

## HAEMOPHILUS INFLUENZAE, INVASIVE DISEASE

### REPORTING INFORMATION

- **Class B:** Report by the close of the next business day after the case or suspected case presents and/or a positive laboratory result to the local public health department where the patient resides. If patient residence is unknown, report to the local public health department in which the reporting health care provider or laboratory is located.
- Reporting Form(s) and/or Mechanism: The Ohio Disease Reporting System (ODRS) should be used to report lab findings to the Ohio Department of Health (ODH). For healthcare providers without access to ODRS, you may use the [Ohio Confidential Reportable Disease Form](#) (HEA 3334, rev. 5/14)
- [CDC National Bacterial Meningitis and Bacteremia Case Report](#) (form 52.15, rev. 10/15) is available for use to assist in local disease investigation and contact tracing activities. Information collected from the form should be entered into the Ohio Disease Reporting System (ODRS) and not sent to the Ohio Department of Health (ODH), unless otherwise requested.
- Key fields for ODRS reporting include: for laboratory – antimicrobial resistance, specimen type, organism, and serotype; for clinical – type of infection; under epidemiology – daycare if <6 years old; for vaccination – patient receive Haemophilus influenzae type b (Hib) vaccine; and case contact information.

### AGENT

*Haemophilus influenzae* is a bacterium that has encapsulated (typable) or unencapsulated (nontypable) strains. Encapsulated strains express 1 of 6 antigenically distinct capsular polysaccharides (type a, b, c, d, e, or f). *Haemophilus influenzae* non-type b strains can cause invasive disease clinically similar to type b (Hib) disease (pneumonia, bacteremia, meningitis, epiglottitis, septic arthritis, cellulitis, or purulent pericarditis). Nontypable strains can also cause invasive disease but more commonly cause mucosal infections such as otitis media, conjunctivitis, and sinusitis.

Prior to the use of effective vaccines, *H. influenzae* type b (Hib) accounted for 95% of systemic *H. influenzae* infections in children. During the influenza pandemic of 1889-92, this organism was isolated from patients who died and was mistakenly claimed to be the cause of influenza. The organism was inappropriately designated *Haemophilus influenzae*. The actual cause of the influenza epidemic, the influenza virus, was not discovered until much later, in 1933. This explanation will aid persons who may confuse Hib, a bacterial disease, with the viral influenza infection commonly referred to as influenza or "flu." Invasive disease due to all types of *H. influenzae* is to be reported.

### CASE DEFINITION

#### Clinical Criteria

Invasive disease caused by *H. influenzae* may produce any of several clinical syndromes, including: meningitis, bacteremia, epiglottitis, pneumonia, cellulitis, purulent pericarditis, septic arthritis; less common infections include endocarditis and osteomyelitis

#### Laboratory Criteria for Diagnosis

- Detection of *H. influenzae* type b antigen in cerebrospinal fluid [CSF].
- Detection of *H. influenzae*-specific nucleic acid in a specimen obtained from a normally sterile site (e.g. blood or CSF), using a validated polymerase chain reaction (PCR) assay.

- Isolation of *H. influenzae* from a normally sterile site (e.g. blood or CSF) or, less commonly, joint, pleural or pericardial fluid).

### **Case Classification**

Probable: Meningitis with detection of *H. influenzae* type b antigen in CSF.

Confirmed: Isolation of *Haemophilus influenzae* from a normally sterile body site (e.g., cerebrospinal fluid [CSF], blood, joint fluid, pleural fluid, pericardial fluid) or 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.

Not a Case: This status will not generally be used when reporting a case, but may be used to reclassify a report if investigation revealed it was not a case.

### **Comment**

Positive antigen test results from urine or serum specimens are unreliable for diagnosis of *H. influenzae* disease.

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

## **SIGNS AND SYMPTOMS**

In unvaccinated children and infants too young to have completed the vaccine series, *H. influenzae* is a leading cause of bacterial meningitis in the United States. It is primarily a disease of children <5 years of age, although it is recognized as a pathogen in adults, particularly those >50 years of age with an underlying disease. Asymptomatic nasopharyngeal colonization with *H. influenzae* is common; occasionally it develops into symptomatic disease. Various types of illness may manifest as described below and are considered reportable invasive disease if the criteria above are met.

Meningitis: Infection of the membranes covering the brain. This is the most common and most serious type of infection due to invasive *H. influenzae*. The illness is usually preceded by an upper respiratory infection and associated otitis media is common. Typical symptoms of meningitis occur. The most common signs of illness are fever and altered central nervous system (CNS) function, including lethargy progressing to stupor or coma. Concurrent Hib infections such as pneumonia, arthritis, osteomyelitis and pericarditis may complicate the clinical picture. Appropriate antibiotic therapy reduces the mortality rate to 5%, but neurologic sequelae, such as hearing loss and language delay, mental retardation and cerebral palsy, occur in 25% - 35% of survivors. The disease occurs now in this country primarily in inadequately vaccinated children and among infants too young to have completed the primary series of vaccinations.

Epiglottitis: An infection and swelling of the epiglottis causing life-threatening airway obstruction. The typically infected person is 2-7 years of age, but illness may also occur in adults. The onset may be insidious, but is usually abrupt. The course is usually rapid, beginning with fever, sore throat and dyspnea. As the illness develops, the child is restless and anxious. Rapid respiratory obstruction results in death within a few hours if treatment is not sought immediately. The disease results in the epiglottis becoming bright red and swollen, resembling a cherry, until it obstructs the pharynx. The airway may need to be maintained by an artificial method. Bacteremia is present in most cases. Concomitant Hib disease, such as pneumonia and meningitis, is unusual but may occur.

Pneumonia: Typically occurs in children 4 months to 4 years of age, but *H. influenzae* has been increasingly recognized as the etiology of pneumonia in adults with primary lung disease or alcohol dependence. The child typically presents with consolidative pneumonia (often with pleural involvement) so severe that hospitalization is necessary. The onset is generally more insidious than other types of bacterial pneumonia. In almost 50% of *H. influenzae* pneumonia cases, there is evidence of infection elsewhere (meningitis, epiglottitis and otitis).

Pericarditis: A rare but important complication, primarily of pneumonia. Pericarditis is an inflammation of the pericardium, the saclike membrane that surrounds the heart. It can be triggered by many conditions. It may also be a purulent producing infection which is common with *H. influenzae*.

Cellulitis: Most often seen in young children, this *H. influenzae* disease frequently begins with an upper respiratory illness, followed by the acute onset of cellulitis. The involvement usually is on the cheek or in the periorbital region. The area is raised, warm and tender and generally has a distinctive reddish-blue color. The disease progresses rapidly over a few hours. Other *H. influenzae* disease (meningitis, arthritis) commonly complicates cellulitis.

Osteomyelitis: Bone infections due to *H. influenzae* are often associated with pre-existing conditions, such as sickle cell anemia.

Septic arthritis: *H. influenzae* is the most common cause of septic arthritis in children 2 months to 2 years of age. Large, weight-bearing joints are typically affected. There may be decreased mobility, pain on movement and swelling of the joint or signs can be more subtle. Residual joint dysfunction may occur, even with adequate antibiotic therapy.

Bacteremia (Septicemia) without focus: Children may develop upper respiratory infections, fever, pharyngitis and lethargy. Examination by a physician is often non-diagnostic. While the child may appear mildly ill, laboratory tests confirm *H. influenzae* disease. These individuals may worsen rapidly and are at substantial risk for developing pneumonia or meningitis. Children with sickle cell disease or previous splenectomy are especially susceptible.

Endocarditis: A less common infection due to *H. influenzae* is an infection of the endocardium, the inner lining of the heart muscle and the heart valves.

Otitis media and conjunctivitis due to *H. influenzae* are not considered invasive disease and are not reportable unless associated with one of the preceding conditions.

## **DIAGNOSIS**

### **Source**

Humans are the only known host. The bacterium resides mainly in the upper respiratory tract, but is also found to a lesser extent on the mucosal surfaces of the eye and lower genital tract. Nasopharyngeal carriage with encapsulated type b strains (those which are most often isolated from children with systemic disease) ranges from 3% - 5%, but is substantially higher in "closed" populations of young children, such as child care centers, and may be as high as 50%. These individuals are usually asymptomatic. Occasionally an individual develops clinically apparent infection. Why certain individuals develop invasive disease is not fully understood; host resistance and virulence of the *H. influenzae* strain may be factors. Hib does not survive in the environment on inanimate surfaces.

### **Occurrence**

Disease due to *H. influenzae* occurs worldwide. The incidence of Hib disease has greatly decreased since the introduction of the Hib vaccine in 1990.

### **Mode of Transmission**

Spread is from person-to-person through airborne respiratory droplets, by direct contact with respiratory secretions or through recently contaminated fomites. Asymptomatic carriers may be a source of infection.

### **Hygiene**

Because Hib is spread through respiratory secretions, individuals (particularly in child care settings) should be educated in the necessity of adopting a consistent program of good hygiene practices. Disposable tissues and towels should be used; hand washing and disinfection procedures should be assessed.

### **Period of Communicability**

The exact period of communicability is unknown, but is thought to be as long as the organism is present. The infected person is non-communicable 24 hours after starting effective antibiotic therapy.

### **Incubation Period**

Unknown, it is thought to be short, probably 2-4 days.

## **PUBLIC HEALTH MANAGEMENT**

### **Case**

Every reported case of invasive *H. influenzae* disease should be evaluated immediately for a child care center/preschool connection, with management as discussed below. **All isolates for persons <5 years of age should be sent to the Ohio Department of Health (ODH) Laboratory for serotyping.** Leftover CSF or blood from patients with negative culture results who were given antibiotics prior to specimen collection can be sent for PCR testing to ODH laboratory. It is important to know how much disease, especially in children, is due to *H. influenzae* type b, regardless of the patient's vaccination status. Please complete the ODH Laboratory Microbiology Specimen Submission Form found at: <http://www.odh.ohio.gov/pdf/IDCM/frm2530.pdf> and the WI VPD Specimen Submission Form found at: <http://www.odh.ohio.gov/pdf/IDCM/frmwivpd.pdf>. Please call the VPD Epidemiology Program at 614/995-5599 to arrange for testing.

### **Treatment**

Without treatment invasive *H. influenzae* disease has a high mortality. The ill individual must seek immediate medical care. Hospitalization and antimicrobial therapy with newer third-generation cephalosporin agents or the combination of ampicillin and chloramphenicol are indicated. Some patients will require rifampin prophylaxis after they have received treatment antibiotics in order to eradicate nasal carriage of Hib, especially if the child will be in close contact with other young children, such as at a child care center.

Treatment course is usually 10-14 days.

Antimicrobial resistance to ampicillin is an increasing problem.

## **Isolation**

Hospitalized patients are placed in respiratory isolation until 24 hours after effective treatment is begun. Any child suspected of having a serious communicable disease in a child care setting should be immediately isolated from other children.

## **Contact Investigation for Invasive Nontypable or Non-Serotype B**

### ***H. influenzae* Disease**

There are no guidelines for control measures around cases of invasive nontypable or non-b *H. influenzae* disease. Chemoprophylaxis is not recommended for contacts of persons with invasive disease caused by nontypable or non-b *H. influenzae* because secondary disease is rare.

## **Comments**

Contact investigations can be difficult when the serotype has not yet been determined for the index case. It may take several days to determine the serotype. Therefore, when waiting for serotype results and determining whether chemoprophylaxis should be administered to contacts, vaccination history for the index case should be taken into consideration. If the index case has documentation of *Haemophilus influenzae* b (Hib) vaccine and resides in a vaccinated community, the risk is low for secondary transmission of Hib. Those at increased risk for invasive Hib disease are unimmunized and underimmunized infants and children and persons with immunocompromising conditions such as: sickle cell disease, asplenia, human immunodeficiency virus (HIV) infection, certain immunodeficiency syndromes, receipt of a hematopoietic stem cell transplant, or malignant neoplasms. Hence, it is important to determine if the index case has had any contact with individuals at high risk for invasive Hib disease. Administering chemoprophylaxis to those individuals at increased risk for Hib may be warranted in certain situations before serotype is identified and should be examined on a case-by-case basis. Consultation by a healthcare provider is also recommended.

## **Contact Investigation for *H. influenzae* Type B (HIB)\***

The following indications and guidelines for rifampin chemoprophylaxis for contacts of index cases of invasive *H. influenzae* type b (Hib) disease are from the *American Academy of Pediatrics' Red Book: 2015 Report of the Committee on Infectious Diseases, 30<sup>th</sup> Edition*. Please refer to this book for a more detailed explanation.

Chemoprophylaxis is recommended for all household contacts in the following circumstances:

- Household with at least 1 contact younger than 4 years of age who is unimmunized or incompletely immunized\*\*;
- Household with a child younger than 12 months of age who has not received the primary Hib series;
- Household with a contact who is an immunocompromised child, regardless of that child's Hib immunization status or age.

## **Comment**

Most secondary cases in households occur during the first week after hospitalization of the index case. Prophylaxis should be administered as soon as possible. However, some secondary cases can occur later so initiation of prophylaxis 7 days or more after hospitalization of the index patient still may be of some benefit.

Chemoprophylaxis is recommended for preschool school and child care center contacts when 2 or more cases of Hib invasive disease have occurred within 60 days and unimmunized or incompletely immunized children attend the child care facility or

preschool. Rifampin prophylaxis for all attendees (irrespective of their age and vaccine status) and child care providers should be considered. In addition, unimmunized or incompletely immunized children should receive a dose of vaccine and should be scheduled for completion of the recommended age-specific immunization schedule.

Data are insufficient on the risk of secondary transmission to recommend chemoprophylaxis for attendees and child care providers when a single case of invasive Hib disease occurs; the decision to provide chemoprophylaxis in this situation is at the discretion of the local health department.

Regardless of whether prophylaxis is given, ALL parents of children in a child care center where a case of Hib disease has been diagnosed should be notified to watch their child for symptoms (see sample parent letter, below). Exposed children in whom a febrile illness develops should receive prompt medical evaluation.

#### New Child Care Center Admissions

Prophylaxis is 90% - 95% effective in eradicating nasopharyngeal carriage. Therefore, regardless of whether prophylaxis is given, for a two-month period following the identification of the index case(s), parents of new enrollees should be informed of the Hib case(s) and signs and symptoms to watch for in their child.

#### Prophylaxing Child Care Center Staff Contacts

When rifampin is given, child care center staff in the same room should also receive prophylaxis. Adults should understand that they are at minimal risk for acquiring Hib disease, but may be carriers of Hib. Therefore, they should receive rifampin prophylaxis in order to protect the young children with whom they have contact.

In addition to discussing gastrointestinal (GI) and CNS side effects with staff, they should be warned that rifampin turns urine orange, stains soft contact lenses and may interfere with the effectiveness of oral contraceptives (alternative birth control methods should be used for the remainder of their oral contraceptive cycle). Rifampin may also interfere with other types of medications; therefore, if rifampin needs to be taken, individuals should check with their physician. Rifampin is not recommended for pregnant women.

Family, friends and siblings of the child care contacts do not need prophylaxis.

**Nasopharyngeal cultures** are of **no benefit** in determining who should receive rifampin. The index case(s) may return to the child care center after hospitalization when they feel well enough and after having received rifampin prophylaxis, if indicated.

Chemoprophylaxis is also recommended for the index case, if younger than 2 years of age or member of a household with a susceptible contact and treated with a regimen other than cefotaxime or ceftriaxone. In these situations, chemoprophylaxis is usually provided just before discharge from the hospital.

#### Recommended rifampin dosage for prophylaxis:

- Doses are given orally once a day for four days
- Each rifampin dose is: 20 mg/kg, with a maximum dose of 600 mg
- The dose for infants < 1 month of age is not established, but the *American Academy of Pediatrics' Red Book: 2015 Report of the Committee on Infectious Diseases, 30<sup>th</sup> Edition* says that some experts recommend lowering the dose to 10 mg/kg.
- For adults, each dose is 600mg

\*Contacts are persons residing with the index patient or nonresidents who spent 4 or more hours with the index case for at least 5 of the 7 days preceding the day of hospital admission of the index case. This time may be lessened in certain situations, such as when infants “share” secretions.

\*\* Complete immunization is defined as having had at least 1 dose of conjugate vaccine at 15 months of age or older; 2 doses between 12 and 14 months of age; or a 2- or 3-dose primary series when younger than 12 months with a booster dose at 12 months of age or older.

## **Prevention and Control**

### Hygiene

Because Hib is spread through respiratory secretions, persons (particularly in child care settings) should be educated about a consistent program of good hygiene practices. Disposable tissues and towels should be used and hand washing and disinfection procedures should be assessed.

### Vaccine

Vaccine is available against Hib disease. Refer to the ODH Vaccine Protocol Manual for details and updated recommendations. There is no evidence that receiving Hib vaccine helps to eradicate nasopharyngeal carriage. Therefore, in the event of an outbreak in a child care center, children who have received Hib vaccine should also be given rifampin. The vaccine should protect the child from invasive disease; the rifampin will protect others in the event the child is a carrier of Hib.

Ohio School Requirements: Vaccination is not required for school entry since Hib is not routinely given to children aged 5 years and older. Childcare facilities and preschools are recommended to follow the Advisory Committee on Immunization Practices (ACIP) guidelines and ensure that children are appropriately vaccinated with the last dose of vaccine being given when the child is between 12 to 15 months of age. Please see the Centers for Disease Control and Prevention (CDC) website for the most current ACIP recommendations: <https://www.cdc.gov/vaccines/hcp/acip-recs/index.html>.

## SAMPLE PARENT LETTER

Dear Parent or Guardian:

A child in our center has been diagnosed as having a disease caused by a bacterium called *Haemophilus influenzae* type b (Hib). The germ is often found in the nose and throat of healthy persons, but occasionally may cause serious illness. Unimmunized and underimmunized children less than four years of age and those with certain immunocompromising conditions such as: sickle cell disease, asplenia, human immunodeficiency virus (HIV) infection, certain immunodeficiency syndromes, receipt of a hematopoietic stem cell transplant, or malignant neoplasms have the highest risk of acquiring this disease. During the next month, if your child develops an illness with a fever, contact your physician IMMEDIATELY. Share this information with him or her.

The following are types of illness caused by Hib and what you should watch for:

- Meningitis is an inflammation of the covering of the brain and spinal cord. Signs of illness to watch for are fever, a change in behavior, loss of appetite, possible vomiting and stiff neck.
- Epiglottitis is an inflammation of the part of the throat that prevents food from entering the airway (epiglottis). Watch for fever with sudden trouble swallowing and trouble with breathing.
- Pneumonia is an inflammation of the lungs. Watch for fever, difficulty breathing and cough.
- Cellulitis is an inflammation of skin tissues, especially on the head (cheek or eye). Watch for fever and a warm reddish or reddish-blue swelling that grows in size quickly.
- Septic arthritis is inflammation of a joint. Watch for fever, pain when an arm or leg is moved or swelling of a joint.

These illnesses must be treated with antibiotics *quickly*. Again, if your child develops any of these signs of infection, CONTACT YOUR DOCTOR IMMEDIATELY.

Hib disease can be prevented by vaccine. Please visit the Centers for Disease Control and Prevention's (CDC) website for the most current vaccination recommendations <https://www.cdc.gov/vaccines/schedules/index.html>.



**What is *Haemophilus influenzae* type b (Hib) disease?**

*Haemophilus influenzae* type b is a bacterium that can cause a variety of different kinds of infections (for example, ear infections, sinus infections, pneumonia, blood stream infections, and infections of the covering of the spinal cord and brain). Before the introduction of an effective Hib vaccine in the late 1980's, Hib was the leading cause of bacterial meningitis (inflammation of the coverings of the spinal cord and brain) and other invasive bacterial diseases (for example, blood stream infections, pneumonia, and joint infections) among children less than 5 years of age.

**Who gets Hib disease?**

Hib disease can occur in any age group. Due to widespread use of Hib vaccine in children, very few cases of Hib in children are reported each year in Ohio. Hib is diagnosed more often in the elderly, in people who are immunocompromised and in incompletely or unvaccinated children.

**How is Hib disease spread?**

A person can get Hib disease by being around children or adults who may have the bacteria and not know it. The germs spread from person to person. If the germs stay in the person's nose and throat, the person probably will not get sick. But sometimes the germs spread into the lungs or the bloodstream and then Hib can cause serious problems.

**What are the symptoms of Hib disease?**

The symptoms depend on the location of the infection. For example, if an individual has Hib meningitis, the symptoms may include fever, lethargy, vomiting and a stiff neck.

**How soon do symptoms appear?**

The incubation period for Hib disease is unknown, but is probably less than one week.

**When and for how long is a person able to spread Hib disease?**

The contagious period varies. As long as the Hib organisms are present in an individual's nose and throat, that individual can spread the Hib bacteria to other persons (even if the individual does not have symptoms). If the individual is treated with antibiotics, though, the spread of Hib will stop 24 hours after the antibiotics were started.

**Does past infection with Hib disease make a person immune?**

Children who had Hib disease before 24 months of age may be at risk of getting Hib disease again. Children and adults who had Hib disease at 24 months of age or older are likely to be immune.

**What is the treatment for Hib disease?**

Antibiotics are used to treat Hib infections. Sometimes individuals exposed to a person with a Hib infection will be given antibiotics to prevent them from becoming infected with the Hib bacteria. (This is called antibiotic prophylaxis.)

**What are the possible complications associated with Hib disease?**

A certain proportion of individuals who get Hib meningitis suffer long-lasting neurologic problems, including deafness. Despite antibiotics, 2% to 5% of individuals who develop Hib meningitis die.

**What can be done to prevent the spread of Hib disease?**

All children should be immunized with an approved Hib vaccine beginning at two months of age. There are currently several Hib vaccines licensed by the U.S. Food and Drug Administration (FDA). Recommendations for scheduling of subsequent doses of Hib vaccine vary depending on the manufacturer of the vaccine. Thus, it is important to consult your physician or local health department about this. In addition, occasionally individuals who have had contact with a person with a Hib infection will need antibiotics to prevent them from developing Hib disease.