

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 asymptotically 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. Detection and isolation laboratory tests can be performed at commercial labs.

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, regardless of age.**
- 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 *H. influenzae* cases, appropriate antibiotic treatment for the patient and good hand hygiene are needed to stop transmission.
- All *H. influenzae* cases should remain on droplet precautions until 24 hours after initiation of effective antimicrobial therapy.
- 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 administered as rapidly as possible to eligible contacts (see below).

Managing Close Contacts

- Household contacts that were exposed within 7 days of the index case's onset date 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, including if the serotype is not available at the time prophylaxis would be administered.
- If more than 14 days have passed since the last contact with the index patient, the benefit of chemoprophylaxis is likely to be decreased.

Prophylaxis Guidelines

- **For *H. influenzae*, type b only:**
 - **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/non-typed *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.

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.**

<input type="checkbox"/> Malaria/Blood Parasite Exam @	<input type="checkbox"/> Worm Identification @	<input type="checkbox"/> Norovirus
<input type="checkbox"/> Schistosoma/Urine Parasite Exam @	<input type="checkbox"/> Other:	
Section 5. BACTERIOLOGY		
<u>Clinical specimen:</u>		Section 9. REQUIRED/REQUESTED SUBMISSIONS
<input type="checkbox"/> Aerobic isolation	<u>Definitive Identification:</u>	<input type="checkbox"/> Corynebacterium diphtheriae ☐
<input type="checkbox"/> Anaerobic isolation	<input type="checkbox"/> Bacillus <input type="checkbox"/> Campylobacter	<input type="checkbox"/> E. coli O157 or other STEC serotypes ☐
<input type="checkbox"/> Culture, stool	<input type="checkbox"/> Enteric Bacteria	<input type="checkbox"/> EHEC, shiga-like toxin assay (Shigatoxin-producing Escherichia coli) ☐
<input type="checkbox"/> Diphtheria Screen	<input type="checkbox"/> Gram Negative Rod	<input type="checkbox"/> Haemophilus influenzae (from sterile sites and <5 years old) ☐
<input type="checkbox"/> GC/CT, amplified RNA probe	<input type="checkbox"/> Gram Positive Rod	<input type="checkbox"/> Listeria ☐
<input type="checkbox"/> Haemophilus, isolation	<input type="checkbox"/> Group B Streptococcus (Beta Strep)	<input type="checkbox"/> Neisseria meningitidis (from sterile sites or lesions) ☐
<input type="checkbox"/> Toxic shock syndrome toxin I assay (TSSST 1)	<input type="checkbox"/> Haemophilus ←	<input type="checkbox"/> Outbreak stool culture ☐
<input type="checkbox"/> <u>Pure culture:</u>	<input type="checkbox"/> Legionella	<input type="checkbox"/> Salmonella ☐
<input type="checkbox"/> Anaerobic identification	<input type="checkbox"/> Neisseria	<input type="checkbox"/> Shigella ☐
<input type="checkbox"/> Organism suspected:	<input type="checkbox"/> Pertussis / Bordetella	<input type="checkbox"/> Staphylococcus aureus (VISA/VRSA) ☐
	<input type="checkbox"/> Staphylococcus	<input type="checkbox"/> Streptococcus pneumoniae (from sterile sites and <5 years old) ☐
	<input type="checkbox"/> Streptococcus <input type="checkbox"/> Other	<input type="checkbox"/> Vibrio cholera ☐
		<input type="checkbox"/> Vibrio sp. ☐

NOTES: All dates must be entered in mm/dd/yyyy format. For culture ID or typing, please provide biochemical reactions on reverse side of form or attach copy of biochemistry printout. Each test section (ex. Bacteriology) requires a separate form and specimen. Please see the form's instructions for details on how to complete this form. Visit our web site at <http://www.dshs.texas.gov/lab/>. @ = Provide patient history on reverse side of form to avoid delay of specimen processing. ☐ = All fields indicated in Section 2 must be completed, if available.

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

REVISION HISTORY

January 2021

- Updated Managing Close Contacts section
- Added Prophylaxis Guidelines Section
- Updated flow chart

January 2022

- Updated Managing Close Contacts section
- Updated Prophylaxis Guidelines

December 2022

- Updated Case Investigation Checklist section

- Updated Laboratory Criteria for Diagnosis
- Updated Control Measures
- Updated Prophylaxis Guidelines

FLOW CHART

