



## **Invasive *Haemophilus influenzae***

### **Invasive *Haemophilus influenzae* disease**

Causative bacterium: *Haemophilus influenzae*

- Gram ( - ) negative coccobacillus
  - Further classified into serotypes:
    - Non-typeable (unencapsulated strains)
    - Serotypes a through f (encapsulated strains)
      - *Haemophilus influenzae* serotype b (Hib) is the most pathogenic

### **Case definition**

- *Haemophilus influenzae* isolated from a normally sterile site: cerebrospinal fluid (CSF), blood, joint, pleural, pericardial fluid or another normally sterile site  
*Isolation from urine, sputum, abscesses or pharyngeal swabs does not meet the case definition.*  
*Gram-negative coccobacilli visualized on Gram stain of CSF or blood are suggestive of invasive *H. influenzae* infection, but this by itself does not meet the case definition.*

*H. influenzae* type b (Hib) infection is generally associated with meningitis, occult febrile bacteremia, pneumonia, epiglottitis, septic arthritis, and also with less serious infections such as otitis media and conjunctivitis. Non-b encapsulated strains and, less commonly, non-typeable unencapsulated strains can cause invasive disease similar to Hib.

### **Signs and symptoms of invasive *H. influenzae* disease**

Signs and symptoms depend on the clinical syndrome associated with invasive *H. influenzae*. Symptoms may commonly include:

- fever
- nausea/vomiting
- lethargy
- anorexia
- headache
- irritability
- epiglottitis
- stiff neck and back in older children
- bulging anterior fontanelle in infants (due to meningeal irritation)

### **Transmission**

Transmission occurs via direct contact with nasal and throat secretions. Transmission to neonates can occur intrapartum from aspiration of amniotic fluid or contact with genital tract secretions containing *H. influenzae*.

**Incubation period:** Unknown, but probably short (2-4 days)

**Period of communicability:** Patient is considered infectious for 7 days prior to onset and until at least 24 hours after the initiation of appropriate antibiotic therapy.

It is estimated that before the widespread use of the Hib conjugate vaccine, 2-4% of young children carried *H. influenzae* type b in their nose and throat without illness (compared to 1% colonization rate among vaccinated populations). While carriage of type b strains is uncommon, colonization without illness by unencapsulated non-typeable strains is much more prevalent (30-80%).

### **Priority for local public health response**

Upon identification of a confirmed or suspect case, do not wait for *H. influenzae* serotype information to begin the investigation of contacts. Serotype determination can take several days or longer from disease onset. **Assume the case has Hib and begin appropriate control measures.**

It is the responsibility of the clinician **and** the diagnosing laboratory to report a case of invasive *H. influenzae* **by telephone** to local and/or state public health officials as soon as possible. Reporting via the Wisconsin Electronic Disease Surveillance System (WEDSS) is not sufficient notification.

1. Ascertain clinical history of patient and how diagnosis was made. Determine or confirm:
  - Clinical signs and symptoms
  - Date of illness onset
  - Laboratory test results (specimen source, culture, Gram stain, antigen test)
    - Refer to *Case definition* on page 1
  - Dates and time of antibiotic treatment that patient received
    - Determine if antibiotic treatment was started prior to collection of specimens for culture. If the patient was seen as an outpatient prior to admission, check whether antibiotics were prescribed at that time.
  - Hib vaccination history (include the date, manufacturer and lot number for each vaccination)
2. Report by phone immediately (per Health Code, HFS 145) all potential cases of invasive *H. influenzae* disease to the Wisconsin Communicable Disease Epidemiology Section (CDES).
  - General number for CDES staff during weekdays: **(608) 267-9003**
  - Emergency number for on-call CDES staff after hours and on weekends: **(608) 258-0099**  
(This number is for local health departments and clinical practitioners only, please do not distribute to the public.)
3. Ensure that the diagnosing lab will send the bacterial isolate (if available) to the Wisconsin State Laboratory of Hygiene (WSLH) for serotype determination. Serotype results should be available within one day. However, serotyping results are rarely received within 48 hours of disease onset, so assume the case has serotype b (Hib) and use appropriate control measures until serotype information is available.
4. Identify all contacts and determine the names, ages, and Hib vaccination histories of contacts less than 5 years of age. Determine if index patient attended day care, and if there is an immunocompromised person in the household.
5. Advise direct contacts of case requiring prophylaxis (see *Contact investigation* on page 3).
6. Enhance surveillance for additional cases:
  - Rapidly investigate suspect cases
  - Alert physicians in area of case
7. Investigate potential links between cases.

### **Contact investigation – Who needs prophylactic treatment?**

*The following control measures apply to H. influenzae type b (Hib). Because of the risk to children and delays with serotype determination, all cases of invasive H. influenzae should be treated assuming the case has serotype b (Hib).*

*Given that most secondary cases in households occur during the first week after hospitalization of the index case, prophylaxis should be initiated as soon as possible.*

Identify contacts of the case patient during the 7 days before illness onset.

#### **Chemoprophylaxis is recommended for the following high-risk contacts:**

- All household contacts in households with at least one child < 4 years of age who is unimmunized or incompletely immunized (See *Recommended immunization schedule for persons aged 0 through 6 years* at: <http://www.cdc.gov/vaccines/recs/schedules/default.htm#child>)
- All household contacts in households with a child < 12 months of age who has not received the 2- or 3-dose primary series (See above link)
- All household contacts in households with a child who is immunocompromised, regardless of child's Hib immunization status and age
- Pre-school or child care contacts and staff when 2 or more cases of invasive Hib disease have occurred within 60 days

#### **Chemoprophylaxis is generally not recommended for the following groups:**

- Household contacts in households with no children < 4 years of age other than index patient
- Household contacts in households with children 12-48 months of age who have completed their Hib immunization series or with children < 12 months of age who have received the 2- or 3-dose primary series
- Pre-school or child care contacts and staff when the index case is the only case in the facility, especially if attendees are older than 2 years of age (secondary disease in child care contacts is rare when all contacts are > 2 years of age – Red Book, 2009)
- Pregnant women (Rifampin is contraindicated during pregnancy)

*Educate the parents of child contacts to monitor all children in the household for signs and symptoms of disease. A febrile child should be evaluated immediately. Children who have not been appropriately immunized for age should receive any required immunizations.*

*Unimmunized children who develop Hib infection before 24 months of age may not develop immunity and are at risk of developing a second episode of disease. They should be immunized with the Hib vaccine according to the age-appropriate schedule for unimmunized children (1 month after onset or as soon as possible thereafter).*

## **Chemoprophylaxis**

- Ideally, provide chemoprophylaxis to contacts within 24 hours of diagnosis of index case.
- Because some secondary cases may occur later, providing chemoprophylaxis 7 or more days after hospitalization of index patient may still be beneficial (Red Book, 2009).

## ***Antibiotic regimens***

The following regimens are appropriate for chemoprophylaxis of contacts.

<b>Agent*</b>	<b>Dose</b>	<b>Duration</b>	<b>Cautions</b>
<b><i>Rifampin*</i></b>			
	Neonates (< 1 month): dose not established; some experts recommend 10 mg/kg, p.o., q.d.	4 days	Not recommended during pregnancy
	Children ≥ 1 month: 20 mg/kg, p.o., q.d. (600 mg is maximum daily dose)	4 days	Stains urine and tears; avoid contact lens use
	Adults: 600 mg, p.o., q.d.	4 days	

\*Rifampin could decrease the effectiveness of oral contraceptives.

\*Rifampin should not be used in pregnant women, as its effect on the fetus has not been established, and it is teratogenic in laboratory animals (CDC and Red Book). The optimal prophylaxis during pregnancy is not clear based on currently available data. Ladhani et al. (2009) recommend providing rifampin prophylaxis to pregnant women when there is a vulnerable individual in the household because the benefits “outweigh any potential risks.” Although ceftriaxone is the alternative for the prophylaxis of pregnant women against meningococcal disease, there is not enough data to support its efficacy against *H. influenzae*; inform physician of this option. Intravenous or intramuscular ceftriaxone q.d. for 2 days has been recommended for people who are unable to tolerate rifampin or develop an adverse reaction (Ladhani et al., 2009).

**Ensure terminal prophylaxis of case patient.** Antimicrobial therapy of invasive *Haemophilus influenzae* with agents other than a third-generation cephalosporin (cefotaxime or ceftriaxone) might not reliably eliminate nasopharyngeal carriage of *H. influenzae*. If the patient is younger than 2 years of age and was not treated therapeutically with a third-generation cephalosporin, ensure that the patient receives rifampin to eliminate Hib colonization (terminal prophylaxis) prior to discharge from hospital. Chloramphenicol in combination with ampicillin may be used as an alternative empiric regimen (consultation with an infectious disease specialist is recommended when treatments other than a third generation cephalosporin are considered).

## **Roles and responsibilities during a case of invasive *H. influenzae* disease**

### ***Local Health Department (LHD)***

See *Priority for local public health response* on page 2

### ***Hospital Infection Preventionist (IP)***

1. Notify LHD about any confirmed or suspect cases of invasive *H. influenzae* by phone immediately. Provide LHD with details about the clinical history and laboratory diagnosis.
2. Ensure case patient receives terminal prophylaxis to eliminate carriage before release from the hospital.
3. Request that the laboratory send the bacterial isolate to the WSLH for serotype determination.

### ***Wisconsin State Laboratory of Hygiene (WSLH)***

1. Serotype the bacterial isolate.
2. Perform PCR, PFGE or antibiotic susceptibility testing on bacterial isolates if requested by CDES.
3. Report results to submitting laboratory and CDES.

### ***Wisconsin Communicable Disease Epidemiology Section (CDES)***

1. Coordinate investigations that are multi-jurisdictional.
2. Assist in determining which persons need chemoprophylaxis.
3. Enhance surveillance for additional cases, as needed. Provide templates of letters to the LHD (e.g., to healthcare providers, to parents of children in school or daycare).
4. Confirm that the bacterial isolate is received at the WSLH for serotype determination.
5. Review historical and prospective data and investigate links between cases.
6. Request PFGE analysis of select isolates when a possible link is identified.
7. Report *H. influenzae* surveillance data to the CDC.

General number for CDES staff during weekdays: **(608) 267-9003**

Emergency number for on-call CDES staff after hours and on weekends: **(608) 258-0099**

(Emergency number is for local health departments and clinical practitioners only, please do not distribute to the public.)

### **References**

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Mandell GL, Bennett JE, Dolin R. *Haemophilus influenzae* epidemiology and respiratory tract colonization. In: *Mandell, Douglas and Bennett's Principles and Practice of Infectious Diseases*. 7th ed. Maryland Heights, MO: Churchill Livingstone, 2009 (Vol. II, Chapter 225).