



Health

Public Health Division/Communicable Disease Control

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Reporting Clarification for Health Care Professionals

Please note: the reporting instructions for the Invasive *Haemophilus influenzae* disease protocol have been modified.

- Same day reporting by telephone (204-788-8666) and secure fax (204-948-3044) to the Public Health Surveillance Unit is required when a health care professional becomes aware that a person meets or has recently met the confirmed case definition for invasive *Haemophilus influenzae* disease (form available at: www.gov.mb.ca/health/publichealth/cdc/protocol/form2.pdf).
- Clinical cases should be reported by following the instructions on the form available at: <http://www.gov.mb.ca/health/publichealth/cdc/protocol/form13.pdf> .

Invasive *Haemophilus influenzae* Disease (IHD)



Communicable Disease Control Unit

This protocol applies only to typeable strains of Invasive *Haemophilus influenzae*. The protocol does not apply to non-typeable *Haemophilus influenzae* (*H. influenzae*) organisms.

Public Health follow-up is indicated for *H. influenzae* type b (Hib) only. The reporting of the other typeable strains is currently for surveillance purposes only; however, as more information becomes available on these strains, further action may be required.

This protocol will need to be revised as more information on the epidemiology, treatment and prophylaxis of non-Hib typeable strains becomes available.

Case Definition

Confirmed Case: Invasive disease including meningitis, bacteremia, epiglottitis, pneumonia, pericarditis, septic arthritis or empyema with isolation of typeable *H. influenzae* or detection of typeable *H. influenzae* by polymerase chain reaction (PCR) from a normally sterile site (e.g., blood, cerebrospinal fluid [CSF] or less commonly, joint, pleural or pericardial fluid) (1, 2, 3).

OR

Isolation of typeable *H. influenzae* from the epiglottis in a person with epiglottitis (1).

Clinical Case: Buccal cellulitis or epiglottitis in a child younger than five years of age with no other causative organisms isolated (1, 3).

Reporting Requirements

- All specimens isolated from sterile sites that are positive for typeable *H. influenzae* are reportable by laboratory to the Director of Communicable Disease Control, Manitoba Health.

- All confirmed cases of invasive Hib are reportable by attending health care professional to the Director of Communicable Disease Control, Manitoba Health.
- Operators of clinical laboratories in Manitoba processing *H. influenzae* isolates obtained from sterile sites, must forward isolate subcultures to the Cadham Provincial Laboratory.

Clinical Presentation/Natural History

Disease caused by *H. influenzae* usually begins in the upper respiratory tract as pharyngitis (4, 5). Invasive disease usually occurs after the organism enters the bloodstream (6). Until widespread use of effective vaccines, *H. influenzae* type b was the leading cause of bacterial meningitis and other invasive bacterial diseases among children younger than five years of age (7). There are strains of *H. influenzae* other than type b that are capable of causing invasive disease; however, their occurrence is relatively rare (8). Next to Hib, *H. influenzae* types e and f are the most frequently encountered typeable strains (8). Invasive disease with *H. influenzae* type a has also been documented (8-12). Disease caused by non-b typeable strains is clinically indistinguishable from Hib disease; however, those infected with non-b typeable strains have a higher frequency of underlying disorders (8, 13).

Meningitis: Meningitis is the most common clinical manifestation of invasive Hib disease (7, 14). Cases of meningitis caused by serotypes a, e and f have been documented (11, 12, 15-18); however, it is not known whether meningitis is the most common clinical presentation of these serotypes. Disease onset may be subtle with low-grade fever for several days but is more frequently sudden; including fever, vomiting, lethargy and

meningeal irritation, with a bulging fontanelle in infants, or stiff neck and back in older children (14). Progressive stupor or coma is common (14). The case-fatality rate of meningitis is approximately five per cent despite antimicrobial therapy (4, 7, 19), and permanent sequelae occur in many of the survivors (4, 7).

Epiglottitis: Hib causes swelling of the epiglottis (7). The disease presents as sudden onset of fever, drooling, and difficulty in swallowing and may progress to life-threatening airway obstruction (6, 7).

Other Diseases: Other common manifestations of invasive disease include septic arthritis, cellulitis (usually involving the face, head or neck) and pneumonia (which can be mild focal or severe empyema) (7). Osteomyelitis and pericarditis are less common forms of invasive disease (7).

Clinically, meningitis, pneumonia, sepsis or arthritis caused by Hib cannot be distinguished from other bacterial causes (6). Laboratory confirmation is required.

Etiology

H. influenzae is a small bacterium (4). The encapsulated strains of *H. influenzae* are classified into serotypes a through f, based on the antigenic characteristics of their polysaccharide capsules (14). Serotype b is the most pathogenic strain (5, 14).

Epidemiology

The epidemiology of *H. influenzae* disease appears to be changing as there have been reports of invasive disease such as meningitis caused by non-Hib typeable strains (8-12, 16, 17, 20).

Reservoir and Source: Humans are the only known natural host for *H. influenzae* organisms (4). Migration from countries where no Hib immunization programs are in place results in a constant source of Hib infection (21). Hib does not survive in the environment on inanimate surfaces (7).

Transmission: Person-to-person transmission of *H. influenzae* occurs by airborne droplets or by direct contact with secretions (4). In neonates (babies up to four weeks of age), infection is acquired intrapartum by aspiration of amniotic fluid or by contact with genital tract secretions containing the organism (22).

Occurrence:

General: Invasive *H. influenzae* infection occurs worldwide and is most prevalent among children two months to three years of age (14). The disease is unusual in children over five years of age (14). The incidence of invasive disease by all typeable strains combined is low (22). With widespread use of Hib vaccines by the late 1990s, most industrialized countries have drastically reduced the incidence of Hib disease (14); however, currently there are no vaccines for the other typeable strains. Hib remains an important pathogen in developing countries where routine vaccination is not widely available (22). Hib is still a leading cause of bacterial pneumonia deaths in children in developing countries (23).

Canada: Prior to the introduction of Hib conjugate vaccines in Canada in 1988, there were an estimated 2,000 cases of Hib disease annually (19). Overall incidence has fallen by more than 99 per cent since then (19). The majority of cases now occur in individuals too old to have received primary immunization (19). As reporting systems have only captured type b infections in the past, it is unclear what effect, if any, the Hib vaccine has had on rates of invasive disease with the other typeable strains (8).

In the past, invasive disease caused by non-serotype b encapsulated organisms occurred more frequently in persons older than five years (8, 9, 24). With reports of invasive disease by non-b typeable strains of *H. influenzae* in children (9-12), there is concern that other serotypes will acquire additional virulence traits and emerge as significant pathogens in children (9).

Manitoba: There was one reported case of invasive Hib disease in 2003, five reported cases in 2004, and a total of four reported cases in 2005 (25). It is not known how many cases of invasive disease occurred due to the other typeable strains of *H. influenzae* as these organisms were not reportable (25). However, 50 per cent of isolates taken from patients with invasive *H. influenzae* disease in a recent Manitoba study were found to be type a (10). Most of the isolates were taken from patients who were ≤ 24 months old (10). These findings support the concept that the epidemiology of invasive *H. influenzae* disease is changing (10). From this study, it appears that *H. influenzae* type a may be the second most clinically virulent type among the six serotypes of *H. influenzae* (10).

Incubation Period: The incubation period is unknown but is believed to be short; probably two to four days (14).

Host Susceptibility and Resistance: Systemic Hib disease is unusual after the age of six years even in the absence of immunization (4). Prior to vaccines, most children acquired natural immunity by five to six years of age through asymptomatic infection by Hib bacteria (7). Children who develop Hib infection at 24 months of age or older do not need immunization, because disease almost always induces a protective immune response (22). Passive protection of some infants from Hib is provided by transplacentally acquired maternal IgG (7). Breastfeeding of infants offers some protection against Hib (7) and other invasive *H. influenzae* strains (24, 26).

The risk of Hib meningitis is at least twice as high for children attending full-time day-care as for children cared for at home (19). The risk is also greater among children with splenic dysfunction (e.g., sickle cell disease, asplenia) or antibody deficiency, and among Inuit children (19).

Period of Communicability:

1) Hib

The exact period of communicability of Hib is unknown (22). However, risk of infection persists for as long as organisms are present whether or not there is nasal discharge (14). Hib disease is considered non-communicable within 24-48 hours after starting effective antibiotic therapy (14).

2) Non –Hib Typeable Strains

The period of communicability for the other typeable strains is unknown.

Diagnosis

All *H. influenzae* specimens taken from invasive sites should be sent to the Cadham Provincial Laboratory for serotyping and/or surveillance analysis (27, 28). Diagnosis is based on the detection of typeable *H. influenzae* organisms from sterile sites including blood, CSF, joint, pleural and pericardial fluid.

Culture: Each specimen is cultured on chocolate agar as soon as possible as viability of *H. influenzae* is lost rapidly (4). *H. influenzae* is differentiated from other *Haemophilus* species in culture by its requirement for both X and V growth factors (4, 27, 28). The porphyrin test is negative for *H. influenzae* (requires X factor for growth), but is positive for *Haemophilus parainfluenzae* (does not require X factor for growth) (27, 28).

Microscopy: A gram stain is performed on the original sample as well as on the cultured specimen (27, 28). *H. influenzae* is a gram negative coccobacillus (14).

Serotyping: Slide agglutination is used to determine serotype on all cultured *H. influenzae* organisms (27, 28).

Key Investigations

- Contact history
- Immunization history

Control

Management of Cases:

1) Hib

For hospitalized patients, Routine and Droplet Precautions are recommended for the first 24 hours after initiation of antimicrobial therapy (22).

Treatment

- Antimicrobial therapy with a third generation cephalosporin (cefotaxime or ceftriaxone) is indicated for Hib disease (4, 7, 22).
- Chloramphenicol in combination with ampicillin may be used as an alternative (7, 22). Consultation with an infectious disease specialist is advised when treatments other than a third generation cephalosporin are considered in serious infections.
- Ampicillin alone should not be used because of frequent resistance (4, 7, 22). Approximately 30 per cent of strains now produce β -lactamase (4, 14).
- The patient should be given rifampin chemoprophylaxis prior to discharge from the hospital to assure elimination of the organism if cefotaxime or ceftriaxone were not used for treatment (3, 4, 14).
- Dexamethasone instituted prior to antibiotics, with both started as early as possible, may reduce the risk of neurologic sequelae in children with Hib meningitis (22).
- Children who develop invasive disease when younger than 24 months of age are at risk of developing a second episode of disease and should be immunized according to the age-appropriate schedule for unimmunized children as if they had received no previous Hib vaccine doses (22). (See *Canadian Immunization Guide*) (19).

2) Non-Hib Typeable Strains

- Limited data exists on the treatment of invasive infections caused by the other typeable strains; however, ceftriaxone (9, 20) and cefotaxime (8, 9) have been used successfully.

Management of Contacts:

1) Hib

- Public Health will determine whether chemoprophylaxis for contacts is indicated and if so, arrange availability. With the advent of effective immunization against Hib, the role of chemoprophylaxis for contacts of Hib cases has diminished (3).
- Education of parents regarding the risk of secondary cases among contacts younger than five years of age, especially infants, and the need for prompt evaluation and treatment if fever or stiff neck develops (3).
- Children who have not been appropriately immunized for age should receive any required immunizations (22).

Chemoprophylaxis is recommended for all household and child care centre contacts¹ in the following circumstances (22):

- Household with at least one contact younger than four years of age who is unimmunized or incompletely immunized (See *Canadian Immunization Guide*).
- Household with an immunocompromised child, regardless of that child's immunization status.

¹ Defined as people residing with the index patient or nonresidents who spent four or more hours with the index case for at least five of the seven days preceding the day of hospital admission of the index case (4, 22).

- Nursery school or child care centre when one case of Hib invasive disease has occurred, for incompletely or unimmunized children younger than four years of age only.
- Nursery school or child care centre, regardless of age and immunization status, when two or more cases of Hib invasive disease have occurred within 60 days.

Rifampin prophylaxis should be considered for all attendees and staff regardless of age and immunization status (even if they do not fit the formal definition of contact), **when two or more cases of disease occur** in a child care setting with inadequately immunized attendees (see first bullet under **Management of Contacts**) (14, 22).

Chemoprophylaxis is not recommended for:

- Household contacts of index cases of invasive Hib infection when the contacts are completely immunized against Hib according to the *Canadian Immunization Guide* (19).
- Nursery school and child care contacts of one index case, especially those older than two years of age.
- Pregnant women as safety has not been determined.

If chemoprophylaxis is indicated (3)(22):

- Persons should be excluded until they are taking rifampin.
- Persons entering a setting (new staff and attendees) where rifampin is being given should also receive it.
- All new attendees entering a setting where rifampin has been used within two months must be age-appropriately immunized.
- Rifampin should be given to contacts within seven days after the index patient is hospitalized in order to be effective in preventing secondary cases (4).

Rifampin Chemoprophylaxis Dosages (22)

Adults: 600 mg orally once daily for four days

Children: 20 mg/kg (maximum 600 mg) orally once daily for four days

Infants younger than one month: 10 mg/kg orally once daily for four days

- Manitoba Health and First Nations and Inuit Health Branch (FNIHB) provide rifampin to contacts of Hib disease at no charge. This can be arranged by contacting the FNIHB Medical Officer of Health or the local provincial Medical Officer of Health. After regular office hours a Medical Officer of Health on-call can be reached by calling (204) 945-0183.
- Children who have not been appropriately immunized for age should receive any required immunizations.

2) Non-Hib Typeable Strains

- Chemoprophylaxis of contacts is not routinely recommended for the other serotypes of *H. influenzae* (12, 14).

Preventive Measures:

- Immunization with Hib conjugate vaccine.
- Currently there are no vaccines available for the other typeable strains of *H. influenzae*.

Appendix: Differences Between Hib and Non-Hib Typeable Strains

	Hib	Non-Hib Typeable Strains a,c,d,e,f
Reportable	Yes	Yes
Public Health Follow-Up	Yes	No
Invasive Disease	More common	Less common
Communicability	Not considered communicable after 24-48 hours of effective antimicrobial therapy.	Unknown
Hospitalized Patients	Routine and droplet precautions until 24 hours after initiation of antimicrobial therapy.	Not defined
Treatment	Third generation cephalosporin or chloramphenicol in combination with ampicillin.	No defined regimen. Ceftriaxone and cefotaxime have been used successfully.
Management of Contacts	Recommended	Not recommended
Prevention	Vaccine	No vaccine

Additional Resources

For Health Care Professionals

- Fact sheet on Rifampin titled *Important notes about Rifampin* (see section on Meningococcal invasive disease).

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