

# ***Haemophilus Influenzae* (meningitis and invasive disease) !**

**Report immediately 24/7 by phone upon initial suspicion or laboratory test order**

## **PROTOCOL CHECKLIST**

- Enter available information into Merlin upon receipt of initial report
  - Review background on disease (see page 2), case definition (see page 4), and laboratory testing (see page 5)
  - Contact provider
  - Facilitate serotyping of *H. influenzae* isolates at Florida Bureau of Public Health Laboratories (BPHL)
    - Determine if the isolate is *H. influenzae* type b (Hib)
  - Interview patient's family or guardian
    - Review disease facts
      - Modes of transmission
      - Incubation period
      - Symptoms/types of infection
    - Ask about exposure to relevant risk factors
      - Exposure to a person with documented *H. influenzae* infection
      - H. influenzae* type B vaccination history
      - Patient with immunocompromised state – HIV, sickle cell, asplenia, malignancy
    - Determine if patient was hospitalized for reported illness
    - Document pertinent clinical symptoms and type of infection
    - Document close contacts\* and family members who may be at risk if Hib is identified.
  - Determine whether patient or symptomatic contact is in a sensitive situation (daycare)
    - Recommend exclusion for patients or symptomatic contacts
    - Recommend prophylaxis and immunization for close contacts\* to Hib as appropriate (see page 6)
  - Provide education on prevention through vaccination and prophylaxis as indicated
  - Address patient family's questions or concerns
- Follow-up on special situations, including exposed contacts or infected persons in sensitive situations
- Enter additional data obtained from interview into Merlin

## Haemophilus Influenzae

### 1. DISEASE REPORTING

#### A. Purpose of reporting and surveillance

1. To correctly identify the serotype of invasive *Haemophilus influenzae* organisms in children under five years old
2. To monitor the effectiveness of immunization programs and vaccines and to assess progress toward elimination of Hib
3. To identify persons exposed to Hib and recommend antibiotic prophylaxis and/or immunization to prevent invasive disease. (see page 6)
4. To establish risk factors for non-Hib cases

#### B. Legal reporting requirements

Laboratories and physicians are required to report persons with *H. influenzae* infection to the county health department (CHD) **immediately 24/7 by phone upon initial suspicion or laboratory test order.**

#### C. County health department investigation responsibilities

1. Begin investigation on the same day as notification.
2. Contact laboratories as soon as possible after a case is reported and request that the *H. influenzae* isolate be submitted to BPHL-Jacksonville for serotyping.
3. Identify close contacts\* of patients with Hib and recommend antibiotic prophylaxis and immunization as appropriate within 24 hours. (see page 6)
4. Report all probable and confirmed infections of *H. influenzae* disease in Merlin, **regardless of serotype** (H. INFLUENZAE, CODE 03841).
  - a. The CDC Active Bacterial Core Surveillance Case Report form is available at: [http://www.floridahealth.gov/diseases-and-conditions/disease-reporting-and-management/disease-reporting-and-surveillance/\\_documents/crf-active-bacterial.pdf](http://www.floridahealth.gov/diseases-and-conditions/disease-reporting-and-management/disease-reporting-and-surveillance/_documents/crf-active-bacterial.pdf)
  - b. Complete the extended data screen in Merlin.

### 2. THE DISEASE AND ITS EPIDEMIOLOGY

Prior to routine vaccination, Hib was the most common cause of bacterial meningitis and was a major cause of other invasive bacterial disease (including epiglottitis) in American children. Prior to the introduction of effective conjugate vaccines in 1988, one child in 200 developed *Haemophilus* disease by the age of five. From 1989 to 2000, there was a 99% reduction in Hib invasive disease among children younger than five years of age. The average incidence rate of Hib in this age group between 2000 to 2004 was 0.14 cases per

100,000. Data from active surveillance sites suggest an expected rate of invasive disease due to non-type-b *H. influenzae* to be 0.9 per 100,000 children younger than five years of age. 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 (nontypable) strains. *H. influenzae* type b (Hib) was responsible for 95% of invasive *H. influenzae* infections among children younger than five 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% to 30% of survivors. Approximately 4% of all 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 of invasive Hib disease. 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%–3.0% of normal infants and children but was not commonly found in adults. *H. influenzae* organisms colonize the nasopharynx and may 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 other, nonencapsulated strains of *H. influenzae*. Asymptomatic carriage of these organisms can be extremely common, especially the non-typeable strains, and can be recovered from the nasopharynx of 40%–80% of children.

**C. Reservoir**

Humans (cases and carriers)

**D. 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 four years-old are considered to be at increased risk of invasive Hib disease, especially

if they have had prolonged close contact with a child with invasive Hib disease. Other predisposing factors are conditions such as sickle cell anemia, asplenia, malignant neoplasms and HIV infection that compromise the immune system. The risk of secondary disease among household contacts is age dependent and is greatest among children less than one year of age (6%). Moreover, secondary attack rates among household contacts are estimated to be 3% for children less than two years of age and 2% for those four years old or less. The overall risk of secondary disease in the childcare setting seems to be less than that in households.

### **E. Incubation period**

Because persons who acquire *H. influenzae* infections are often asymptotically colonized, the incubation period is unknown but is probably short, possibly two to four days. Most secondary infections in households occur during the first week after hospitalization of the index patient, although some secondary infections occur later.

### **F. 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 which may be a prolonged period, even without active nasal discharge. Communicability ends within 24 hours after initiation of appropriate chemoprophylaxis. Note, however, that treatment of invasive disease does not necessarily eradicate the organism from the nasopharynx. Appropriate chemoprophylaxis for the purpose of eliminating nasopharyngeal carriage should be given to the index patient with invasive Hib disease just before discharge from the hospital.

### **G. 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. Antimicrobial treatment of other invasive *H. influenzae* infections is similar. Duration of therapy is usually a minimum of 10 days; longer duration of therapy may be indicated in complicated cases. For Hib disease, index patients who are treated with an antibiotic other than cefotaxime or ceftriaxone and are aged < 2 years should receive rifampin.

### **H. Prophylaxis**

Chemoprophylaxis with rifampin is recommended for *all* members of the immediate household of Hib cases when the household includes members that meet certain criteria (see page 6). **For invasive *H. influenzae* infections caused by serotypes other than b, no prophylaxis is needed for household contacts. When serotype information is delayed, or unknown, prophylaxis of close contacts\* is generally not recommended.**

### **I. *Haemophilus influenzae* type b in Florida**

From 1997 to 2011, there were 27 cases of invasive disease caused by Hib in those under the age of five. From 2007 to 2011, an average of one Hib case under the age of five per year was reported. During this same time frame a total of 910 invasive *H. influenzae* infections were reported.

### 3. CASE DEFINITION

#### 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

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

Confirmed: a clinically compatible case that is laboratory confirmed

Probable: a clinically compatible case with detection of *H. influenzae* type b antigen in CSF

#### D. Comment

Cases of all ages should be reported. Serotype should be determined for all *Haemophilus influenzae* isolates because Hib vaccines protect against serotype b organisms only. This testing is especially important for children less than 15 years of age to determine possible vaccine failure or failure to vaccinate. Positive antigen test results from urine or serum samples are unreliable for diagnosis of *H. influenzae* disease. Sputum cultures are not confirmatory as sputum is not obtained from a sterile site.

**Isolates from cases, especially those under the age of 15 years, must be sent to the Bureau of Public Health Laboratories (BPHL) for typing to determine if they are type b.**

### 4. LABORATORY TESTING

#### A. Criteria for diagnosis

Confirming the diagnosis of invasive *H. influenzae* disease requires culturing *H. influenzae* 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). *H. influenzae* isolates from normally sterile sites must be forwarded to the BPHL for serotyping or must retain a subculture of the isolate on suitable media for at least six months after receipt of the specimen in the laboratory.

#### B. Services available at the Bureau of Public Health Laboratories

BPHL can provide isolate confirmation and serotyping for *H. influenzae*. Clinical laboratories should be contacted for each reported case to assure that all *H. influenzae* isolates are forwarded to the BPHL. All submissions should be accompanied by a:

1. Clinical Lab Submission Form:  
[http://www.floridahealth.gov/diseases-and-conditions/disease-reporting-and-management/disease-reporting-and-surveillance/surveillance-and-investigation-guidance/\\_documents/dh1847clinicallabsubmissionform.pdf](http://www.floridahealth.gov/diseases-and-conditions/disease-reporting-and-management/disease-reporting-and-surveillance/surveillance-and-investigation-guidance/_documents/dh1847clinicallabsubmissionform.pdf)
2. Packaging and shipping
  - a. Flowchart: [http://www.floridahealth.gov/diseases-and-conditions/disease-reporting-and-management/disease-reporting-and-surveillance/surveillance-and-investigation-guidance/\\_documents/packagingflowchar0422051.pdf](http://www.floridahealth.gov/diseases-and-conditions/disease-reporting-and-management/disease-reporting-and-surveillance/surveillance-and-investigation-guidance/_documents/packagingflowchar0422051.pdf)
  - b. Flowchart Notes: [http://www.floridahealth.gov/diseases-and-conditions/disease-reporting-and-management/disease-reporting-and-surveillance/surveillance-and-investigation-guidance/\\_documents/packagingflowchartnotes0422051.pdf](http://www.floridahealth.gov/diseases-and-conditions/disease-reporting-and-management/disease-reporting-and-surveillance/surveillance-and-investigation-guidance/_documents/packagingflowchartnotes0422051.pdf)
3. Contact the regional laboratory liaison with questions:  
[http://www.floridahealth.gov/diseases-and-conditions/disease-reporting-and-management/disease-reporting-and-surveillance/\\_documents/investigationunitmap\\_11-22-13color.pdf](http://www.floridahealth.gov/diseases-and-conditions/disease-reporting-and-management/disease-reporting-and-surveillance/_documents/investigationunitmap_11-22-13color.pdf)

## **5. CASE INVESTIGATION**

### **A. Confirm 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 to BPHL for 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 childcare 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 young children (under the age of five) who are household or childcare contacts of patients and assess their immunization status. This will help identify persons who should receive antimicrobial prophylaxis if Hib disease is confirmed, or who should be immunized (see Section 6).
2. Determine whether the patient had prolonged contact with other children less than two years of age in a childcare setting in the week prior to onset of illness. If so, refer to Section 7. Secondary transmission in childcare centers is rare if all the contacts of the case are older than two years of age.

See recommendation for contact management in Section 6 if the isolate is determined to be Hib.

**D. Environmental evaluation—None****6. CONTROLLING FURTHER SPREAD**

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

**A. Infection control recommendations/case management**

1. Persons with known or suspected Hib disease should be cared for using droplet precautions until 24 hours after initiation of appropriate antibiotic therapy.
2. Persons with Hib disease who are younger than two years-old, 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. Treatment with meropenem, ampicillin or chloramphenicol does not eradicate carriage, thus, children receiving these antibiotics should be treated with rifampin.
3. Children developing Hib invasive disease before the age of two years are at increased risk of recurrent Hib disease. They should be immunized according to an age-appropriate schedule initiated as soon as possible during convalescence. Any earlier doses of Hib vaccine received by such children should be discounted.

**B. Contact management****1. Education**

If children under four years old are potentially exposed to a patient with 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 febrile illness occur. Most secondary cases in households occur during the first week after hospitalization of the index case although some secondary cases occur later.

**2. Antibiotic prophylaxis**

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

- A child under age four years who is not fully immunized (defined as at least one dose of conjugate vaccine at 15 months of age or older, or two doses at 12–14 months, or a two or three dose primary series at less than 12 months with a booster dose at 12 months or older);
- An infant that is less than 12 months of age who has not completed the primary Hib series;
- An immunocompromised child (< 18 years of age) regardless of this child's Hib immunization status.

In general, chemoprophylaxis is not recommended for contacts of a single case of Hib in a childcare center. However, rifampin chemoprophylaxis is recommended in childcare settings when two or more cases of invasive Hib disease have occurred within 60 days and unimmunized or underimmunized children attend the facility. Prophylaxis should be prescribed for all attendees, regardless of age or vaccine status, and for childcare providers.

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

The rifampin dosage is 20 mg/kg (maximum 600 mg) once daily for four days. For neonates (less than one month old) the dose is not established, some experts recommend lowering the dose to 10 mg/kg once daily for four days. Rifampin is available in 150 mg and 300 mg capsules, which can be mixed with applesauce, following the manufacturer's instructions. 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.

Antibiotic prophylaxis should begin as soon as possible. "Because some secondary cases occur later, initiation of chemoprophylaxis seven days or more after hospitalization of the index case may be of some benefit (*Red Book 2012*, Report of the Committee on Infectious Disease, p. 347)."

For additional information regarding indications for rifampin chemoprophylaxis for contacts of patients with Hib disease, please see the *Red Book 2012*, Report of the Committee on Infectious Disease, pp. 347-348.

\*Examples of **close contact** with H. flu patients include:

- a) Direct face-to-face contact with a symptomatic case patient during the contagious period; this includes household and immediate family members, boyfriends/girlfriends, and childcare contacts (those who spend many hours together or sleep under the same roof) or who are at increased risk for contact with respiratory secretions of the case patient.
- b) An obvious exposure that involves direct contact with respiratory, oral, or nasal secretions from a case patient during the contagious period (e.g., a cough or sneeze in the face, sharing eating utensils, sharing water bottles, kissing, mouth-to-mouth resuscitation, or performing intubation or nasotracheal suctioning without a mask). Health care workers who have not had direct contact with the case patient's nasopharyngeal secretions are not at increased risk, and prophylaxis is not indicated.
- c) Close proximity for a prolonged period of time with a case patient during the contagious period (i.e., sitting next to an infected individual for eight hours or more on an airplane). Risk of droplet exposure increases with longer duration and closer proximity of contact.

### 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 and be scheduled to complete the series.

### C. Environmental measures

None

## 7. MANAGING SPECIAL SITUATIONS

### A. Case attends childcare (*H. influenzae* type b only)

Ascertain if the patient was in any childcare setting during the week prior to onset. The overall risk of secondary disease in childcare settings seems to be less than that in households, and is rare when all child-care contacts are older than two years.

1. The operator of the facility should be asked about other attendees with meningitis or other suspect invasive disease occurring among other children during the past two months.
2. The parents of children in the same classroom as the patient 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. Identify un- or under-immunized children and instruct the parents to have immunizations updated as age appropriate. Documentation of receipt of age appropriate Hib vaccine is required for childcare entry and attendance.
4. Instruct the childcare operator to notify the CHD immediately if another child becomes ill with similar symptoms. When two or more infections of Hib have occurred within 60 days and un- or under-immunized children attend the child-care facility, rifampin prophylaxis for workers and attendees is generally recommended regardless of vaccine status.
5. 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* type b (Hib) vaccine is recommended for all children. The primary series consists of either three doses given at two, four and six months or two doses given at two and four months depending on the type of vaccine. A booster dose is recommended at 12–15 months of age. Fewer doses are recommended if the series is initiated at an older age.

For more information regarding the types of Hib vaccines and recommended schedules for different Hib vaccines, see <http://www.cdc.gov/vaccines/vpd-vac/hib/default.htm>.

**B. Prevention recommendations**

Vaccination is the best way to protect against invasive disease caused by Hib.

**9. REFERENCES**

- A. Heymann, D.L. (Ed.). (2008). *Control of Communicable Diseases Manual* (19<sup>th</sup> ed.). Washington: American Public Health Association.
- B. American Academy of Pediatrics. (2012). *Red Book: 2012 Report of the Committee on Infectious Diseases* (29<sup>th</sup> Ed.). Grove Village, IL: American Academy of Pediatrics.
- C. Briere EC, Rubin L, Moro PL, et al. (2014). Prevention and Control of *Haemophilus influenzae* Type b Disease: Recommendation of the Advisory Committee on Immunization Practices (ACIP). MMWR. 63(RR01);1-14.  
[http://www.cdc.gov/mmwr/preview/mmwrhtml/rr6301a1.htm?s\\_cid=rr6301a1\\_e](http://www.cdc.gov/mmwr/preview/mmwrhtml/rr6301a1.htm?s_cid=rr6301a1_e)

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