

Haemophilus influenzae

(Invasive)

REPORT IMMEDIATELY

Section 1:

ABOUT THE DISEASE

A. Etiologic Agent

Haemophilus influenzae is a small gram-negative coccobacillus that may be either encapsulated (types a–f) or unencapsulated (non-typeable). *Haemophilus influenzae* type b (Hib) is the only type for which there is a vaccine and for which control measures are considered necessary.

B. Clinical Description

Invasive disease due to *H. influenzae* may produce various clinical syndromes including meningitis, bacteremia or sepsis, epiglottitis, pneumonia, septic arthritis, osteomyelitis, pericarditis, empyema, and abscesses. 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.

C. Vectors and Reservoirs

Humans are the only known host.

D. Modes of 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.

E. Incubation Period

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

F. Period of Communicability or Infectious Period

If the case 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. If the case is on antibiotic therapy, disease is non-communicable within 24–48 hours after starting effective 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, daycare center, or institutional setting), can lead to outbreaks of Hib or direct secondary transmission of the disease. Asymptomatic carriage is known to occur.

G. Epidemiology

Invasive *H. influenzae* disease is most prevalent among children aged two months to three years and is unusual in healthy individuals over the age of five years. The introduction of Hib vaccine in 1988 resulted in a 99% decrease in invasive Hib disease in children younger than 5 years of age. Currently, Hib disease occurs primarily in infants too young to have completed a primary series of immunization. Secondary cases may occur in households, daycare centers, and other institutional settings.

Before the widespread use of Hib conjugate vaccines, Hib was a leading cause of bacterial meningitis in the U.S. among children <5 years of age and a major cause of other life-threatening invasive bacterial disease in this age group. Meningitis occurred in approximately two-thirds of children with invasive Hib disease, resulting in hearing impairment or severe permanent neurologic sequelae, such as mental retardation, seizure disorder, cognitive and developmental delay, and paralysis in 15–30% of survivors. Approximately 5% of all cases were fatal.

Since the introduction of Hib vaccine, the incidence of all infection due to the encapsulated and nontypeable strains combined have decreased. However, *H. influenzae* type f has become the most common serotype causing invasive infections in the U.S.

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. 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.

H. Bioterrorist Potential

This pathogen is not considered to be of risk for use in bioterrorism.



Section 2:

REPORTING CRITERIA AND LABORATORY TESTING

A. What to Report to the Massachusetts Department of Public Health (MDPH)

Report any of the following:

- ◆ A case clinically compatible with invasive *H. influenzae* infection (e.g., with meningitis, bacteremia, epiglottitis, or pneumonia), as diagnosed by a health care provider; or
- ◆ Isolation (culture) of *H. influenzae* from a normally sterile body site (e.g., blood, cerebrospinal fluid [CSF], or less commonly, joint, pleural, or pericardial fluid), or detection of Hib capsular antigen in CSF.

B. Laboratory Testing Services Available

Because Hib has become rare as the cause of invasive *H. influenzae* infection in the U.S., there is an increased need to identify the serotype of all cases of invasive *H. influenzae* disease, especially in children <15 years of age. Confirmatory identification and serotyping of *H. influenzae* isolates are performed at the MDPH State Laboratory Institute (SLI). All strains of *H. influenzae* isolated from normally sterile sites must be serotyped in order to identify

the strain and to differentiate between vaccine (type b) and non-vaccine serotypes (for which there are no control measures).

For more information on submitting specimens, contact the SLI Reference Laboratory at (617) 983-6607. Subcultures should be sent along with the SLI *Specimen Submission Form*, (which can be found at the end of this chapter or on the MDPH website at www.mass.gov/dph/bls/generalform.pdf) to the SLI Reference Laboratory.

*Note: Positive antigen results from tests of urine and/or serum samples are not reliable for diagnosis of *H. influenzae* disease and should not be used as a substitute for culture.*



Section 3:

REPORTING RESPONSIBILITIES AND CASE INVESTIGATION

A. Purpose of Surveillance and Reporting

- ◆ To ensure that all cases of invasive *H. influenzae* disease have their etiologic agent serotyped and to identify all cases of Hib (particularly in those <15 years of age).
- ◆ To identify household and daycare contacts of Hib cases who need antimicrobial prophylaxis and/or immunization, and to prevent further spread of disease.
- ◆ To identify the emergence of other *H. influenzae* types as causes of invasive disease.
- ◆ To monitor Hib vaccine effectiveness, and to assess progress toward disease elimination.

B. Laboratory and Health Care Provider Reporting Requirements

Invasive *H. influenzae* infection is reportable to the local board of health (LBOH). The MDPH requests that health care providers immediately report to the LBOH in the community where the case is diagnosed, all confirmed or suspect cases of invasive *H. influenzae* infection, as defined by the reporting criteria in Section 2A.

Laboratories performing examinations on any specimens derived from Massachusetts residents that yield evidence of *H. influenzae* infection shall immediately report such evidence of infection, directly by phone, to the MDPH Division of Epidemiology and Immunization at (617) 983-6800 or (888) 658-2850.

Due to the potential severity of the disease, the MDPH requests that information about any case of invasive *H. influenzae* infection also be reported immediately to an epidemiologist at the MDPH Division of Epidemiology and Immunization by calling (617) 983-6800 or (888) 658-2850.

C. Local Board of Health (LBOH) Reporting and Follow-Up Responsibilities

Reporting Requirements

MDPH regulations (*105 CMR 300.000*) stipulate that invasive *H. influenzae* infection is reportable to the LBOH and that each LBOH must report any case of invasive *H. influenzae* disease or suspect case of invasive *H. influenzae*

disease, as defined by the reporting criteria in Section 2A. After the initial notification to MDPH, cases should be reported to the MDPH Bureau of Communicable Disease Control, Office of Integrated Surveillance and Informatics Services (ISIS) using an official MDPH *Invasive Haemophilus Influenzae Case Report Form* (found at the end of this chapter). Refer to the *Local Board of Health Timeline* at the end of this manual's *Introduction* section for information on prioritization and timeliness requirements of reporting and case investigation.

Due to the potential severity of invasive *H. influenzae* as well as national surveillance and reporting requirements, the MDPH will take the lead on invasive *H. influenzae* infection case investigations in children <15 years of age. This includes filling out the official case report form and making disease control recommendations. This will be done in collaboration with the LBOH. The MDPH will keep the LBOH informed of all significant developments and will request the assistance of LBOH as needed. For cases older than 15 years of age, the LBOH will usually take the lead.

Case Investigation

1. Ensure that typing of the *H. influenzae* isolate has been or is being done, preferably at the SLI. Call an epidemiologist at the MDPH Division of Epidemiology and Immunization at (617) 983-6800 or (888) 658-2850 for help.
2. Collect pertinent information (demographic, clinical, exposure setting, transmission setting, detailed immunization history, and other pertinent history on the case), and record on the MDPH *Invasive Haemophilus Influenzae Case Report Form* (found at the end of this chapter). To assess and prepare for the possibility of a Hib case, it is important to collect complete information about Hib vaccination history, whether the case had contact with another case of invasive Hib disease, whether a childcare setting was involved, and the ages and Hib vaccination histories of children exposed to the case in the household and the childcare center.
3. If Hib is identified as the etiologic agent, notify an epidemiologist at the MDPH Division of Epidemiology and Immunization at (617) 983-6800 or (888) 658-2850, and fax the case report form to ISIS, even if incomplete at that time. If non-type b is identified, no additional control measures are necessary and once completed, the case report form can be faxed to ISIS.
4. After completing the form, attach laboratory report(s) and fax or mail (in an envelope marked "Confidential") to ISIS. The confidential fax number is (617) 983-6813. Call ISIS at (617) 983-6801 to confirm receipt of your fax. The mailing address is:

**MDPH, Office of Integrated Surveillance and Informatics Services (ISIS)
305 South Street, 5th Floor
Jamaica Plain, MA 02130
Fax: (617) 983-6813**

5. Institution of disease control measures is an integral part of case investigation. It is the responsibility of the LBOH to understand, and if necessary, institute the control guidelines listed in Section 4.



Section 4:

CONTROLLING FURTHER SPREAD

NOTE: Control measures are for H. influenzae type b (Hib) infection only. There are no control measures for other types.

A. Isolation and Quarantine Requirements (105 CMR 300.200)

Minimum Period of Isolation of Patient

Isolate the case until 24 hours after initiating appropriate antimicrobial treatment.

Minimum Period of Quarantine of Contacts

Personal surveillance and prophylaxis with an appropriate antimicrobial when indicated by clinical situation of the contact or potential for future transmission. Otherwise, no restrictions.

B. Protection of Contacts of a Case

1. Isolate the case 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. Also, note that Hib disease does not necessarily confer immunity to subsequent disease. 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. For additional information, please refer to the table in Section 4B.
 - 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.
2. Antimicrobial prophylaxis for close contacts. Although several antibiotics are useful for *treatment* of invasive Hib disease and elimination of carriage in the case, rifampin is the appropriate drug to use for antibiotic *prophylaxis* of contacts. Several studies have shown that rifampin eradicates Hib carriage in $\geq 95\%$ of contacts of primary Hib cases, including children in daycare facilities.

When indicated, prophylaxis should be initiated as soon as possible. Most secondary cases in households occur in the first week after hospitalization of the index case. Prophylaxis of household contacts that begins ≥ 1 week after hospitalization of the case may still be of benefit, although initiation of prophylaxis beyond 4 weeks after that date is probably of limited utility. Prophylaxis is not recommended for pregnant women who are contacts because the effect of rifampin on the fetus has not been established.

Rifampin Prophylaxis Against Hib

Age Group	Dosage/Schedule
Children ¹	20 mg/kg PO QD x 4 days (Maximum: 600 mg/dose)
Adults	600 mg PO QD x 4 days

¹ The dose for infants <1 month of age is not established; some experts recommend lowering the dose to 10 mg/kg.

The risk of secondary disease in children attending childcare centers appears to be lower than that observed for age-susceptible household contacts, and secondary disease in childcare contacts is rare when all contacts are older than two years. Also, the efficacy of rifampin in preventing disease in childcare groups is not established. Nevertheless, rifampin prophylaxis is recommended in certain situations, as indicated in the table below.

Indications and Guidelines for Rifampin Chemoprophylaxis for Contacts of Index Cases of Invasive *Haemophilus influenzae* Type b (Hib) Disease

<p>Chemoprophylaxis Recommended</p>	<p>In certain index cases:</p> <ul style="list-style-type: none"> ◆ Index case, if younger than two years of age or member of a household with a susceptible contact and treated with regimens other than cefotaxime or ceftriaxone, chemoprophylaxis usually is provided just before discharge. <p>In certain household situations:</p> <ul style="list-style-type: none"> ◆ All household contacts (except pregnant women),¹ irrespective of age, in households where at least one contact is <4 years of age and is unimmunized or incompletely immunized. ◆ All household contacts (except pregnant women),¹ irrespective of age, in households where a child is <12 months of age and if the child has not received the primary series.² ◆ All household contacts (except pregnant women),¹ irrespective of age, in households with an immunocompromised child, regardless of the child's Hib immunization status. <p>In certain childcare situations:</p> <ul style="list-style-type: none"> ◆ Nursery and childcare center contacts, regardless of age, when ≥2 cases have occurred within 60 days.^{3,4}
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Chemoprophylaxis NOT Recommended

In certain individuals:

- ◆ Pregnant women.

In certain household situations:

- ◆ Occupants of households with no children <4 years of age, other than the index patient.
- ◆ Occupants of households when all household contacts 12–48 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.

In certain childcare situations:

- ◆ Nursery and childcare contacts of one index case, especially contacts >2 years of age.

1 Defined as persons residing with the index patient or nonresidents who spent ≥ 4 hours with the index case for ≥ 5 of the 7 days preceding the day of hospital admission of the index case.

2 The primary series consists of 2–3 doses, depending on the Hib vaccine formulation. See the table on the next page for more details.

3 Only 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 the daycare center or other setting during the time prophylaxis is given should also receive rifampin, as should supervisory personnel.

4 When 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.

5 Complete immunization is defined as having had ≥ 1 dose of conjugate vaccine at ≥ 15 months of age; 2 doses between 12–14 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.

3. 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 <5 years of age should be scheduled for completion of the recommended age-specific immunization schedule (see definition of “complete immunization” in Footnote 5 above). Infants should be placed on an accelerated schedule using minimum intervals between doses. Unvaccinated high-risk individuals >5 years of age should receive 1 dose.

The accelerated schedule for situations in which an incompletely vaccinated child has been exposed is as follows:

Hib Vaccine Recommendations for Children Not Up-To-Date

Age at Presentation	Previous Vaccination History	Recommended Regimen
7–11 months	0 doses	3 doses given with a 1 month minimum interval between dose 1 and dose 2; third dose given at least 2 months after dose 2, at 12–15 months
	1 dose of HbOC, PRP-T, or PRP-OMP ¹	1 or 2 doses of conjugate vaccine at 7–11 months (depending on age), with a booster dose given at least 2 months later, at 12–15 months
	2 doses of HbOC or PRP-T	1 dose of conjugate vaccine at 7–11 months, with a booster dose given at least 2 months later, at 12-15 months of age
12–14 months	0 doses	2 doses of any conjugate vaccine, with a minimum interval of 2 months ²
	1 dose before 12 months of HbOC, PRP-T, or PRO-OMP ¹	2 additional doses of any conjugate vaccine, with a minimum interval of 2 months ²
	2 doses before 12 months of HbOC, PRP-T, or PRP-OMP ¹	1 dose of any conjugate vaccine ²
15–59 months	Any incomplete schedule	1 dose of any conjugate vaccine ²
≥60 months	Any incomplete schedule	1 or 2 doses of any conjugate vaccine ³

1. HbOC (HibTITER®), PRP-T (ActHIB®), PRP-OMP (PedvaxHIB®).
2. For children 12–59 months of age with an underlying condition predisposing them to Hib disease (e.g., sickle cell disease, asplenia, HIV infection, AIDS, other immunosuppressive conditions and treatments) who are not immunized or have received only 1 dose of conjugate vaccine before age 12 months, 2 additional doses of licensed conjugate vaccine (separated by 2 months) are recommended. If they have received 2 doses before age 12 months, only 1 dose is recommended.

Note: Some experts recommend that a reinforcing dose of Hib vaccine should be administered to children receiving treatment for malignancy, to be administered three months after completion of treatment.

3. Children ≥60 months of age with an underlying condition predisposing them to Hib disease (e.g., sickle cell disease, asplenia, HIV infection, AIDS, other immunosuppressive conditions and treatments), who are not fully immunized, should receive 1 dose of Hib vaccine. Some experts recommend 2 doses (separated by 1–2 months) for those with HIV infection or IgG2 deficiency.
4. Conduct surveillance. Careful observation of exposed contacts, especially children <4 years of age, is essential. Those in whom a febrile illness develops should receive prompt medical attention, regardless of Hib vaccination status.

D. Preventive Measures

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

Please 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 >5 years of age, with underlying conditions predisposing them to Hib disease may need additional doses. Other relevant resources, including the MDPH's Immunization Guidelines and Massachusetts *Immunization Program-State Supplied Vaccines and Patient Eligibility Criteria*, are available through the MDPH Division of Epidemiology and Immunization at (617) 983-6800 or (888) 658-2850 or on the MDPH website at www.mass.gov/dph.

A *Haemophilus influenzae* type b Public Health Fact Sheet for the general public can be obtained from the MDPH Division of Epidemiology and Immunization or on the MDPH website at www.mass.gov/dph. Click on the "Publications and Statistics" link, and select the "Public Health Fact Sheets" section under "Communicable Disease Control."



ADDITIONAL INFORMATION

The following is the formal Centers for Disease Control and Prevention (CDC) surveillance case definition for invasive *H. influenzae* disease. It is provided for your information only, and should not affect the investigation or reporting of a case that fulfills the criteria in Section 2A of this chapter. (The MDPH and the CDC use the CDC case definitions to maintain uniform standards for national reporting.) For reporting to the MDPH, always use the criteria outlined in Section 2A of this chapter.

Note: The most up-to-date CDC case definitions are available on the CDC website at www.cdc.gov/epo/dphsi/casedef/case_definitions.htm.

Clinical Description

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

Laboratory Criteria for Diagnosis

Isolation of *H. influenzae* from a normally sterile site (e.g., blood or CSF, or less commonly, joint, pleural, or pericardial fluid).

Case Classification

Probable	A clinically-compatible case with detection of Hib antigen in CSF.
Confirmed	A clinically-compatible case that is laboratory-confirmed.

Note: Positive antigen test results from urine or serum samples are unreliable for diagnosis of H. influenzae disease.



REFERENCES

- American Academy of Pediatrics. [*Haemophilus influenzae* Infections.] In: Pickering L.K., ed. *Red Book: 2003 Report of the Committee on Infectious Disease, 26th Edition*. Elk Grove Village, IL, American Academy of Pediatrics; 2003: 293–301.
- CDC. Progress Toward Elimination of *Haemophilus influenzae* type b Disease among Infants and Children—United States, 1998–2000. *MMWR*. 2002; 51: 234–37.
- CDC. Case Definitions for Infectious Conditions Under Public Health Surveillance. *MMWR*. 1997; 46(RR-10).
- CDC. *Manual for the Surveillance of Vaccine-Preventable Disease*. CDC, 2002.
- Heymann D., ed. *Control of Communicable Diseases Manual, 18th Edition*. Washington, DC, American Public Health Association, 2004.
- MDPH. *Regulation 105 CMR 300.000: Reportable Diseases, Surveillance, and Isolation and Quarantine Requirements*. MDPH, Promulgated November 4, 2005.



FORMS & WORKSHEETS

Haemophilus influenzae (Invasive)

Haemophilus influenzae

(Invasive)

REPORT IMMEDIATELY



LBOH Action Steps

*This form does not need to be submitted to the MDPH with the case report form. It is for LBOH use and is meant as a quick-reference guide to *H. influenzae* case investigation activities.*

LBOH staff should follow these steps when *H. influenzae* is suspected or confirmed in the community. For more detailed information, including disease epidemiology, reporting, case investigation, and follow-up, refer to the preceding chapter.

*Note: Due to the potential severity of *H. influenzae* as well as national surveillance and reporting requirements, MDPH epidemiologists will usually take the lead on *H. influenzae* investigations in children <15 years of age. This includes filling out the official case report form and making disease control recommendations, in collaboration with the LBOH. MDPH epidemiologists will keep the LBOH informed of all significant developments and will request the assistance of the LBOH as needed. For cases older than 15 years of age, the LBOH will usually take the lead.*

Reporting

- Immediately notify the MDPH Division of Epidemiology and Immunization at (617) 983-6800 or (888) 658-2850 to report any confirmed or suspect case(s) of *H. influenzae*.

Case Investigation

- Work with the MDPH to ensure that appropriate clinical specimens are collected and submitted to the MDPH State Laboratory Institute (SLI) for confirmation.
- Ensure that typing of the *H. influenzae* isolate has been or is being done, preferably at the SLI.
- Fill out the case report form for non-type b cases (attach laboratory results).
- If *H. influenzae* type b is identified as the etiologic agent, work with the MDPH to obtain the information necessary to complete a case report form, including possible source of exposure, clinical information, vaccination history, and laboratory results. (MDPH will complete the form and submit to the MDPH Bureau of Communicable Disease Control, Office of Integrated Surveillance and Informatics Services [ISIS].)
- For non-type b cases, send the completed case report form (with laboratory results) to ISIS.

Prevention and Control

- If *H. influenzae* type b is identified as the etiologic agent:
 - Work with MDPH to institute isolation and quarantine requirements (*105 CMR 300.200*) and other control measures, as they apply to a particular case.

- Determine if there are high-risk contacts (e.g., infants, immunocompromised individuals) or susceptible individuals.
- Vaccinate if indicated (if not contraindicated).
- Consult with MDPH to see if chemoprophylaxis is recommended in a particular situation.
- Emphasize hand hygiene, respiratory hygiene, and cough etiquette.
- Conduct surveillance for two incubation periods.
- If type b is not identified, no additional control measures are necessary.

Managing *H. influenzae* type b in Childcare and School Settings

In addition to prevention and control measures described above:

- Assess immunization status of contacts, and ensure they are up-to-date for age.
- Notify and educate staff and students.
- Conduct surveillance of exposed contacts, especially those <4 years of age.
- Encourage ill individuals to stay at home.