Haemophilus influenzae, Invasive Disease (including Type B)

1. **Agent**: *Haemophilus influenzae* is an encapsulated (types a-f) and non-encapsulated or "non-typeable" Gram-negative rod. Immunization prevents only serotype b (Hib) infection. Before effective vaccination, one in 200 children developed invasive Hib disease by age 5 and Hib was the most common cause of childhood bacterial meningitis.

2. **Identification**:

   a. **Clinical presentation:**
   - Non-typeable strains generally can affect the respiratory tract with milder disease including conjunctivitis and otitis media
   - Encapsulated *H. influenzae* causes invasive diseases including sepsis, meningitis, bacteremia, epiglottitis, pneumonia, osteomyelitis, pericarditis, peritonitis, or septic arthritis.

   b. **Differential Diagnosis**: Other bacterial or viral agents of meningitis, sepsis, or pneumonia.

   c. **Diagnosis**: Isolation of organisms from cerebrospinal fluid, blood, joint aspirate or other normally sterile site. Diagnosis can also be made by several rapid methods for capsular antigen detection.

3. **Incubation**: Unknown.

4. **Reservoir**: Human.

5. **Source**: Nose and throat secretions of case and/or carriers.

6. **Transmission**: Person-to-person by inhalation of respiratory droplets or by direct contact with respiratory tract secretions from nasopharyngeal carrier or case patient. Neonates can become infected by aspiration of amniotic fluid or by contact with genital tract secretions containing the organism.

7. **Communicability**: Individuals are contagious as long as organisms are present in nose and throat.

8. **Specific Treatment**:

   a. Initial therapy for children with invasive *H influenzae* infection is a 3rd/4th generation cephalosporin (cefotaxime or ceftriaxone) and can be narrowed according to susceptibilities are identified. Therapy depends on the type and severity of infection
   b. Dexamethasone is beneficial for treatment of infants and children with Hib meningitis to diminish the risk of hearing loss, if administered before or concurrently with the first dose of antimicrobial agent(s).
   c. Decolonization: For individuals who do not receive at least one dose of a cephalosporin and are younger than 2 years of age, they should receive rifampin prophylaxis for decolonization after their therapy is completed as described for close contacts below.

   Chemoprophylaxis for close contact:
   The risk of invasive Hib disease is increased among un- or under-immunized household contacts <4 years of age. Factors that predispose to invasive disease include sickle cell disease, asplenia, HIV infection, certain immunodeficiency syndromes, and malignant neoplasms.

   Prophylaxis should be initiated as soon as possible. Additionally, clinicians may consider chemoprophylaxis of contacts of index cases of invasive H. influenzae disease while serotyping is being processed in order to avoid delays. See **Contact section**.

9. **Immunity**: Immunity is age-dependent and associated with the presence of circulating bacterial antibody. Vaccination with any of the polysaccharide Hib vaccines is highly effective in preventing invasive infections.

REPORTING PROCEDURES

1. **Reportable (with all serotypes)**. (Title 17, Section 2500, *California Code of Regulations*). Report within 1 working day of identification of case or suspected case by mail, telephone, fax, or electronic transmission. **Ordinarily, only suspected cases under 5 years of age are to be investigated. In some instances, the state will recommend investigation of a case that is older.**

2. **Report Form**: **INVASIVE *HAEMOPHILUS INFLUENZAE* DISEASE CASE REPORT (PM 401).**

3. **Epidemiologic Data**:

   a. Source of specimen.

   b. Serotype of isolate.

   c. Location of infection.

   d. Hib immunization history only for cases under age ten years and known to be due to serotype b, including manufacturer and lot number of each vaccine dose.

CONTROL OF CASE, CONTACTS & CARRIERS

Public Health Nursing Protocol:

Home visit is required – a face to face interview is required.

Refer to "Public Health Nursing Home Visit REQUIRED Algorithm" (B-73 Part IV Public Health

Investigate cases of invasive Hib disease on the day of report. Non-invasive cases including conjunctivitis and positive sputum culture without pneumonia or epiglottitis, and cases confirmed not to be serotype b do not require investigation.

CASE:
Precautions: Respiratory secretion precautions should be taken until 24 hours after initiation of appropriate treatment.

CONTACTS:

See **Case Report Form (PM 401).** In summary:

Care of Exposed People
Secondary cases of Hib disease have occurred in unimmunized or incompletely immunized children exposed in a childcare or household setting to invasive Hib disease. Such children should be observed carefully for fever or other signs/symptoms of disease. Exposed young children in whom febrile illness develops should receive prompt medical evaluation. Indications and guidelines for chemoprophylaxis in different circumstances are summarized in the **Table 1**.

CARRIER:

Nasopharyngeal carriage studies should not be used as a guide for implementation of chemoprophylaxis. Carriage of the disease has not been proven to correlate with risk of the disease. Furthermore, performing such a study would delay implementation of chemoprophylaxis.

PREVENTION-EDUCATION

1. Concurrent disinfection of fomites contaminated with nose and throat discharges. Assure the separation and ventilation of living and sleeping quarters.

2. Several Hib vaccines are licensed for infants beginning at 2 months of age. Follow the recommended vaccine schedule for series and booster doses. (See **Table 2**)

3. Un-immunized or incompletely immunized children, under the age of 24 months who develop invasive Hib disease should complete the recommended vaccine schedule beginning 1-2 months after acute illness.

DIAGNOSTIC PROCEDURES

Few laboratories in LAC perform serotyping of *H. influenzae* isolates any more. Request laboratories to forward all sterile-site isolates from all patients to the Public Health Laboratory for serotyping.

Culture and sensitivities
The diagnosis of invasive disease is established by the growth of H. influenzae from a normally sterile body site (e.g., cerebrospinal fluid (CSF), blood, joint fluid, pleural fluid, pericardial fluid, peritoneal fluid, subcutaneous tissue fluid, placenta, and amniotic fluid). Gram stain can facilitate presumptive diagnosis. All isolates should be tested for antimicrobial susceptibility.

Polymerase chain reaction (PCR) detection
Although culture is the gold standard for confirming H. influenzae, real-time PCR is an accepted alternative. Real-time PCR assays are available to detect DNA of all six H. influenzae serotypes in blood, CSF, or other clinical specimens. A major advantage of PCR is that it allows for detection of H. influenzae from clinical samples in which the organism could not be detected by culture methods, such as when a patient has been treated with antibiotics before a clinical specimen is obtained for culture.

Serotyping
All H. influenzae isolates associated with invasive disease in children <5 years of age should be serotyped to identify the strain, monitor epidemiologic trends, and differentiate between type b and other serotypes for which control measures are not required. The six encapsulated types have distinct capsular polysaccharides that can be differentiated by slide agglutination with type-specific antisera.

Antigen detection
The type b capsular antigen can be detected in body fluids, including urine, blood, and CSF of patients. Antigen detection may be used as an adjunct to culture, particularly in the diagnosis of patients who have received antimicrobial agents before specimens are obtained for culture. Methods for antigen detection include latex agglutination and counterimmunoelectrophoresis. If Hib antigen is detected in CSF but a positive result is not obtained from culture or PCR, the patient should be considered as a probable Hib case and reported as such. Because antigen detection tests can be positive in urine and serum of persons without invasive Hib disease, persons who are identified exclusively by positive antigen tests in urine or serum should not be reported as cases.

Table 1: Indications and Guidelines for Rifampin Chemoprophylaxis for Contacts of Index Cases of Invasive *Haemophilus Influenzae* Type b (Hib) Disease[a]

Chemoprophylaxis Recommendations:

- For all household contacts[b] in the following circumstances:
  - Household with at least 1 child younger than 4 years who is unimmunized or incompletely immunized[c]
  - Household with a child younger than 12 months who has not complete the primary Hib series
  - Household with an immunocompromised child, regardless of that child's Hib immunization status or age
  - For all preschool and child care center contacts with 2 or more cases of Hib invasive disease have occurred within 60 days
  - For index patient, if younger than 2 years or members of a household with a susceptible contact and treated with a regimen other than cefotazime, chemoprophylaxis as the end of therapy for invasive infection

Chemoprophylaxis Not Recommended:

- For occupants of households with no children younger than 4 years other than the index patient
- For occupants of households when all household contacts are immunocompetent, all household contacts 12 through 28 months of age have completed their Hib immunization series, and when household contacts younger than 12 months have completed their primary series of Hib immunizations
- For preschool and childcare contacts of 1 index case
- For pregnant women

[a] Similar criteria may be used for Hia; however, the criteria for Hib immunization are not applicable.
[b] Defined as people residing with the index patient or nonresidents who spent 4 or more hours with the index patient for at least 5 of the 7 days preceding the day of hospital admission of the index case
[c] Complete immunization is defined as having had a least 1 dose of conjugate vaccine at 15 months of age or older; 2 doses between 12 and 14 months of age; or the 2- or 3-dose primary series when younger than 12 months with a booster dose at 12 months of age or older.

Table 2. Recommended Regimens for Routine *Haemophilus influenzae* Type b (Hib) Conjugate Immunization for Children Immunized at 2 Months Through 4 Years of Age[a]

Vaccine Product	Primary Series	Booster Dose	Catch-up Doses[b]
PRP-T (ActHIB, Sanofi Pasteur)	2, 4, 6 mo	12 through 15 mo	16 mo through 4 y
PRP-T (Hiberix, GlaxoSmithKline)	2, 4, 6 mo	12 through 15 mo	16 mo through 4 y
PRP-OMP (PedvaxHIB, Merck)[c,d]	2, 4 mo	12 through 15 mo	16 mo through 4 y
Combination vaccine			
DTaP-IPV-Hib (Pentacel, Sanofi Pasteur)	2, 4, 6 mo	12 through 15 mo	16 mo through 4 y
DTaP-IPV-Hib-HepB (Vaxelis, Sanofi Pasteur, Merck & Co, Inc)	2, 4, 6 mo	Use other Hib containing vaccine for booster, at least 6 months after last priming dose	

PRP-T indicates polyribosylribotol phosphate-tetanus toxoid; OMP, outer membrane protein complex from *Neisseria meningitidis;* DTaP, diphtheria and tetanus toxoids and acellular pertussis; IPV, inactivated poliovirus vaccine; Hep B, hepatitis B vaccine.

[a] See text and Table 3.10 for further information about specific vaccines and Table 1.10 (p 37) for information about combination vaccines.

[b] See Catch-up Immunization Schedule **(https://redbook.solutions.aap.org/SS/Immunization_Schedules.aspx)** for additional information.

[c] If a PRP-OMP(PedvaxHIB) vaccine is not administered as both doses in the primary series, a third dose of Hib conjugate vaccine is needed to complete the primary series.

[d] Preferred for American Indian/Alaska Native children.