# Invasive Haemophilus influenzae Management



#### Invasive Haemophilus influenzae disease:

Caused by the bacterium *Haemophilus influenzae*, a Gram-negative coccobacillus.



- There are 6 identifiable types of *H. influenzae* (named a through f) and other non-identifiable types (called non-typeable).
- *H. influenzae* type b or Hib is the most pathogenic. Before the Hib vaccine, Hib disease was the leading cause of bacterial meningitis among children under 5 years of age in the United States.
- While H. influenzae can cause many illness types, we will be focusing on "invasive disease" which include sepsis and meningitis.

#### **SIGNS AND SYMPTOMS may include:**

Fever/chills

- Stiff/immobile neck
- Headache

Nausea/vomiting

Diarrhea

Photophobia (aversion to light)

- Altered mental status/anxiety
- Fatigue

· Shortness of breath

#### TRANSMISSION is through direct contact with respiratory droplets

People spread *H. influenzae* to others through their respiratory droplets, during close contact, or when a person coughs or sneezes. The majority of *H. influenzae* is spread by people who are not sick but have the bacteria in their nose and throat.





Asymptomatic carriage of Hib is uncommon; however, the non-b types are common colonizers of the respiratory tract. Transmission of these non-b types are frequent causes of ear infections, conjunctivitis, sinusitis, and bronchitis.

**INCUBATION PERIOD:** It is not known exactly how long it takes after *H. influenzae* bacteria enters a person's body for someone to get sick. It could take as little as a few days before symptoms appear.

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

The United States began using Hib vaccine for children in 1987 and for infants in 1990. Since then, the annual incidence of invasive Hib disease in children aged younger than 5 years decreased by **99%**.





#### **CASE DEFINITION:**

#### Confirmed

- 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 *H. influenza* specific nucleic acid in a specimen obtained from a normally sterile body site (CSF, blood, joint fluid, pleural fluid, pericardial fluid), using a validated polymerase chain reaction (PCR) assay

#### **Probable**

Meningitis with the detection of *H. influenzae* type b antigen in CSF\*

\*Positive antigen test results from urine or serum samples are unreliable for diagnosis of *H. influenzae* disease and should not be used as a basis for case classification.

Urine, sputum, bronchial lavage (BAL), eye, ear and throat specimens are not considered sterile sites.

#### **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. Specimens may not be sent and serotype determination can take several days from disease onset. Assume that the case has serotype b and begin appropriate control measures.

It is the responsibility of the clinician, infection control practitioner (IP) **and** the laboratory to ensure the reporting of a suspect case of meningococcal disease **by phone** to their local health department (LHD) and/or state public health staff as soon as possible. Entering the case into the Wisconsin Electronic Disease Surveillance System (WEDSS) is **not** sufficient notification.

## 1) Gather clinical history of the patient:

- Clinical signs and symptoms
- Date of illness onset
- Laboratory test results
  - $\Rightarrow$  Specimen source
  - ⇒ Gram stain results
  - ⇒ Culture results
  - ⇒ CSF analysis if applicable.
- Hib vaccination history (include the date, manufacturer and lot number for each vaccination)
   The "Search WIR" button will upload vaccine data into the WEDSS record.

- 2) Report by phone immediately (per Health Code, HFS 145) all suspected 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 LHDs and clinical practitioners only; please do not distribute this phone number to the public.)
- 3) Ensure that the diagnosing laboratory will send the bacterial isolate to the Wisconsin State Laboratory of Hygiene (WSLH) for serotype determination.
  - Serotype results should be available within one day of arriving at WSLH. However, serotyping
    results are rarely received within 48 hours of disease onset.
  - Assume that the case has serotype b (Hib) and try to determine exposures to unvaccinated children under 5 years of age.



- 4) Identify all contacts of the case, less than 5 years of age, with direct saliva contact in the 7 days prior to patient illness onset.
  - Determine the names, ages, and Hib vaccination histories.
  - Determine if the case attended day care (in home or facility run).
  - Identify if there is an immunocompromised person in the household.
- 5) Advise direct contacts of the case on how to acquire prophylaxis (see Contact investigation on page 4).
- 6) Enhance surveillance for additional cases.
  - Rapidly investigate additional suspect cases.
  - Consider alerting clinicians, health, and school officials in your area of the case, especially if the case had a lot of contacts in a group childcare or play environment.
- 7) Investigate potential links between any additional cases identified.
- 8) If there are multiple cases, investigate potential links between them.

CDES will help the LHD in situations where there are additional cases in other jurisdictions, counties, or states.

# Who needs prophylactic treatment?

The following control measures apply only 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 (Red Book, 2018-2021, p. 370).

#### Chemoprophylaxis is recommended for:

- All household contacts<sup>a</sup> in the following circumstances:
  - Households with at least 1 contact younger than 4 years who is unimmunized or incompletely Immunized.<sup>b</sup>
  - Household with a child younger than 12 months who has not completed the primary Hib series.
  - Household with a contact who is an immunocompromised child, regardless of that child's immunization status or age.
- Pre-school and child care center contacts when 2 or more cases of Hib invasive disease have occurred within 60 days (see text).
- The index patient, if younger than 2 years or member of a household with a susceptible contact and treated with a regimen other than cefotaxime or ceftriaxone, chemoprophylaxis at the end of therapy for invasive infection.

# Chemoprophylaxis is generally not recommended for the following groups:

- Occupants of households with no children younger than 4 years other than index patient
- Occupants of households when all household contacts are immunocompetent, all household contacts 12-48 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
- Preschool and child care contacts of 1 index case
- Pregnant women

<sup>&</sup>lt;sup>a</sup> 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.

b Complete immunization is defined as having had at least 1 dose of conjugate vaccine at 15 months of age or older; two 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.

# **Antibiotic regimens**

#### Chemoprophylaxis

- The risk of invasive Hib disease is increased among unimmunized household contact young than four years.
- Rifampin eradicates Hib from the pharynx in approximately 95 percent of carriers.
- Ideally, provide chemoprophylaxis to contacts within 24 hours of diagnosis of index case.
- Because some secondary cases may occur later, providing chemoprophylaxis seven or more days after hospitalization of index patient may still be beneficial (Red Book, 2018-2021, p.371).

#### **Antibiotic regimens**

The following regimens are appropriate for chemoprophylaxis of contacts.

AGENT	DOSE	DURATION	CAUTIONS
Rifampin*	Taken orally		
	Neonates (< 1 month): dose not established; some experts recommend Lowering dose to 10 mg/kg, p.o., q.d.	1 x per day for 4 days	
	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
	<b>Adults:</b> 600 mg, p.o., q.d.	4 days	Not recommended during pregnancy

<sup>\*</sup>Rifampin could decrease the effectiveness of oral contraceptives.

# Ensure terminal prophylaxis of case patient.

- Treatment of Hib disease with cefotaxime or ceftriaxone eradicates Hib colonization, eliminating the need for prophylaxis of the index patient.
- Antimicrobial therapy of invasive *H. influenzae* with agents other than cefotaxime or ceftriaxone might not reliably eliminate nasopharyngeal carriage of *H. influenzae*.
- Patients who did not receive at least 1 dose of cefotaxime or cephtriaxone and who are younger than 2 years should receive rifampin prophylaxis at the end of therapy for invasive Infection.

# Roles and responsibilities during a case investigation



#### **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.

The 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 this number to the public.)

There are several vaccines that can help prevent Haemophilus influenzae type b or Hib disease.

These vaccines do not provide protection against other types of <u>Haemophilus influenzae disease</u>.

CDC recommends Hib vaccination for all children younger than 5 years old in the United States. CDC does not recommend Hib vaccination for most people 5 years or older unless they:

- Have certain medical conditions and are unvaccinated
- Receive a bone marrow transplant

Talk with your or your child's doctor if you have questions about Hib vaccines.

Below are summaries of recommendations from CDC's Advisory Committee (ACIP) on Immunization Practices. For the full text of the recommendations, see <u>Haemophilus influenzae</u> type b (Hib) ACIP Vaccine Recommendations.

#### **Routine Vaccination of Infants and Children**

The Centers for Disease Control and Prevention (CDC) recommends routine administration of a conjugate Hib vaccine series beginning at age 2 months.

- Infants 2 through 6 months of age should receive either:
  - A 3-dose series of ActHIB®, Hiberix®, Pentacel®, or Vaxelis™
  - A 2-dose series of PedvaxHIB®
- You can administer the first dose as early as age 6 weeks.
- CDC recommends a booster dose of any licensed conjugate Hib vaccine at age 12 through 15 months.
  - Administer the booster dose at least 8 weeks after the most recent Hib vaccination.
  - The booster dose will be dose 3 or 4 depending on vaccine type used in the primary series.

#### **Contraindications and Precautions**

You should **not** administer Hib vaccines to:

- A person who has ever had a severe allergic reaction (e.g., anaphylaxis) after a previous dose
- A person who has a severe allergy to any vaccine component
- A person younger than 6 weeks

You may administer Hib vaccines, if you and the parent or patient deem the benefits of vaccination to outweigh the risks, to a person who has a moderate or severe acute illness with or without fever.

#### References:

American Academy of Pediatrics *Haemophilus influnezae* infections. In: RKimberlin DW, Brady MT, Jackson MA, Long SS, eds. *Red Book: 2018- Report of the Committee on Infectious Diseases.* 31st ed. Itasca, IL: American Academy of Pediatrics, 2018:367-375.

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Centers for Disease Control and Prevention. Recommendations and guidelines: 2010 Child and adolescent immunization schedules for persons aged 0-6 years and "catch-up schedule."

Available at: http://www.cdc.gov/vaccines/recs/schedules/default.htm#child.

CSTE. <u>Revision of the national surveillance case definition for invasive *Haemophilus influenzae* disease [7 pages]. CSTE position statement 14-ID-05. Atlanta, GA: CSTE; 2014.</u>

CDC. <u>Progress toward elimination of *Haemophilus influenzae* type b invasive disease among infants and children—United States, 1998–2000</u>. *MMWR Morb Mortal Wkly Rep* 2002;51(11):234–7.