



Haemophilus influenzae Invasive Disease

Haemophilus influenzae is transmitted person to person by inhalation of respiratory tract droplets or by direct contact with respiratory tract secretions¹. Children under 5 years of age who have not been vaccinated are at increased risk for invasive *H. influenzae* serotype b (Hib) disease². Before the introduction of effective Hib conjugate vaccines, Hib was the most common cause of bacterial meningitis in children in the United States¹⁻³.

The epidemiology of invasive *H. influenzae* disease in the United States has shifted in the post-Hib vaccination era¹. Nontypeable *H. influenzae* is now the most common cause of invasive *H. influenzae* disease in all age groups¹. In addition to invasive disease, nontypeable *H. influenzae* causes approximately 50% of episodes of acute otitis media and sinusitis in children and is a common cause of recurrent otitis media¹. *H. influenzae* type a (Hia) has emerged as the most common encapsulated serotype causing invasive disease, with a clinical presentation similar to Hib¹. In some North American Indigenous populations (eg, Alaska Native children, northern Canadian Indigenous children), the rate of invasive Hia infection has been increasing and there is evidence of secondary cases having occurred¹.

Certain factors can predispose an individual to invasive disease; including sickle cell disease, asplenia, HIV infection, certain immunodeficiency syndromes, and malignant neoplasms¹. Only Hib is preventable through vaccination².

A. Agent:

H. influenzae is a pleomorphic gram-negative coccobacillus¹⁻². The strains are either encapsulated (serotypes a-f) or unencapsulated (non-typeable)¹⁻². Encapsulated strains express 1 of 6 antigenically distinct capsular polysaccharides (a through f); nonencapsulated strains lack complete capsule genes and are designated nontypeable¹.

B. Clinical Description:

Invasive disease due to *H. influenzae* may produce any of several clinical syndromes, including pneumonia, bacteremia, meningitis, epiglottitis, septic arthritis, cellulitis, or purulent pericarditis; less common infections include endocarditis and osteomyelitis¹. Symptoms include fever, vomiting, anorexia, epiglottitis, nausea, irritability, lethargy, and/or meningeal irritation, consisting of bulging fontanel in infants or a stiff neck and back in older children². Otitis media or sinusitis may be a precursor of illness². Unencapsulated strains may cause noninvasive respiratory infections in healthy children, and community acquired pneumonia and chronic bronchitis in adults². Infections peak in September-December and March-May². The case-fatality rate of Hib is 3%-6% even with appropriate treatment².

C. Reservoirs:

Humans (asymptomatic carriers) are the only known reservoir of *H. influenzae*². It does not survive on inanimate surfaces or in the environment². The major reservoir of Hib is young infants and toddlers who carry the organism in the upper respiratory tract, which is the natural habitat of *H. influenzae* in humans¹⁻².

D. Mode of Transmission:

Mode of transmission is person-to-person by inhalation of respiratory tract droplets or by direct contact with respiratory tract secretions¹. In neonates, infection is acquired intrapartum by aspiration of amniotic fluid or by contact with genital tract secretions containing the organism. Most of the time *H. influenzae* is spread by people who have the bacteria in their noses and throats but who asymptomatic⁴.

E. Incubation Period:

Unknown¹.

F. Period of Communicability:

H. influenzae is communicable as long as organisms are present in the upper respiratory tract⁴. Communicability ends within 24–48 hours after the initiation of effective antibiotic therapy¹. The potential of spread of invasive *H. influenzae* is considered to be limited². However, certain circumstances, particularly close contact with a case (e.g., household, child care, or institutional setting) can lead to outbreaks or direct secondary transmission of the disease².

G. Susceptibility and Resistance:

H. influenzae susceptibility is universal and immunity may be acquired transplacentally, from prior infection, or from appropriate immunization². Hib disease is not common beyond 5 years of age². In the pre-vaccine era, peak attack rates occurred at 6–7 months of age, and most children acquired immunity by 5–6 years of age through asymptomatic infection².

3 or 4 doses of Hib are recommended at 2 months, 4 months, 6 months (depending on which Hib primary vaccine series is used), and 12–15 months^{5–6}.

Hib efficacy:

≥ 95% immune after primary series of vaccine (either 2 or 3 doses depending on the series)².

H. Treatment:

Patients with life-threatening *H. influenzae* illness should receive initial therapy with an effective third-generation cephalosporin (i.e. cefotaxime or ceftriaxone) or chloramphenicol in combination with ampicillin^{1–2}. Rifampicin is received prior to discharge from the hospital to ensure elimination of the organism from the nasopharynx¹.

Disease Management

I. Clinical Case Definition⁷:

Invasive disease due to *H. influenzae* may produce any of several clinical syndromes, including pneumonia, bacteremia, meningitis, epiglottitis, septic arthritis, cellulitis, or purulent pericarditis; less common infections include endocarditis and osteomyelitis.

J. Laboratory Criteria for Diagnosis⁷:

Confirmatory results

- Isolation of *H. influenzae* from a normally sterile body site (e.g., cerebrospinal fluid (CSF), blood, joint fluid, pleural fluid, pericardial fluid), OR
- Detection of *Haemophilus influenzae*-specific nucleic acid in a specimen obtained from a normally sterile body site, using a validated polymerase chain reaction (PCR) assay.

Presumptive results

- Detection of *Haemophilus influenzae* type b antigen in CSF.

Case Classification⁷

Confirmed	A case that meets either of the confirmatory laboratory criteria for diagnosis.
Probable	Meningitis with detection of Haemophilus influenzae type b antigen in CSF.

K. Classification of Import Status:

N/A

L. Laboratory Testing:

Biotyping of *H. influenzae* is accomplished with biochemical (PCR) testing or by matrix assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF), and confirmed with serologic agglutination (where applicable)^{6,10}. Gram stains and cultures are performed routinely by clinical laboratories. Serotyping of invasive *H. influenzae* isolates in children <5 years of age is done at the Arizona State Public Health Laboratory (ASPHL). Serotyping distinguishes encapsulated strains, including Hib, from unencapsulated strains, which cannot be serotyped⁶.

TEST	SPECIMEN TYPE	COLLECTION TIME Prior to the initiation of antibiotics.
Culture & PCR^{2,6}	Blood, CSF or less commonly, synovial, pleural or pericardial fluid.	Collect and culture as soon as possible – organism does not survive well
Gram stain^{2,6}	Blood, CSF or less commonly, synovial, pleural or pericardial fluid.	Collect as soon as possible

M. Assessing Laboratory Results:

The diagnosis of invasive disease is established by growth of *H. influenzae* from CSF, blood, synovial fluid, pleural fluid, or pericardial fluid⁶. Gram stain of an infected body fluid specimen can facilitate presumptive diagnosis². All *H. influenzae* isolates in children <5 years of age with invasive infection should be serotyped; this test determines whether an isolate is serotype b^{2,6}. Antigen detection may be used as an adjunct to culture, particularly in diagnosing *H. influenzae* infection in patients who have been partially treated with antimicrobial agents, in which case the organism may not be viable on culture^{2,6}.

N. Outbreak Definition:

An increase in cases of Hib, confirmed by ASPHL, in time or place that is greater than expected⁸. Two cases more than 14 days apart may be considered an outbreak if there is epidemiological evidence¹.

O. Time Frame⁹:Invasive *H. influenzae*

Providers	Submit a report to the Local Health Department within 1 working day after a case or suspect case is diagnosed, treated, or detected.
Schools, Childcare establishments, Shelters	Submit a report to the Local Health Department within 24 hours after detecting a case or a suspect case.
Laboratories	<ul style="list-style-type: none"> - Submit a report to ADHS within 1 working day after obtaining a positive test result. - Submit an isolate or specimen when a positive result is obtained for an individual <5 years of age within 1 working day. - For those >5 years of age, laboratories must submit an isolate or specimen, as applicable, only by request.
Local Health Agencies	<ul style="list-style-type: none"> - Notify ADHS within 1 working day after receiving a report. - Submit an epidemiologic investigation report to ADHS within 30 calendar days after receiving a report.

P. Forms:

- [ADHS Haemophilus influenzae Invasive Disease Investigation Form](#)

Q. Investigation Steps:For a local health agency⁸:**A.A.C. .R9-6-344 . *Haemophilus influenzae*: Invasive Disease**

A. Case control measures:

1. A local health agency shall:

- a. Upon receiving a report of a *Haemophilus influenzae* invasive disease case or suspect case, notify the Department within one working day after receiving the report and provide to the Department the information contained in the report;
- b. Conduct an epidemiologic investigation of each reported *Haemophilus influenzae* invasive disease case or suspect case; and
- c. For each *Haemophilus influenzae* invasive disease case, submit to the Department, as specified in Table 2.4, the information required under R9-6-206(D).

B. Contact control measures: A local health agency shall evaluate the level of risk of transmission from each contact's exposure to a *Haemophilus influenzae* invasive disease case and, if indicated, shall provide or arrange for each contact to receive immunization or treatment.

Confirm Diagnosis

Use current case definition to verify diagnosis.

Conduct Case Investigation⁶

- Epidemiological investigation report should be submitted in MEDSIS by filling out the full DSO.
- Collect case's demographic data and contact information:
 - Note any daycare attendance.
- Obtain information from the provider or medical chart.
 - If patient was hospitalized, obtain medical records, including admission notes, progress notes, lab report(s), and discharge summary.
- Examine the symptoms and clinical history, especially:

- Date of illness onset, type of infection, hospitalization records (reason, location and duration of stay), and outcome status (survived or date of death).
- Examine the laboratory testing that was done, especially:
 - Collection date, date first positive culture obtained, type of specimen from which organism isolated, gram stain results, and serotyping (if needed, coordinate sending isolate to the ASPHL).
- Travel history should be captured in the travel table in MEDSIS with dates of travel.

Conduct Contact Investigation^{1,6}

- Contacts to consider when dealing with a Hib investigation include:
 - Household and close contacts:
 - All persons residing with index case, **OR**
 - Nonresidents who spent >4 hours with the index case for at least 5 of the 7 days preceding the case's date of hospital admission.
 - Daycare: All direct caregivers and roommates of a case.
 - School: All close personal contacts, educators and classmates of case.
 - Incompletely immunized contacts that do not have:
 - At least 1 dose of conjugate vaccine at ≥15 months old; **OR**
 - 2 doses between 12 and 14 months old; **OR**
 - 2 or 3 dose primary series when <12 months old, followed by booster at ≥12 months old
- Interview case, case's family, or close acquaintances to identify activities 7 days prior to hospital admission:
 - Case's daily activities, living, and/or sleeping accommodations, association with young children or infants in childcare or nursery school.
- Identify and create a line listing of close contacts collecting information on each contact's:
 - Age, Hib Immunization status, occupation, school, or childcare attendance (include facility and location), any immunocompromised conditions.

Initiate Control and Prevention Measures

Isolate and institute droplet precautions for a *H. influenzae* meningitis or epiglottitis case or suspected case for 24 hours after the initiation of treatment⁷.

Isolation, Work and Child Care Restrictions

For a health care provider or an administrator of a healthcare institution⁸:

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A. Case control measures:

1. A diagnosing health care provider or an administrator of a health care institution, either personally or through a representative, shall isolate and institute droplet precautions for a *Haemophilus influenzae* meningitis or epiglottitis case or suspect case for 24 hours after the initiation of treatment.

Case Management^{1,6}

- Cases should be followed to determine compliance of control measures. Assure that the Hib case received a regimen including cefotaxime or ceftriaxone before returning to a child care or nursery school setting.
- Hib cases treated with a regimen other than cefotaxime or ceftriaxone should receive rifampin chemoprophylaxis prior to hospital discharge if:
 - Case is <2 years of age, OR
 - Case is a member of the household of a susceptible contact.

Contact Management, including Susceptible Contacts^{1,2,6}

- Evaluate the level of risk of transmission from each contact's exposure to a suspect case.
 - The level of urgency for follow-up depends on: serotype or when it will be available, ages of the contacts, Hib immunization status of contacts <4 years of age, and presence of immunocompromised contacts <18 years of age, regardless of vaccination status.
 - Not all Hib contacts will need chemoprophylaxis but all should be:
 - Informed about their risk of disease and benefits of vaccination.
 - Educated on the unknown incubation period and the need to seek immediate medical attention if febrile illness or other symptoms develop.
- Rifampin chemoprophylaxis use should be evaluated on an individual basis.
- The following guidelines are presented for Hib infections:
 - For household and close contacts meeting the following criteria, rifampin is recommended for all household and close contacts:
 - Households with ≥ 1 contact younger than 4 years of age who is unimmunized or incompletely immunized, OR
 - Households with a child <12 months of age who has not received the primary Hib series, OR
 - Households with an immunocompromised individual <18 years of age, regardless of immunization status.
 - For child care establishments:
 - ≥2 cases of invasive Hib disease occur within 60 days: rifampin prophylaxis is recommended for all attendees and staff.
 - All unimmunized and underimmunized children should receive one dose of vaccine and are recommended to complete their age-specific immunizations schedule.
- Rifampin is generally not recommended in the following circumstances:
 - For household or close contacts with no children ≤ 4 years of age other than the index case.
 - For household or close contacts that are:
 - 12–48 months of age that are immunocompetent and have completed their Hib immunization series, OR
 - <12 months of age and have completed the primary Hib series.
 - Child care establishment contacts when there is only 1 case of invasive Hib disease within 60 days.
 - Discretion for rifampin prophylaxis is with the local health agency in this situation; however, there is limited data on effectiveness.
 - For pregnant women.

R. Outbreak Guidelines:

Refer to the general outbreak guidelines section for general information on conducting an outbreak investigation.

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