

# *Haemophilus Influenzae* Invasive Disease (under age 5 years)

## 1. DISEASE REPORTING

### A. Purpose of Reporting and Surveillance

1. To correctly identify the serotype of invasive *Haemophilus influenzae* (HI) organisms in children under 5 years old.
2. To monitor the effectiveness of immunization programs and vaccines and to assess progress toward elimination of pediatric *H. influenzae* serotype B (Hib) invasive disease.
3. To identify children exposed to Hib cases and closely observe them for signs of illness.
4. To recommend antibiotic prophylaxis and/or immunization to appropriate contacts of Hib cases.
5. To identify additional cases and establish risk factors for cases of non-Hib invasive *H. influenzae* disease.

### B. Legal Reporting Requirements

1. Health care providers: **immediately notifiable to local health jurisdiction; only cases under 5 years old are reportable**
2. Health care facilities: **immediately notifiable to local health jurisdiction; only cases under 5 years old are reportable**
3. Laboratories: **immediately notifiable to local health jurisdiction; only cases under 5 years old are reportable**; specimen submission is required — culture, from sterile sites only, when type is unknown (2 business days); see Section C2 below
4. Local health jurisdictions: notifiable to the Washington State Department of Health (DOH Communicable Disease Epidemiology (CDE) within 7 days of case investigation completion or summary information required within 21 days

### C. Local Health Jurisdiction Investigation Responsibilities

1. Begin investigation on the same day as notification.
2. Contact laboratories as soon as possible after a case is reported to assure that **all** *H. influenzae* isolates are submitted to Washington State Public Health Laboratories for serotyping.

**Note:** The need to correctly identify the serotype of *H. influenzae* isolates from children under 5 years old with invasive disease has increased because Hib has become a rare disease.

3. Identify close contacts of patients with Hib and recommend antibiotic prophylaxis as appropriate within 24 hours.
4. Report all *confirmed* and *probable* cases to CDE. Complete the *Haemophilus influenzae*

case report form (<http://www.doh.wa.gov/Portals/1/Documents/5100/210-027-ReportForm-Hflu.pdf>) and enter the data into the Washington Disease Reporting System (WDRS). Note that **all** cases of invasive *H. influenzae* disease in children under 5 years old are reportable regardless of serotype.

## 2. THE DISEASE AND ITS EPIDEMIOLOGY

Prior to the introduction of effective conjugate vaccines in 1988 and the recommendation for routine vaccination, *H. influenzae* serotype b (Hib) was the most common cause of bacterial meningitis and was a major cause of other invasive bacterial disease (including epiglottitis) in young American children. Invasive disease is markedly age dependent, with peak rates at age 6–18 months. One child in 200 developed invasive Hib disease by the age of 5 years. From 1989 to 2000 there was a 99% reduction in Hib disease among children younger than 5 years of age. Between 2000 and 2004, the average incidence of invasive Hib disease in this age group was 0.14 cases per 100,000 in the United States. Data from active surveillance sites suggest an expected rate of invasive disease due to non-type-b *H. influenzae* (non-Hib invasive *H. influenzae* disease) to be 0.9 per 100,000 children younger than 5 years. This rate can be used as a surveillance indicator for monitoring the completeness of invasive *H. influenzae* case reporting.

### A. Etiologic Agent

*Haemophilus influenzae* is a small, gram-negative coccobacillus bacterium. There are at least six serotypes of *H. influenzae* (designated types a–f) distinguished by their capsular antigens, as well as unencapsulated (nontypeable) strains. *H. influenzae* serotype b (Hib) was responsible for 95% of invasive *H. influenzae* infections among children younger than 5 years of age in the prevaccine era. Meningitis occurred in approximately two thirds of children with invasive Hib disease resulting in hearing impairment or severe permanent neurologic sequelae in 15–30% of survivors. Approximately 4% of all invasive Hib cases were fatal.

### B. Description of Illness

Invasive disease caused by *H. influenzae* can affect many organ systems. Meningitis is the most common clinical manifestation. Bacteremia, periorbital or other cellulitis, epiglottitis (which may cause life-threatening airway obstruction), septic arthritis, osteomyelitis, pericarditis and pneumonia are other manifestations of invasive *H. influenzae* disease. Onset of symptoms is usually abrupt, and may include fever, headache, lethargy, anorexia, nausea, vomiting, irritability or laryngeal stridor, depending on the system involved. 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 history of recent upper respiratory tract infection may facilitate invasion. Having had a recent cochlear implant procedure also has been identified as a possible risk factor for invasive disease.

In the prevaccine era, Hib could be isolated from the nasopharynx of 0.5%–3% of normal infants and children but was not commonly found in adults. *H. influenzae* organisms can colonize the nasopharynx and may either be transient or remain for months in the absence of symptoms (asymptomatic carriage). Thus, isolates from sputum or other non-sterile sites are *not* indicative of invasive disease.

Non-invasive upper respiratory tract diseases, including otitis media, sinusitis, and bronchitis, are often caused by nontypeable strains of *H. influenzae*. Asymptomatic carriage of *H. influenzae* organisms, especially the nontypeable strains, can be common; the organism can be recovered from the nasopharynx of 40 to 80% of children.

**C. Haemophilus influenzae in Washington State**

In 2000, due to the dramatic reduction in the rate of invasive Hib disease that followed the implementation of routine childhood immunization in 1990, Washington State mandated reporting of invasive *H. influenzae* disease due to any serotype. Annually, from 2005 through 2014 DOH received 4 to 11 reports of invasive *H. influenzae* disease due to all serotypes in children under 5 years of age with two deaths, as compared to 1986 when there were 319 reports of invasive disease due to serotype b only, most in young children, with 11 deaths in that year alone.

From 2005-2014, a total of 68 cases of invasive *H. influenzae* disease were reported to DOH. Of these, 13 cases were due to Hib. Isolates from an additional 4 cases were not tested for serotype and so those cases must be considered as possible Hib cases. The remaining 51 reported cases had invasive *H. influenzae* disease due to other identified serotypes or the isolates were non-typeable. The immunization status of these cases is shown in the table below. Among the five Hib cases considered UTD for vaccine, none were old enough to have had the opportunity to finish the full childhood series: 2 cases had received just one dose, and 1 case had received two doses at the time of onset, and 2 cases had underlying conditions putting them at high-risk.

<b>Immunization Status of Washington State cases of invasive <i>Haemophilus influenzae</i> disease 2005-2014 by Serotype</b>						
<b>Serotype</b>	<b>No. cases</b>	<b>Up-to-date for age for Hib vaccine?</b>				<b>% UTD</b>
		<b>Too young (&lt;2mos)</b>	<b>No</b>	<b>Yes</b>	<b>Unknown</b>	
Type B	13	3	5	5	0	38%
Non-B	22	1	6	13	2	59%
Nontypeable	29	10	6	13	0	45%
Unknown serotype	4	2	0	2	0	50%
<b>All serotypes</b>	<b>68</b>	<b>16</b>	<b>17</b>	<b>33</b>	<b>2</b>	

**D. Reservoir**

Humans (cases and carriers)

**E. Modes of Transmission**

*H. influenzae* organisms are transmitted person to person by inhalation of respiratory droplets or by direct contact with respiratory tract secretions. Unimmunized children less than 4 years old are considered to be at increased risk of invasive Hib disease, especially if they have had prolonged close contact with another child with invasive Hib disease. Other predisposing factors are conditions such as sickle cell anemia and HIV infection that lead to compromise of the immune system. The risk of secondary disease among household contacts is age

dependent and estimated to be 4% for children less than 2 years of age, 1.5% for children 2 to 3 years of age, 0.1% for children 4–5 years of age, and 0% among immunocompetent contacts over the age of 6 years. The overall risk of secondary disease in the child care setting seems to be less than that seen in households.

#### F. Incubation Period

Because persons who acquire *H. influenzae* infections are often asymptotically colonized, the incubation period is unknown but probably short, possibly 2–4 days. Most secondary cases in households occur during the first week after hospitalization of the index case although some secondary cases do occur later.

#### G. Period of Communicability

The exact period of communicability is unknown. A person is communicable as long as the organism is present in discharges from the nose or throat. This may be a prolonged period, even without active nasal discharge. Communicability ends within 24–48 hours after initiation of appropriate chemoprophylaxis. Note, however, that treatment of invasive disease does not necessarily eradicate the organism from the nasopharynx. Chemoprophylaxis for the purpose of eliminating nasopharyngeal carriage should be given to the index case with invasive Hib disease just before discharge from the hospital if younger than two years of age or if the case lives in a household with a susceptible contact and has been treated for invasive disease with a regimen other than cefotaxime or ceftriaxone.

#### H. Treatment

Initial therapy for children with meningitis potentially caused by Hib includes cefotaxime or ceftriaxone. Alternative therapies are meropenem or the combination of ampicillin and chloramphenicol administered intravenously. For antimicrobial treatment of epiglottitis, arthritis, and other clinical syndromes due to invasive *H. influenzae* infections, including infections caused by strains other than serotype b, recommendations are similar. Duration of therapy is usually a minimum of 10 days; longer duration of therapy may be indicated in complicated cases.

### 3. CASE DEFINITIONS

#### A. Clinical Description

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

#### B. 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 *H. influenzae* from a normally sterile site (e.g., blood or cerebrospinal fluid [CSF] or, less commonly, joint, pleural, or pericardial fluid)

### C. Case Definition (2015)

*Probable:* meningitis with detection of *H. influenzae* serotype b (Hib) antigen in CSF

*Confirmed:*

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

### D. Comments

**In Washington, only cases under 5 years of age must be reported.**

Positive antigen test results from urine or serum samples are unreliable for diagnosis of *H. influenzae* disease. Because antigen detection tests can be positive in urine and serum of person without invasive Hib disease, a case that is identified exclusively by positive antigen tests in urine or serum should not be reported as a true case, but can be considered a suspect case if clinical symptoms are compatible with invasive bacterial disease.

Isolates of *Haemophilus influenzae* are important for serotype and antimicrobial susceptibility testing.

## 4. DIAGNOSIS AND LABORATORY SERVICES

### A. Diagnosis

Confirming the diagnosis of invasive *H. influenzae* disease requires culturing *H. influenzae* or detecting *Haemophilus influenzae*-specific nucleic acid in a specimen obtained from a body site which is normally sterile (e.g., CSF, blood, joint fluid, pleural effusion, pericardial effusion, peritoneal fluid, subcutaneous tissue fluid, placenta, and amniotic fluid). All *H. influenzae* isolates from normally sterile sites in children under 5 years old are required to be submitted to PHL for serotyping and antimicrobial susceptibility testing.

### B. Tests Available at Washington State Public Health Laboratories (PHL)

PHL provide isolate confirmation and serotyping for *H. influenzae*. Clinical laboratories should be contacted promptly for each reported case to assure that all pediatric *H. influenzae* isolates are forwarded to PHL.

Note that PHL require all clinical specimens have two patient identifiers, a name **and** a second identifier (e.g., date of birth) both on the specimen label and on the submission form. Due to laboratory accreditation standards, specimens will be rejected for testing if not properly identified. Also include specimen source and collection date.

### C. Specimen Collection

Isolates should be submitted to PHL on media that support growth. In the event of an outbreak, contact Communicable Disease Epidemiology (877-539-4344 or 206-418-5500) for assistance in determining which additional specimens should be collected for laboratory

study. Include the correct microbiology form with all specimens:

<http://www.doh.wa.gov/Portals/1/Documents/5230/302-013-Micro.pdf>.

## 5. ROUTINE CASE INVESTIGATION

### A. Evaluate the Diagnosis

Review the clinical presentation, risk factors for exposure, and immunization status of the patient. Assure that laboratories submit all *H. influenzae* isolates obtained from a sterile site in children under 5 years old to Washington State Public Health Laboratories for confirmation and serotyping.

### B. Identify Source of Infection

Usually, identification of the source of infection is not possible because asymptomatic persons can carry the organism in their nose and throat. It is important to verify whether any household or child care contacts have had any illness suggestive of *H. influenzae*-caused invasive disease within the previous 60 days.

### C. Identify Potentially Exposed Persons

While awaiting the serotype result:

1. Identify children younger than 4 years of age who are household or childcare contacts of patients and assess their immunization status. This will help identify persons who should receive antimicrobial prophylaxis if *H. influenzae* serotype b (Hib) disease is confirmed, or who should be immunized. See recommendation for contact management in Section 6 if the serotype is determined to be type b.
2. Determine whether the case had prolonged contact with other children under 2 years of age in a child care setting in the week prior to onset of illness. Secondary transmission in child care centers is rare if all the contacts of the case are older than 2 years of age.

If the serotype is determined to be type b, see recommendation for contact management in Section 6. If the serotype b case attends a child care also refer to Section 7.

### D. Environmental Evaluation — None

## 6. CONTROLLING FURTHER SPREAD

The following recommendations to control further spread pertain only to cases of *H. influenzae* invasive disease due to serotype B (Hib).

### A. Infection Control Recommendations / Case Management

1. Children with known or suspected *H. influenzae* serotype b (Hib) disease should be cared for using droplet precautions until 24 hours after initiation of appropriate antibiotic therapy.
2. Children with Hib disease who are younger than 2 years or who have a susceptible household contact should receive appropriate treatment to eliminate respiratory carriage for at least 24 hours before resuming contact with any susceptible persons. Treatment of Hib invasive disease with ceftriaxone or cefotaxime will also eradicate nasal carriage. Index patients who are treated with an antibiotic other than cefotaxime or ceftriaxone and

are aged <2 years should receive rifampin prior to hospital discharge.

3. Children developing Hib invasive disease before the age of 2 years may remain at risk of recurrent Hib disease. Any earlier doses of Hib vaccine received by such children should be disregarded. They should be immunized according to the age-appropriate schedule for unimmunized children beginning one month after onset, or as soon as possible thereafter.

## **B. Contact Management**

### **1. Antibiotic Prophylaxis**

**Household Contacts:** Chemoprophylaxis with rifampin is recommended for all members of the immediate household of Hib cases when the household includes members that meet either of the following:

- A child under age 4 years who is not fully immunized [See tables in section 8A for immunization recommendations.]
- An immunocompromised member under 18 years regardless of Hib vaccination status.

If indicated, antibiotic prophylaxis should begin as soon as possible. “Because some secondary cases occur later, initiation of chemoprophylaxis 7 days or more after hospitalization of the index case may be of some benefit” (Red Book 2009 p. 316).

**Child Care Contacts:** In general, chemoprophylaxis is not recommended for contacts of a single case of Hib in a child care center. However, when two or more cases have occurred within 60 days and unimmunized or incompletely immunized children are in attendance at a child care facility, rifampin prophylaxis should be considered. When prophylaxis is indicated, it should be prescribed for all attendees, regardless of age or vaccine status, and for all child care providers. In addition, unimmunized or incompletely immunized children should receive a dose of vaccine and be scheduled to complete an age-specific catch up schedule.

The rifampin dosage is 20 mg/kg (maximum 600 mg) once daily for 4 days. For neonates (<1 month), the dose is 10 mg/kg once daily for 4 days. Rifampin is available in 150 mg and 300 mg capsules which can be mixed with applesauce, following the manufacturer’s instructions. A limited number of pharmacies specialize in compounding and can make a liquid suspension for young children. Rifampin chemoprophylaxis is not recommended for pregnant women. Those taking rifampin should be informed that gastrointestinal upset, orange discoloration of urine, discoloration of soft contact lenses, and decreased effectiveness of oral contraceptives can occur.

For additional information regarding indications for rifampin chemoprophylaxis for contacts of patients with Hib disease, please see the Red Book 2009 Report of the Committee on Infectious Disease pp. 316–17.

Chemoprophylaxis is **not** recommended for contacts of patients with invasive disease caused by non-type b strains of *H. influenzae*.

### **2. Education**

If children under 4 years old are potentially exposed to a patient with invasive Hib disease, their parents or guardians should be instructed to monitor their children for signs

of illness (e.g., fever, lethargy, irritability, loss of appetite, vomiting), and to seek medical care immediately should any illness occur. Most secondary cases in households occur during the first week after hospitalization of the index case although some secondary cases have occurred later.

### 3. Active Immunization

Because of the length of time necessary to develop antibodies, vaccination does not play a major role in the management of contacts. However, unvaccinated or incompletely vaccinated children who are contacts of persons with Hib should receive a dose of Hib vaccine as soon as possible and be scheduled to complete the series.

### C. Environmental Measures — None

## 7. MANAGING SPECIAL SITUATIONS

### A. Case Attends Child Care (*H. influenzae* invasive disease due to serotype b [Hib] only)

Ascertain if the case was in any child care setting during the week prior to onset.

(The overall risk of secondary disease in child care settings seems to be less than that in households, and is rare when all child care contacts are older than 2 years.)

1. The operator of the facility should be asked about other cases of meningitis or other suspect invasive disease occurring among other children during the past 2 months.
2. The parents of children in the same classroom as the case should be notified (preferably in writing) of the occurrence of Hib disease in the facility. The notice should advise parents to:
  - monitor their children carefully for signs of illness such as fever, irritability, lethargy, and loss of appetite; and
  - seek medical care immediately should such symptoms occur.
3. Instruct the child care operator to notify the local health jurisdiction immediately if another child becomes ill with similar symptoms. When 2 or more cases of Hib have occurred within 60 days and unimmunized or under-immunized children attend the child care facility, rifampin prophylaxis for workers and attendees is generally recommended.
4. Chemoprophylaxis is **not** recommended for contacts of cases of invasive *H. influenzae* disease due to serotypes other than b.

## 8. ROUTINE PREVENTION

### A. Immunization Recommendations

*Haemophilus influenzae* serotype b (Hib) vaccine is recommended for all children. The primary series consists of either 3 doses given at 2, 4 and 6 months or 2 doses given at 2 and 4 months depending on the type of vaccine. A booster dose is recommended at 12–15 months of age.



**Table 1. Hib monovalent conjugate vaccines currently available and recommended regimens for routine vaccination of children in the United States.**

Licensed vaccine	Trade name	Primary Series	Booster Dose
PRP-T	ActHIB	2, 4, 6 months	12-15 months
PRP-OMP	PedvaxHIB	2, 4 months	12-15 months
PRP-T	Hiberix	Not licensed for primary series	12-15 months

**Table 2. Combination vaccines currently available and recommended regimens for routine vaccination of children in the United States.**

Licensed vaccine	Trade name	Primary Series	Booster Dose
PRP-OMP + HepB	COMVAX	2, 4 months	12-15 months
PRP-T + DTaP+IPV	Pentacel	2, 4, 6 months	12-15 months

**\*Note:** An additional combination vaccine, Hib-MenCY-TT, is available for vaccination of children aged 2-23 months who are at increased risk for meningococcal disease. See <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6324a2.htm>.

**Table 3. Recommended schedule for Hib conjugate vaccine administration among previously unvaccinated children.**

Age at first dose	Primary Doses	Booster Dose
<12 months	2-3* doses, 1 month apart	At 12-15 months**
12-15 months	2 doses, 2 months apart	NR
>15 - 72 months	1 dose	NR
>72 months	NR	NR

**\*Note:** 2-3 doses depending on whether PRP-T or PRP-OMP vaccine was used

**\*\*Only necessary if 3 primary doses received before age 12 months**

Tables reproduced from: Centers for Disease Control and Prevention. Manual for the Surveillance of Vaccine-Preventable Diseases. Chapter 2: *Haemophilus influenzae* type b (Hib), Briere, E, Mayer, L, Messonnier, N., 2014.

For more information regarding the types of Hib vaccines and recommended schedules for different Hib vaccines, see: <https://www.cdc.gov/vaccines/vpd/hib/index.html>

## B. Prevention Recommendations

Vaccination is the best way to protect against invasive disease caused by *Haemophilus influenzae* serotype b.

**ACKNOWLEDGEMENTS**

This document is a revision of the Washington State Guidelines for Notifiable Condition Reporting and Surveillance published in 2002 which were originally based on the Control of Communicable Diseases Manual (CCDM), 17<sup>th</sup> Edition; James Chin, Ed. APHA 2000. We would like to acknowledge the Oregon Department of Human Services for developing the format and select content of this document.

**UPDATES**

January 2011:

The Legal Reporting Requirements section has been revised to reflect the 2011 Notifiable Conditions Rule revision.

In particular, labs are now required to immediately notify local health jurisdictions of *Haemophilus influenzae* in children under five years old and submit sterile site culture to PHL for serotyping.

Section 3C: Case classification changed; criteria for probable cases were updated to include language from the 2010 case definition.

January 2015:

Sections 3 and 4A updated to reflect new 2015 CSTE case definition which includes PCR as a confirmatory laboratory test.

Section 5.A. Updated language about rifampin use in index cases.

Section 5.B. Updated language about chemoprophylaxis of contacts.

Section 8.A. Updated vaccine recommendation section to include information about combination vaccines now available including Hib-MenCY-TT.