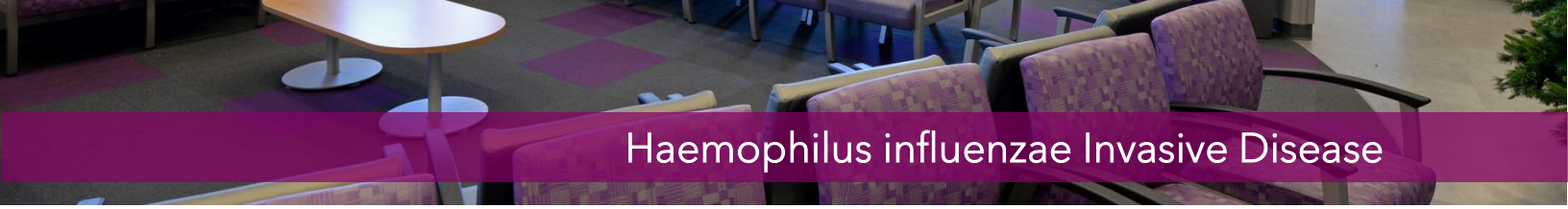

Haemophilus influenzae Invasive Disease

Haemophilus influenzae is transmitted person to person by inhalation of respiratory tract droplets or by direct contact with respiratory tract secretions[1]. Children under 5 years of age who have not been vaccinated are at increased risk for invasive *H. influenzae* serotype b (Hib) disease[2]. Before the introduction of effective Hib conjugate vaccines, Hib was the most common cause of bacterial meningitis in children in the United States[1–3]. Certain factors can predispose an individual to invasive disease; including sickle cell disease, asplenia, HIV infection, certain immunodeficiency syndromes, and malignant neoplasms[1]. Only Hib is preventable through vaccination[2].

A. Agent:
H. influenzae is a pleomorphic gram-negative coccobacillus[1–2]. The strains are either encapsulated (serotypes a-f) or unencapsulated (non-typeable)[1–2]. It is generally aerobic but can grow as a facultative anaerobe[2].

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 osteomyelitis[1]. 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 children[2]. Otitis media or sinusitis may be a precursor of illness[2]. Unencapsulated strains may cause noninvasive respiratory infections in healthy children, and community acquired pneumonia and chronic bronchitis in adults[2]. Infection peaks in September-December and March-May[2]. The case-fatality rate of Hib is 3%-6% even with appropriate treatment[2].

C. Reservoirs:
Humans (asymptomatic carriers) are the only known reservoir of *H. influenzae*[2]. It does not survive on inanimate surfaces or in the environment[2]. 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 humans[1–2].

D. Mode of Transmission:
Mode of transmission is person-to-person by inhalation of respiratory tract droplets or by direct contact with respiratory tract secretions[1]. In neonates, infection is acquired intrapartum by aspiration of amniotic fluid or by contact with genital tract secretions containing the organism[1]. Most of the time *H. influenzae* is spread by people who have the bacteria in their noses and throats but who asymptomatic[4].

E. Incubation Period:
Unknown[1]

F. Period of Communicability:
H. influenzae is communicable as long as organisms are present in the upper respiratory tract[4]. Communicability ends within 24–48 hours after the initiation of effective antibiotic therapy[1]. The potential of spread of invasive *H. influenzae* is considered to be limited[2]. 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 disease[2].

G. Susceptibility and Resistance:
H. influenzae susceptibility is universal and immunity may be acquired transplacentally, from prior infection, or from appropriate immunization[2]. Hib disease is not common beyond 5 years of age[2]. 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 infection[2].

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 nasopharynx[1].

I. Clinical Case Definition[7]:

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 Diagnosis[7]:

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 Classification[7]	
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[6]. 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 serotyped[6].

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 fluid[6]. Gram stain of an infected body fluid specimen can facilitate presumptive diagnosis[2]. 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:

Diagnosis or detection of 1 or more cases of Hib, confirmed by ASPHL, within a 14-day period[8]. Two cases more than 14 days apart may be considered an outbreak if there is epidemiological evidence.

O. Time Frame[9]:

Invasive *H. influenza*

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	- 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	- 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 agency[8]:

A.A.C. R9-6-339. *Haemophilus influenzae*: Invasive Disease

A. Case control measures:

1. A local health agency shall:
   a. Upon receiving a report under R9-6-202 or R9-6-203 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 Investigation[6]

- 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 epiglottis case or suspected case for 24 hours after the initiation of treatment[7].

Isolation, Work and Child Care Restrictions

For a health care provider or an administrator of a health care institution[8]:

A.A.C. R9-6-339. *Haemophilus influenzae*: Invasive Disease

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 will it 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:

For patients with invasive Hib disease, droplet precautions are recommended for 24 hours after initiation of effective antimicrobial therapy[7].

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