Haemophilus Influenzae 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 for people <5 years old
- ☐ Review background on disease (see page 2), case definition (see page 4), and laboratory testing (see page 5)
- ☐ For cases in people ≥5 years old, interviews/investigations are not recommended unless the illness is known to be caused by *H. influenzae* type B. Surveillance for *H. influenzae* invasive disease in people ≥5 years old is now conducted only through electronic laboratory reporting (ELR) surveillance
- ☐ Contact health care provider to obtain pertinent information including demographics, medical records, vaccination history, and laboratory results
- ☐ Facilitate serotyping of *H. influenzae* isolates for people <5 years old at Florida Bureau of Public Health Laboratories (BPHL) Jacksonville
  - ☐ 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 (see page 7) and family members who may be at risk if Hib is identified
  - ☐ Determine whether patient or symptomatic contact is in a sensitive situation (daycare or other settings with infants or unvaccinated children)
    - ☐ Recommend exclusion for patients or symptomatic contacts until 24 hours of effective antibiotic treatment.
    - ☐ 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 Invasive Disease

1. DISEASE REPORTING

A. Purpose of reporting and surveillance

1. To identify the serotypes of invasive *Haemophilus influenzae* organisms that cause disease in children under 5 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 among children under 5 years old

B. Legal reporting requirements

Laboratories and physicians are required to report persons <5 years old 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 for cases in people <5 years old.
2. Contact laboratories as soon as possible after a case that is <5 years old 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 people <5 years old in Merlin, **regardless of serotype** (H. INFLUENZAE, CODE 03841).
   a. The Centers for Disease Control and Prevention (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.
   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 5. From 1989 to 2000, there was a 99% reduction in Hib invasive disease among children younger than 5 years of age. The national average incidence

rate of Hib in this age group from 2010 to 2013 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 5 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. 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 5 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 5 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 1 year of age (6%). Moreover, secondary attack rates among household contacts are estimated to be 3% for children less than 2 years of age and 2% for those 4 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 asymptomatically 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. Ampicillin should be substituted if the Hib isolate is susceptible. Antimicrobial treatment of other invasive *H. influenzae* infections is similar. Duration of therapy is continued for 7 to 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, prophylaxis is generally not needed for household contacts. When serotype information is delayed, or unknown, prophylaxis of close contacts (See Section B. Contact Management) is generally not recommended.**

I. *Haemophilus influenzae* type b in Florida

From 2001 to 2015 there were 14 cases of invasive disease caused by Hib in those under the age of 5. During this same time frame a total of 336 invasive *H. influenzae* infections cases were reported.

3. CASE DEFINITION

A. Clinical description

Invasive disease may manifest as pneumonia, bacteremia, meningitis, epiglottitis, septic arthritis, cellulitis, or purulent pericarditis; less common infections include endocarditis and osteomyelitis.

B. Laboratory criteria for diagnosis

Confirmatory:

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

OR

- Detection of *H. influenzae*-specific nucleic acid in a specimen obtained from a normally sterile body site (e.g., blood or CSF), using polymerase chain reaction (PCR) assay

Presumptive:

- Detection of *H. influenzae* type b antigen in CSF

C. Case definition

Confirmed: A person with confirmatory laboratory evidence

Probable: Meningitis in a person with presumptive laboratory evidence

D. Comments

***H. influenzae* invasive disease cases in people ≥5 years old are only reportable for laboratories participating in electronic laboratory reporting (ELR).** Cases in people ≥5 years old will be automatically created and reported in Merlin based on ELR results, and will not require symptoms to meet case definition. For case reports in people ≥5 years old received from health care providers or via paper laboratory results, cases do not need to be investigated or created in Merlin; however, county health departments can choose to enter and report these cases.

Cases in children <5 years old are reportable for all laboratories and health care providers. All cases in children <5 years old need to be investigated and reported, regardless of the method through which the case reports were received. **Extended data in Merlin is only required for those cases in people <5 years old.**

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. Sputum cultures are not confirmatory as sputum is not obtained from a sterile site.

Serotype should be determined for all *Haemophilus influenzae* isolates in people <5 years old because Hib vaccines protect against serotype b organisms only. This testing is

especially important for children <5 years of age to determine possible vaccine failure or failure to vaccinate.

Isolates from cases <5 years old must be sent to the BPHL-Jacksonville 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 in people <5 years old must be forwarded to the BPHL for serotyping.

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:
   a. 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. Contact BPHL for packaging and shipping training dates. BPHL conducts approximately 20, face-to-face trainings per year all over Florida, free of charge. DOH employees must register for the classes in the DOH online training system called, TRAIN. For shipping guidance, please contact BPHL.
   b. Contact the appropriate regional laboratory with questions: http://www.floridahealth.gov/programs-and-services/public-health-laboratories/locations/index.html

3. Contact the regional laboratory liaison with questions: http://www.floridahealth.gov/diseases-and-conditions/disease-reporting-and-management/disease-reporting-and-surveillance/_documents/investigation-unit-map.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 in persons <5 years old 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* invasive disease within the previous 60 days.

C. Identify potentially exposed persons

While awaiting serotype results for children less than 5 years of age:

1. Identify young children (under the age of 5) 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).

   Determine whether the patient had prolonged contact with other children less than 2 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 2 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. Chemoprophylaxis is recommended for patients with Hib disease that are younger than 2 years old with a susceptible household contact and treated with a regimen other than ceftriaxone or cefotaxime.

3. Children developing Hib invasive disease before the age of 2 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 4 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 4 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 under-immunized 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 1 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 prophylaxis seven days or more after hospitalization of the index patient still may be of some benefit (*Red Book 2015*, Report of the Committee on Infectious Disease, p. 372)."

For additional information regarding indications for rifampin chemoprophylaxis for contacts of patients with Hib disease, please see the *Red Book 2015*, Report of the Committee on Infectious Disease.

*Examples of **close contact** with *H. influenzae* 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 under-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 childcare contacts are older than 2 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 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 2, 4 and 6 months or two doses given at 2 and 4 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

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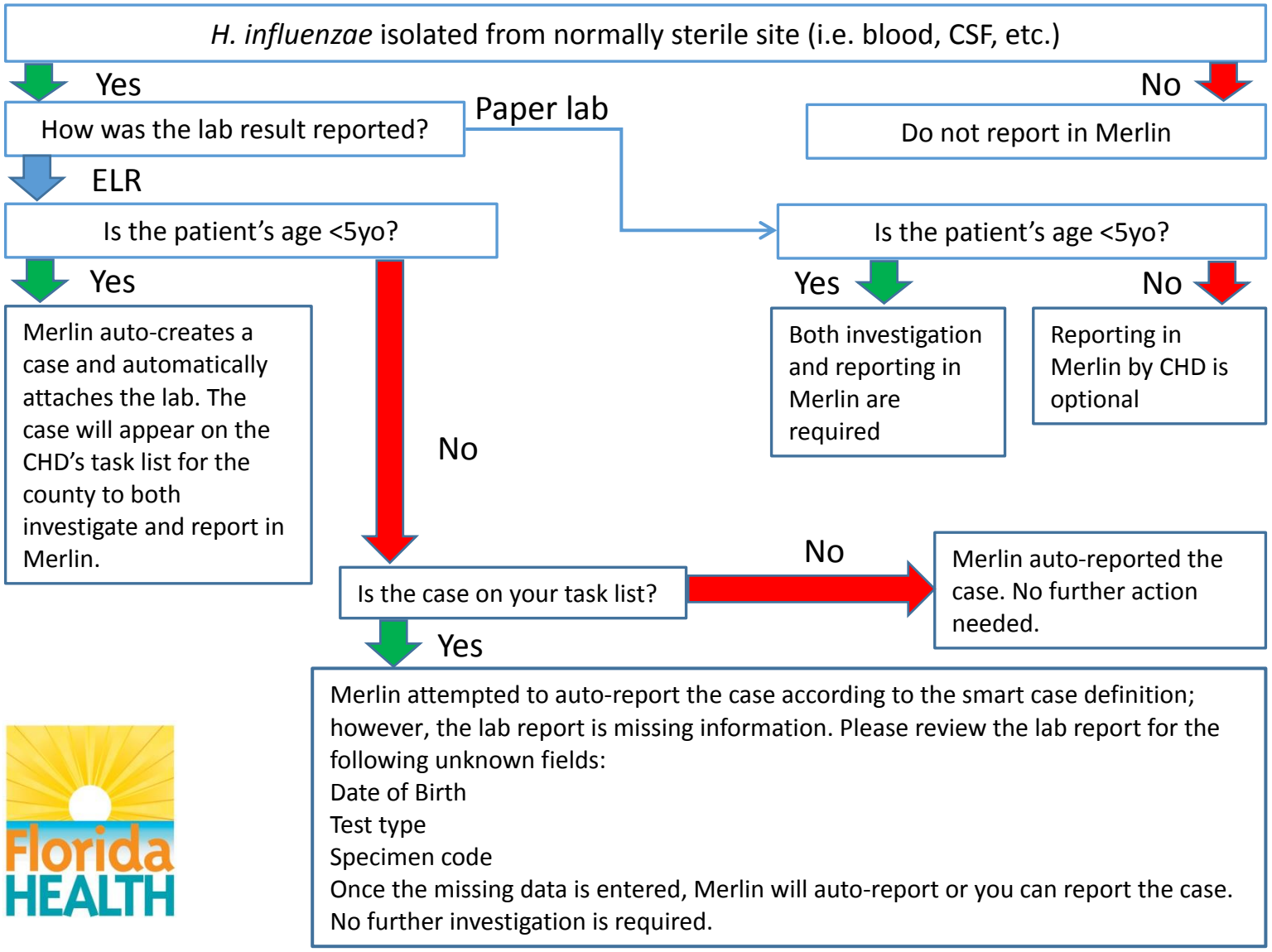
H. influenzae Merlin Reporting Algorithm



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