Invasive *Haemophilus influenzae*

H. flu

IMMEDIATELY REPORTABLE DISEASE

Per N.J.A.C. 8:57, health care providers and administrators shall immediately report **by telephone** confirmed and suspected cases of H. flu to the health officer of the jurisdiction where the ill or infected person lives, or if unknown, wherein the diagnosis is made. The health officer (or designee) **must immediately institute the control measures listed below in section 6, "Controlling Further Spread**," regardless of weekend, holiday, or evening schedules.

Directory of Local Health Departments in New Jersey and

Directory of After Hour Emergency Contact Phone Numbers for Local Health Departments in New Jersey, both available at:

http://www.nj.gov/health/lh/community/index.shtml#1

If the health officer is unavailable, the health care provider or administrator shall make the report to the New Jersey Department of Health by telephone to 609.826.5964, between 8:00 A.M. and 5:00 P.M. on non-holiday weekdays or to 609.392.2020 during all other days and hours.

Invasive *Haemophilus influenzae* (H. flu)

1 THE DISEASE AND ITS EPIDEMIOLOGY

A. Etiologic Agent

Haemophilus influenzae is a pleomorphic gram-negative coccobacillus that has encapsulated (typeable) or unencapsulated (nontypeable) strains. Encapsulated strains express 1 of 6 antigenically distinct capsular polysaccharides (a through f). The one that is most pathogenic, and that people are most familiar with, is *H. influenzae* type b (Hib). There is a vaccine that can prevent disease caused by **Hib**, but not the other types of *H. influenzae* bacteria. Before the introduction of the Hib conjugate vaccine, Hib invasive disease was the leading cause of bacterial meningitis among children younger than 5 years of age in the United States.

All invasive *H. influenzae* cases are **immediately reportable** to the New Jersey Department of Health (NJDOH), regardless of serotype.

B. Clinical Description and Laboratory Diagnosis

In spite of its name, *Haemophilus influenzae* (H. flu) bacteria do not cause influenza (the "flu"). *H. influenzae* non-type b strains can cause **invasive** disease clinically similar to type Hib disease (pneumonia, bacteremia, meningitis, epiglottitis, septic arthritis, cellulitis, or purulent pericarditis). Nontypeable strains can also cause invasive disease but more commonly cause **non-invasive** mucosal infections such as otitis media, conjunctivitis, and sinusitis. Only invasive disease is reportable to NJDOH, not non-invasive disease.

Laboratory diagnosis is typically made by isolation of the organism (culture) from normally sterile sites, such as blood or cerebrospinal fluid (CSF), or, less commonly, joint, pleural, or pericardial fluid. A list of normally sterile sites is available on the *Haemophilus influenzae* page on the NJDOH website located at:
http://www.nj.gov/health/cd/topics/haemophilus.shtml

Culture remains the gold standard laboratory test for identification of *H. influenzae* from normally sterile sites with virtually 100% specificity. However, a variety of laboratory tests are

available, including antigen detection by latex agglutination and polymerase chain reaction (PCR). PCR assays that can detect serotype are important since determining serotype is crucial for identifying potential outbreaks and determining appropriate public health responses, such as chemoprophylaxis for contacts of cases of Hib.

As per New Jersey Administrative Code (N.J.A.C.) 8:57-1.7(e), *H. influenzae* isolated from normally sterile sites **must** be submitted within 3 days of identification to the NJDOH Public Health and Environmental Laboratories (PHEL) for confirmation and serotyping. Approval to submit isolates is not necessary as submission is required by regulation.

Detection of *H. influenzae* via real-time **PCR** is becoming increasingly common. A major advantage of PCR is that it allows for detection of *H. influenzae* from clinical samples in which the organism could not be detected by culture methods, such as when a patient has been treated with antibiotics before a clinical specimen is obtained for culture. Even when the organisms are nonviable following antimicrobial treatment, PCR can still detect *H. influenzae* DNA. Real-time PCR assays are available to detect DNA of all six *H. influenzae* serotypes in blood, CSF, or other clinical specimens – unfortunately, NJDOH is currently unaware of any NJ medical facilities who have the capability to detect the serotype in addition to the organism via PCR. Therefore, if *H. influenzae* has been identified via PCR, it is important to determine whether there is also a culture result, if a culture result is pending, or if there is remaining CSF clinical sample material that can be submitted for testing:

- If the culture result is **positive**, the *H. influenzae* isolate MUST be sent to NJDOH PHEL, as described above and as required by N.J.A.C. 8:57-1.7(e).
- If there is no pending culture or the culture result is negative (e.g., no growth), and result was on **CSF**, it is very important to request from the testing facility that any remaining CSF clinical sample yielding the positive PCR result be sent to NJDOH PHEL for serotype testing at CDC or an approved VPD reference laboratory. PLEASE NOTE: currently, facilities are currently not required to submit specimens other than those specified within N.J.A.C. 8:57-1.7, however most facilities are agreeable to submitting the CSF samples in order to facilitate serotype testing for surveillance and public health response. While approval is not required, it is still important to notify NJDOH that a CSF clinical sample will be submitted instead of an isolate.

C. Reservoir

Humans (asymptomatic carriers) are the only known reservoir of *H. influenzae*. *H. influenzae* does not survive in the environment on inanimate surfaces.

D. Modes of Transmission

H. influenzae is transmitted person-to-person by inhalation of respiratory droplets or through direct contact with respiratory secretions of an infected person. The most common portal of entry is the nasopharynx. Newborns can become infected by inhaling amniotic fluid or genital tract secretions containing the organism.

E. Incubation Period

The exact incubation period is unknown but is most likely 2 to 4 days.

F. Period of Communicability

H. influenzae is communicable as long as organisms are present and the person is not receiving antibiotic therapy. Organisms may be present in the upper respiratory tract, sometimes for a prolonged period even without symptoms (e.g., nasal discharge).

If the person is on antibiotic therapy, *H. influenzae* is noncommunicable within 24 to 48 hours after effective antibiotic therapy is started.

G. Epidemiology

H. influenzae invasive infection occurs worldwide and is most prevalent among children aged 2 months to 3 years of age and is uncommon in healthy persons older than 5 years of age. Before the widespread use of *Haemophilus influenzae* type b (Hib) conjugate vaccine, *H. influenzae* serotype b was the most pathogenic strain of *Haemophilus* bacterium and was the leading cause of bacterial meningitis and other life-threatening invasive bacterial disease in the United States among children < 5 years of age. Meningitis occurred in approximately two thirds of children and often resulted in severe permanent neurologic sequelae that included hearing impairment, seizures, paralysis, and cognitive or developmental delay. Since 1991 in the United States, the incidence of *H. influenzae* serotype b disease in infants and children < 5 years of age has decreased by 99%. The incidence of invasive infection caused by all other serotypes combined is similarly low. Currently, invasive *H. influenzae* serotype b disease usually occurs primarily in children who have not been immunized or have not completed their Hib vaccine series. However, all strains —a, b, c, d, e, f, and nontypeable—still can cause invasive disease. Factors predisposing children and other persons to *H. influenzae* invasive disease include certain immunodeficiency syndromes, sickle cell disease, asplenia, HIV infection, and certain malignancies.

2 REPORTING CRITERIA AND LABORATORY TESTING SERVICES

A. New Jersey Department of Health Case Definition

Haemophilus influenzae cases (all serotypes) are reported by states to CDC through the National Notifiable Diseases Surveillance System (NNDSS). The New Jersey Department of Health (NJDOH) Communicable Disease Service (CDS) follows the most current case definition as published on the CDC NNDSS website. For the most recent case definition please visit:

https://ndc.services.cdc.gov/conditions/haemophilus-influenzae-invasive-disease/

CASE CLASSIFICATION (as of 2015)

Clinical Description:

Invasive disease caused by *H. influenzae* may produce any of several clinical

syndromes, including pneumonia, bacteremia, meningitis, epiglottitis, septic arthritis, cellulitis, or purulent pericarditis; less common infections include endocarditis and osteomyelitis.

Laboratory Criteria for Diagnosis:

- Isolation of *H. influenzae* from a normally sterile body site (e.g., cerebrospinal fluid [CSF], blood, joint fluid, pleural, pericardial fluid); OR
- Detection of *H. influenzae* type b antigen in cerebrospinal fluid (CSF); OR
- Detection of *H. 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

CONFIRMED

- Isolation of *H. influenzae* from a normally sterile body site (e.g., CSF, blood, joint fluid, pleural fluid, pericardial fluid); OR
- Detection of *H. influenzae*-specific nucleic acid in a specimen obtained from a normally sterile body site (e.g., CSF, blood, joint fluid, pleural fluid, pericardial fluid), using a validated PCR assay

PROBABLE

- Meningitis WITH detection of *H. influenzae* type b antigen in CSF

POSSIBLE

- Not used

NOTES:

- **PCR assays that can detect serotype are important since determining serotype is crucial for determining appropriate public health response, such as chemoprophylaxis for contacts of cases of *Haemophilus influenzae* type b (Hib) disease.**
- **Positive antigen test results from urine or serum samples are unreliable and, therefore, not confirmatory.**

B. Laboratory Testing Services Available

The PHEL will confirm and serotype isolates of invasive *H. influenzae.* Serotyping aids in public health surveillance. While PHEL is currently unable to perform serotype testing on PCR-positive specimens, they will facilitate additional testing at CDC or one of the approved VPD Reference Centers.

For more information about submitting specimens, please see Section 4B below or contact NJDOH Communicable Disease Service (CDS) at 609.826-5964.

NOTE: Only invasive *H. influenzae* infections (identified in a specimen collected from a normally sterile body site) are reportable. Per New Jersey Administrative Code (N.J.A.C. 8:57-1.7), ALL isolates from invasive *H. influenzae* must be submitted within three (3) working days to New Jersey Department of Health, Division of Public Health and Environmental Laboratories, Attn: Specimen Receiving, 3 Schwarzkopf Drive, Ewing, NJ 08628.

http://www.nj.gov/health/phel/

3 PURPOSE OF SURVEILLANCE AND REPORTING REQUIREMENTS

A. Purpose of Surveillance and Reporting

- Ensure that all cases of invasive *H. influenzae* are serotyped to identify *H. influenzae* serotype b;
- Identify close contacts of a case and provide recommendations for appropriate preventive measures, such as chemoprophylaxis, thus preventing further spread of infection;
- Increase understanding about the disease, its transmission, and methods of prevention;
- Identify clusters or outbreaks of disease promptly and initiate appropriate prevention and control measures;
- Monitor the impact of the Hib vaccine.

B. Laboratory Reporting Requirements

The N.J.A.C. 8:57-1.7 states that a laboratory director (or designee) shall report any positive culture, test, or assay result specific for invasive *H. influenzae* disease **immediately by telephone** to the local Health Officer having jurisdiction over the locality where the patient lives or, if unknown, to the Health Officer in whose jurisdiction the healthcare provider who requested the laboratory examination is located.

If this is not possible, the report may be made immediately by telephone to the NJDOH at 609.826.5964 during business hours and at 609.392.2020 after business hours and on weekends and holidays. Such report shall be followed within 24 hours by a written or electronic lab report.

C. Health Care Provider Reporting Requirements

According to N.J.A.C. 8:57-1.4, a physician, advanced practice nurse, physician's assistant, or a person having control or supervision over a hospital or other healthcare institution shall **immediately report by telephone** a known or suspect case of invasive *H. influenzae* disease to the Health Officer of the jurisdiction where the individual lives or if unknown, wherein the diagnosis is made. If the Health Officer is unavailable, the report shall be made to the NJDOH by telephone at 609.826.5964 during business hours, or 609.392.2020 after business hours and on weekends and holidays.

D. Local Health Department Reporting and Follow-up Responsibilities

The N.J.A.C. 8:57-1.9 states that a Health Officer (or designee) who is notified of the existence of a known or suspect case of invasive *H. influenzae* disease shall **immediately notify NJDOH by telephone** at 609.826.5964 during business hours and 609.392.2020 after business hours and on weekends and holidays.

Institution of disease control measures is an integral part of follow-up. It is the Health Officer's responsibility to understand and, if necessary, **immediately institute the control guidelines listed below in section 6**, "Controlling Further Spread."

4 CASE INVESTIGATION

A. Objectives of the investigation

The primary objective of the case investigation is to ensure that at-risk close contacts of the patient are identified and referred to their healthcare provider for chemoprophylaxis to prevent further spread of illness (see section 5C, below, for definition of an at-risk close contact}.

If the individual does not have a healthcare provider or cannot obtain the recommended medication, the Health Officer should assist in obtaining the medication. Agents and dosages for prophylaxis can be found in section 5C, below.

A second objective of the case investigation is to document information obtained and actions taken. Thorough and timely documentation in Communicable Disease Reporting and Surveillance System (CDRSS) will facilitate communication between disease investigators and assist with public health surveillance. Refer to section 4B, below, for specific information on filing the report in CDRSS.

Case investigations typically include review of laboratory, medical, and immunization records, as well as interviewing the medical provider/deignee to obtain information about clinical presentation. Investigations **also** include interviews of cases, or their guardian, which are necessary to verify onset dates, symptoms, and to identify sources of infection and contacts at risk.

B. Investigation guidelines

A VPD General Case Investigation Checklist and *Haemophilus influenzae* Case Investigation Checklist for Local Health Departments were developed to be used by case investigators as a supplement along with this chapter. They include high level steps of investigation, not necessarily in order, when investigating *H. flu* reports. The checklist can be accessed at: https://www.nj.gov/health/cd/topics/haemophilus.shtml

1. Verify the diagnosis/laboratory report

i) Review reported laboratory result(s) to ensure source is from a normally sterile site. Often, reported cases of *H. influenzae* are ultimately found to be results from laboratory tests performed on specimens that are considered non-sterile (e.g., eye swab). If a positive result is reported for a specimen that is not normally sterile, it is not invasive disease, is not reportable, and no public health response is necessary. The case can be closed as Not A Case/Does Not Meet Case Definition.

If unsure whether a result is sterile vs non-sterile, inquire with the testing laboratory or NJDOH.

ii) If PCR positive is reported in CDRSS first, inquire if culture result is pending*

iii) When *H. influenzae* has been identified via culture of a normally sterile specimen,
- An isolate MUST be submitted to NJ PHEL for serogroup testing, as required per N.J.A.C. 8:57-1.7(e), REGARDLESS of patient's mortality
  - Approval by NJDOH for isolate submission is not necessary as it is required by regulation.
- Contact testing laboratory (or facility IP) as soon as possible after a case is reported to assure *H. influenzae* isolate will be submitted to PHEL. In the laboratory test section of CDRSS, document the date and method the isolate will be sent to PHEL.
  - This may necessitate calling a commercial laboratory to request submission
- Facility/laboratory should create an order via PHEL's Online Ordering Portal:
  - If online ordering is not available, a completed BACT-109 form must accompany the isolate submitted to PHEL.
  - Print requisition form and include with sample in shipment to PHEL. Name and DOB must be correct and match between form and sample or PHEL will reject it.

iv) *When *H. influenzae* has been identified via PCR on **CSF** and no culture is pending OR culture result is negative:
- Please request remaining CSF clinical sample (minimum volume: 300-500µL) be sent on cold ice packs (4°C) or dry ice (-20°C) to PHEL for forwarding to Wisconsin State Laboratory of Hygiene (our VPD Reference Center).
  - Notify NJDOH REP/SME that clinical sample is being submitted instead of isolate.
- Facility/laboratory should create an order via PHEL's Online Ordering Portal:
  - Search for "*Reference Laboratory Test Request*", select "*Other*" under test type; enter "*H. flu PCR testing*"; select specimen type (*CSF*); and select appropriate reference laboratory location (*Wisconsin*).
  - If online ordering is not available, a completed BACT-109 form must accompany the specimens sent to PHEL. In "Tests Requested" section of the form, indicate "*Reference Laboratory*" and write in "*Wisconsin*".
  - Print requisition form and include with sample in shipment to PHEL. Name and DOB must be correct and match between form and sample or PHEL will reject it.

v) Do not await serotype results in order to initiate case investigation, close contact identification, and public health response. If *H. influenzae* was identified in a specimen from a normally sterile site, at-risk close contacts of the case should be identified and referred to their healthcare provider for prophylaxis, as appropriate. (See section 5C, below, for prophylaxis recommendations.)

2. Identify exposed at-risk close contacts and refer them to a healthcare provider for prophylaxis, as necessary

Close contacts are 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. For guidelines on prophylaxis of close contacts, please see section 5C below or the AAP Red Book chapter on *Haemophilus influenzae*.

Prophylaxis should be administered as soon as possible after identification of the index patient.

3. Disease Control Measures

Institution of disease control measures is an integral part of case investigation. It is the Health Officer's responsibility to understand and institute the control guidelines listed below in section 6, "Controlling Further Spread".

4. Document case investigation in CDRSS

The local Health Officer must immediately report the case to NJDOH. After notification to NJDOH, it is the Health Officer's responsibility to ensure the case is entered into CDRSS and investigated. Use the following guidelines to accurately record all case information into CDRSS:

- demographic information – at minimum, document/verify the patient's name, date of birth, sex, race/ethnicity, home address, and telephone number(s).
- clinical information, including:
  - illness onset date,
  - admission and discharge dates (when available)
  - presenting signs/symptoms,
  - treatment (antibiotics only related to treating *H. flu*),
  - Hib vaccine dates (via NJIIS, PMD, patient/parent/school record)
  - mortality (was patient alive upon discharge?)
- laboratory data, including:
  - specimen collection date,
  - specimen type (verify collected from normally sterile site),
  - specimen tests results,
  - date and method isolate will be sent to PHEL for serotyping.
- epidemiologic information, including:
  - risk factors,
  - industry and occupation
    - add employer name and address and click GEOCODE.
      - If unknown, enter 'Unknown' or 'Unwilling to provide' for both
    - add current occupation (what's the person's job?) and current industry (what does the company make or do?) then click SUBMIT

  - If the person does not work, enter occupation as: 'retired', 'unemployed', 'homemaker', 'volunteer', 'student', 'child', or 'did not work'. And enter 'none' for industry.
  - If unknown, enter 'unknown' for occupation and industry
- contact tracing – document whether case has any at-risk close contacts, if they are up to date with Hib immunizations, have been referred for/received prophylaxis.

5 CONTROLLING FURTHER SPREAD

A. Isolation and Quarantine Requirements (N.J.A.C. 8:57-1)

1. Minimum period of isolation of patient

In addition to standard precautions, droplet precautions are recommended for 24 hours after the initiation of appropriate antibiotic therapy.

2. Minimum period of quarantine of contacts

None.

B. Treatment of the Case

- Antimicrobial therapy with an effective third-generation cephalosporin (cefotaxime or ceftriaxone), or chloramphenicol in combination with ampicillin should be begun immediately. Ampicillin-resistant strains of Hib are now common throughout the United States. Children with life-threatening illness in which Hib may be the etiologic agent should not receive ampicillin alone as initial empiric therapy.
- Vaccination: unimmunized or incompletely immunized children should receive a dose of vaccine and should be scheduled for completion of the recommended age-specific immunization schedule as per ACIP guidelines.
- For additional guidelines on treatment for invasive *H. influenzae* disease, see the AAP Red Book.

C. Prophylaxis for Contacts of Index Cases of Hib Disease

- Rifampin prophylaxis is recommended only for household contacts (defined below). In certain circumstances, prophylaxis might be recommended for childcare contacts of confirmed and probable *H. influenzae* serotype b cases.
  - There may be occasions when prophylaxis of childcare contacts is indicated prior to obtaining serotype information. Please contact the NJDOH for guidance.
- Prophylaxis is not recommended for contacts of *H. influenzae* serotype nontypeable or serotypes a, c, d, e, and f.
  - Do not wait for serotype information to begin the identification of contacts.
- Regardless of serotype, testing of contacts is not recommended.

Prophylaxis Guidelines for Close Contacts of an Invasive Hib Case

Rifampin Prophylaxis against Hib	
Age Group	**Dosage/Schedule**
Infants < one month of age	10 mg/kg PO QD × 4 days
Children	20 mg/kg PO QD × 4 days (maximum: 600 mg/dose)
Adults	600 mg PO QD × 4 days

Close contacts are defined as persons 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. For unique circumstances, such as a death occurring at home or delayed hospitalization of the case, please contact NJDOH for further guidance.

Chemoprophylaxis Recommended

- For all household contacts in the following circumstances:
  - Household with at least 1 child younger than 4 years of age (48 months) who is unimmunized or incompletely immunized* for Hib.
  - Household with a child younger than 12 months who has not completed the primary Hib series.
  - Household with an immunocompromised child, regardless of that child's Hib immunization status or age
- For preschool and childcare center contacts when 2 or more cases of Hib invasive disease have occurred within 60 days and unimmunized or underimmunized children attend the facility. When prophylaxis is indicated, it should be prescribed for all attendees, regardless of age or vaccination status, and for childcare providers.
- For index patient, if younger than 2 years of age or a 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 NOT Recommended

- For occupants of households with no children younger than 4 years of age other than the index patient
- For occupants of households when all household contacts are immunocompetent, all household contacts 12 through 48 months of age have completed their Hib immunization series, and when household contacts younger than 12 months of age have completed their primary series of Hib immunizations
- For preschool and childcare contacts of 1 index case
- For index patients over age 2 years or treated with a full course of cefotaxime or ceftriaxone for *H influenzae* type b invasive disease
- For pregnant women

*Complete immunization is defined as having had at least 1 dose of Hib conjugate vaccine at 15 months of age or older; 2 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.

NOTE: If there is a delay in obtaining the serotype, prophylaxis of at-risk close contacts should be started without serotype information.

D. Managing Special Situations: Child Care Contacts

- The risk of secondary disease in children attending childcare centers appears to be lower than that observed for age-susceptible household contacts, and secondary disease in childcare contacts is rare when all contacts are older than 2 years.
- Data are insufficient on the risk of secondary transmission to recommend chemoprophylaxis for attendees and childcare providers when a single case of invasive Hi disease occurs; the decision to provide chemoprophylaxis in this situation is at the discretion of the local health department.
- Childcare or nursery school contacts, regardless of age (children and staff), should receive prophylaxis when 2 or more cases of invasive Hib disease have occurred within 60 days.
- Careful observation of the exposed unimmunized or incompletely immunized childcare or nursery school contact is imperative. If a child/contact develops a febrile or respiratory infection, ensure the child/contact is medically evaluated.
- Unimmunized or incompletely immunized children should receive a dose of vaccine and be scheduled to complete the age-appropriate Hib immunization.

Ensure appropriate immunization of household and childcare contacts. The number of doses required is determined by the current age of the child and the number, timing, and type of Hib vaccine doses previously received.

The recommended schedule for Hib conjugate vaccine administration can be found at: https://www.cdc.gov/vaccines/hcp/imz-schedules/downloads/child/0-18yrs-child-combined-schedule.pdf

Unvaccinated and under vaccinated children younger than 5 years should be scheduled for completion of the recommended age-specific immunization schedule. Infants should be placed on an accelerated schedule using minimum intervals between doses. The accelerated schedule for situations in which an incompletely vaccinated child has been exposed follows:
https://www.cdc.gov/vaccines/hcp/imz-schedules/child-adolescent-catch-up.html

E. Preventive Measures

- Routine childhood vaccination is the best preventive measure against Hib disease. Visit the CDC National Immunization Program at https://www.cdc.gov/vaccines/index.html to print the most recent childhood immunization schedule.
- Please consult the chapter on *Haemophilus influenzae* in the Red Book of the American Academy of Pediatrics for a full discussion of vaccines, immunization

schedules, and special circumstances. For example, children with underlying conditions predisposing them to Hib disease, including children 5 years of age or older, may need additional doses.

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