event of a death, copies of the hospital discharge summary, death certificate, and autopsy report should also be faxed or emailed to DSHS.
- All confirmed and probable *Haemophilus influenzae* case investigations must be entered and submitted for notification in the NEDSS Base System (NBS). Please refer to the NBS Data Entry Guidelines for disease specific entry rules.
Control Measures

- Control measures are primarily needed for Hib cases (see Prophylaxis Guidelines section below). For all other H. influenzae cases, appropriate antibiotic treatment for the patient and good hand hygiene are the only control measures needed.
- Appropriate vaccination is the best control measure.
- Children <24 months of age who have had invasive Hib disease (culture confirmed) should still receive Hib vaccine, since many children of that age fail to develop adequate immunity following natural disease.
- Rifampin prophylaxis should be instituted as rapidly as possible, to eligible contacts (see below).

Managing Close Contacts

- Household contacts should be evaluated for appropriate prophylaxis (see below).
- The risk of Hib invasive disease for childcare center contacts of a patient with Hib invasive disease case is thought to be lower than that for a susceptible household contact.
- There are no guidelines for control measures around cases of invasive non-typeable or non-b H. influenzae disease.

Prophylaxis Guidelines

- For H. influenzae type b:
  - Rifampin chemoprophylaxis is recommended for index case-patients (unless treated with cefotaxime or ceftriaxone) and all household contacts in households with members less than 4 years of age who are not fully vaccinated or members less than 18 years of age who are immunocompromised, regardless of their vaccinated status.
    - The recommended dose of rifampin is 20 mg/kg as a single daily dose (maximum daily dose 600 mg) for 4 days. Some providers recommend that neonates (<1 month of age) receive 10 mg/kg once daily for 4 days.
  - If the case is part of a household with a child younger than 12 months of age who has not received the three-dose primary series of Hib conjugate vaccine, all household members should receive rifampin prophylaxis.
  - If the case is part of a household with at least one contact that is younger than 48 months of age and unvaccinated or incompletely vaccinated against Hib, rifampin prophylaxis is recommended for all household contacts regardless of age.
  - If the case is part of a household with an immunocompromised child, even if the child is older than 48 months and fully vaccinated, all members of the household should receive rifampin because of the possibility that the vaccination may not have been effective.
  - Chemoprophylaxis is not recommended for occupants of households that do not have children younger than 48 months of age (other than the index case) or when all household contacts 12 to 48 months of age are immunocompetent and have completed their Hib vaccination series.
  - In childcare facilities, prophylaxis is recommended when there have been 2 or more cases in a 60 day period AND there are under or unimmunized children at the daycare. Attendees and providers should receive rifampin prophylaxis. Additionally, under or unimmunized children should receive a dose of vaccine and should be scheduled to complete the recommended series.
  - Index patients younger than 2 years or that live with a susceptible contact, should also receive rifampin prophylaxis preferably just before hospital discharge, if the patient was not treated with cefotaxime or ceftriaxone.
  - Hospital personnel exposed to a child with invasive Hib disease do not need
prophylaxis.

- For non-b *H. influenzae*:
  Chemoprophylaxis is not recommended for contacts of persons with invasive disease because cases of secondary transmission have not been documented.

Treatment
Antibiotic treatment is available to treat infection with *Haemophilus influenzae*.

Exclusion
Children with a fever from any infectious cause should be excluded from school/daycare for at least 24 hours after fever has subsided without the use of fever suppressing medications. Do not exclude exposed asymptomatic children and staff as long as they have no other reasons for exclusion.
**MANAGING SPECIAL SITUATIONS**

**Outbreaks**
If an outbreak of *Haemophilus influenzae* is suspected, notify EAIDU at (800) 252-8239 or (512) 776-7676.

**REPORTING AND DATA ENTRY REQUIREMENTS**

**Provider, School & Child-Care Facilities, and General Public Reporting Requirements**
Confirmed, probable and clinically suspected cases are required to be reported within 1 week to the local or regional health department or to DSHS EAIDU at (800) 252-8239 or (512) 776-7676.

Local and regional health departments should:

- Enter the case into NBS and submit an NBS notification on all confirmed and probable cases to DSHS within 30 days of receiving a report of a confirmed or probable case.
  - Please refer to the *NBS Data Entry Guidelines* for disease-specific entry rules.
  - A notification can be sent as soon as the case criteria have been met. Additional information from the investigation may be entered upon completing the investigation.
- Fax, send a secure email, or mail a completed Investigation Form within 30 days of completing the investigation.
  - In the event of a death, copies of the hospital discharge summary, death certificate, and autopsy report should also be sent to DSHS EAIDU.
  - Investigation forms may be faxed to 512-776-7616, securely emailed to VPDTexas@dshs.texas.gov or mailed to:
    - Emerging and Acute Infectious Disease Unit
    - Texas Department of State Health Services
    - Mail Code: 1960
    - PO Box 149347
    - Austin, TX 78714-9347
  - Cases (Hib and children under 5) should be monitored until hospital discharge, even if all investigation and control measures have been completed.

When an outbreak is investigated, local and regional health departments should:

- Report outbreaks within 24 hours of identification to the regional DSHS office or to EAIDU at 512-776-7676.
LABORATORY PROCEDURES

Serotyping of *H. influenzae* isolates is an important part of the diagnostic process, but also to aid in understanding the epidemiology of *H. influenzae* in Texas. The Texas Administrative Code mandates the submission of *H. influenzae* isolates on children under 5 years old to the DSHS laboratory. *H. influenzae* isolates from patients of any age can be submitted to the DSHS lab and we encourage the submission of all *H. influenzae* isolates. Serotyping of *H. influenzae* isolates allow us to understand the epidemiology of *H. influenzae* and how the vaccine has affected Hib and all other *H. influenzae* types in Texas. The DSHS laboratory can perform serotyping for *H. influenzae* isolates collected from sterile sites. DO NOT submit isolates from sputum for serotyping.

Isolate Submission

- Submit isolates of *Haemophilus influenzae* on chocolate agar slants (or media that has the necessary growth requirements for *Haemophilus*) at ambient temperature.
- Ship isolate to the DSHS laboratory via overnight delivery. The viability of the organism is short lived; therefore, isolate must arrive at the DSHS lab in Austin within 48 hours after subculture.
- If a delay of more than 48 hours in transport is anticipated, use a CO₂ generator bag.
- Use Specimen Submission form G-2B.
  - When submitting isolate from sterile site and <5 years old make sure to check the box in Section 9 shown below in addition to the correct box in Section 5. Bacteriology.

![Section 5. BACTERIOLOGY](image-url)
**Specimen Shipping**

- DO NOT mail on a Friday or a day before a state holiday unless special arrangements have been pre-arranged with DSHS Laboratory.
- Ship specimens to:
  
  Laboratory Services Section, MC-1947  
  Texas Department of State Health Services  
  Attn. Walter Douglass (512) 776-7569  
  1100 West 49th Street  
  Austin, TX 78756-3199

*Haemophilus influenzae* is considered an infectious agent, biosafety level 2. The isolate should be triple contained in accordance with federal regulations.

**Causes for Rejection**

- Discrepant or missing information between isolate and paperwork
  - There must be 2 identifiers such as patient first and last name AND date of birth on the specimen media.
- Expired media used

**FLOW CHART**

- See next page

**UPDATES**

January 2021

- Updated Managing Close Contacts section
- Added Prophylaxis Guidelines Section
- Updated flow chart
Haemophilus influenzae
Case Status Classification

FLOW CHART rev Jan 2018

Notified of suspect case of H. influenzae

Texas Resident?

Yes

Was specimen from a sterile site?

Yes

Was H. influenzae isolated by culture or detected by PCR?

No

Was specimen from CSF?

Yes

Detection of H. influenzae type B (Hib) antigen in CSF?

No

Confirmed Case

Probable case

Not a Case

Yes

Not a Texas case. Report case to EIDB for referral to case’s residential state.

See Sterile Site and Invasive Disease Determination flow chart