Haemophilus influenzae serotype b, Invasive

Revision Dates

Case Definition	August 2011
Reporting Requirements	August 2011
Remainder of the Guideline (i.e., Etiology to References sections inclusive)	June 2005

Case Definition

Confirmed Case

Clinical evidence of invasive disease[1] with laboratory confirmation of infection:

- Isolation of *Haemophilus influenzae* serotype b from a normally sterile[2] site.

**The following probable case definition is provided as a guideline to assist with case finding and public health management, and should not be reported to AHW.*

Probable Case

Clinical evidence of invasive disease[1] with laboratory evidence of infection:

- Detection of *H. influenzae* serotype b antigen[3] in cerebrospinal fluid

OR

- Detection of *H. influenzae* DNA[3] by specific nucleic acid test (e.g., PCR) in a normally sterile[2] site

OR

Buccal cellulitis or epiglottitis in a child < 5 years of age with no other causative organisms isolated.

[1] Clinical evidence of invasive disease due to *H. influenzae* includes meningitis, bacteremia, epiglottitis, pneumonia, pericarditis, septic arthritis, or empyema.

[2] Specimens from a normally sterile site are defined as:

- blood,
- cerebrospinal fluid (CSF),
- pleural fluid,
- peritoneal fluid,
- pericardial fluid,
- bone,
- joint fluid
- specimens taken during surgery (e.g., muscle collected during debridement for necrotizing fasciitis or fluid from a deep abscess). **NOTE:** A specimen collected from a non-sterile site during a sterile procedure is not considered a “normally sterile site”.

[3] Detection of *H. influenzae* DNA is considered probable, not confirmed, because Hib may be present in a non-pathogenic role and thus, depending on the site, may NOT reflect the actual pathogen. Additionally, detection of *H. influenzae* DNA in a sterile site does NOT indicate that it is type b since this test does not differentiate between serotypes.

Reporting Requirements

1. **Physicians, Health Practitioners and others**
   Physicians, health practitioners and others listed in Sections 22(1) or 22(2) of the *Public Health Act* shall notify the Medical Officer of Health (MOH) (or designate) of all confirmed cases by the Fastest Means Possible (FMP) i.e., direct voice communication.

2. **Laboratories**
   All laboratories, including regional laboratories and the Provincial Laboratory for Public Health (PLPH) shall, in accordance with Section 23 of the *Public Health Act*, report all positive laboratory results by FMP to the:
   - Chief Medical Officer of Health (CMOH) (or designate),
   - MOH (or designate) and
   - Attending/ordering physician.

3. **Alberta Health Services and First Nations Inuit Health**
   - The MOH (or designate) shall notify the CMOH (or designate) of all confirmed cases by FMP.
   - The MOH (or designate) of the zone where the case currently resides shall forward the preliminary Notifiable Disease Report (NDR) of all confirmed cases to the CMOH (or designate) within seven days (one week) of notification and the final NDR (amendments) within two weeks of notification.
   - For out-of-zone reports, the MOH (or designate) first notified shall notify the MOH (or designate) of the zone where the case currently resides by FMP and immediately fax a copy of the positive laboratory report.
   - For out-of-zone contacts, the MOH (or designate) first notified shall notify the MOH (or designate) of the zone where the contact resides by mail, fax or electronic transfer including:
     - name,
     - date of birth,
     - personal heath number and
     - contact information i.e., address and phone number.
   - For out-of-province and out-of-country reports, the following information should be forwarded to the CMOH (or designate) by FMP, including:
     - name,
     - date of birth,
     - out-of-province health care number,
     - out-of-province address and phone number,
     - attending physician (locally and out-of-province) and
     - positive laboratory report (faxed).

Etiology (1)

Haemophilus influenzae serotype b bacterium. It does not survive in the environment or on inanimate surfaces.

Clinical Presentation (1)

Prior to the introduction of an effective vaccine, Hib was the leading cause of bacterial meningitis and other invasive bacterial disease among children less than five years of age. Almost all serious Hib infections were in children less than five; two thirds of these cases were in children less than 18 months old.

Haemophilus influenzae type b is a bacterial infection. The organism enters the body through the nasopharynx. Here the organism colonizes and may remain only transiently or may persist for several months with no symptoms. In some individuals the organism causes an invasive infection but the exact mode of invasion into the bloodstream is unknown. An infection of the upper respiratory tract may be a contributing factor. This organism has the ability to cause meningitis (usually associated with a bacteremia), epiglottitis, pneumonia, septic arthritis, bacteremia, cellulitis, pericarditis, empyema, and osteomyelitis. The onset may be subacute but is typically acute. Symptoms can include fever, vomiting, lethargy, and meningeal irritation with a bulging fontanelle in infants or a stiff neck/back in other children. Progressive stupor or coma is common. Three to 6% of cases are fatal and up to 20% of survivors have permanent hearing loss.

Diagnosis

The diagnosis is made by the isolation of the *Haemophilus influenzae* organism from a normally sterile site. Clinical specimens should be inoculated onto appropriate culture media as soon as possible following collection as the viability of the organism is lost quickly. The organism is typed (to identify serotype b) at the PLPH, or at a regional laboratory and confirmed at the PLPH. (G Tyrell, personal communication, December 8, 2003)

Epidemiology

Reservoir

Humans.

Transmission

Transmission is person to person via droplet infection, and direct or indirect contact with discharges from the nose and throat during the infectious period. Typically the nasopharynx is the portal of entry. In neonates the source of infection may be the aspiration of amniotic fluid or genital tract secretions containing the organism.

Incubation Period

The incubation period remains unknown but is believed to be between two and 10 days, probably 2-4 days.

Period of Communicability

The exact period of communicability is unknown but is thought to be communicable for up to seven days prior to the onset of illness, remaining communicable until the organism is no longer present. The individual becomes non-infectious approximately 24 hours after starting effective antibiotic therapy.

Host Susceptibility (1,2)

Universal susceptibility in children less than five years of age. Most at risk are infants and young children, household and daycare contacts. Immunity is associated with the presence of circulating

bactericidal and/or anticapsular antibody that is acquired transplacentally, from prior infection or from immunization. Children who acquire an invasive Hib infection prior to two years of age may not develop immunity.

Risk factors for disease include host factors (chronic diseases) and exposure factors (household crowding, large household size, child care or nursery school attendance, low socioeconomic status, low parental education levels, and school-aged siblings).

Occurrence

General (3,4)

Worldwide distribution. It is not a common disease in children over five years of age in developed countries, but continues to be a major cause of lower respiratory tract infections in infants and children in developing countries due to the absence of vaccination programs.

In the United States from 1980 to 1990, the incidence of invasive Hib disease was 40 to 100/100,000 children less than five years of age. Conjugate vaccine was introduced for children in 1987 and infants in 1990. In 1995, the incidence dropped to less than 2/100,000 children. From 1996 to 2000 there were a total of 341 cases (average of 68 per year) of Hib reported in the United States. The majority of these cases were in unvaccinated or incompletely vaccinated children.

The United Kingdom (UK) saw a rapid reduction of invasive Hib cases when the vaccine was introduced as a routine infant immunization (given at two, three and four months of age) in October of 1992. In 1999, there was a notable resurgence of cases of invasive Hib although the incidence remained well below the pre-vaccine levels. The majority of those infected were fully immunized children. Several studies are underway to look for an explanation for the increase.

Canada (5-7)

Invasive Hib disease became reportable in Canada in 1979. The first Hib vaccine, a polysaccharide, was licensed in 1985 for children over two years of age. A conjugate vaccine (for children two months of age and over) was licensed in 1988. Prior to the introduction of Hib conjugate vaccine there were approximately 2,000 cases of Hib disease reported annually. The number of cases has declined since 1988.

From 1995 to 1999 fewer than 65 cases of invasive Hib were reported annually. Of the few cases reported annually, the highest numbers were reported in children less than nine years of age and in adults over the age of 40 years.

The number of cases of Hib infection in children less than 16 years of age has a remarkable decline beginning in 1995 (as observed by IMPACT). Monitoring of disease in children up to 16 years old is done through IMPACT in 12 pediatric hospitals across Canada. This program reported a reduction from 485 cases in 1985 to only 20 cases in 1995 and fewer yet in 1997 with eight cases being reported. Nine cases were reported in each 1998 and 1999. In 2000, only four cases of invasive Hib were admitted to IMPACT centres; one in each Ontario, Alberta, Manitoba and Quebec. This was a historic low. In 2001 and 2002 a total of 26 cases were reported by IMPACT sites. Seven cases were considered immunization failures and 20 had received no or incomplete immunization. Parent refusals or failure to ensure their children are immunized outnumber vaccine failures by three to one.

Alberta (6,8)

In 1987, 141 cases of Hib were reported. Rates were highest in children less than one year of age followed by children aged one to four years. A polysaccharide vaccine (Hib-PRP) was introduced in Alberta in 1987 for children over the age of two years. The number of cases reported began to decrease. In 1989, 76 cases of *H. influenzae* infection were reported. The number of reported cases decreased annually to 34 in 1992 and rates in children one to four years of age had declined. In 1992, a new conjugate Hib vaccine (Hib-Hboc) was introduced that provided protection for children two months of age and older. By 1993 rates in children less than one year of age had drastically declined. There were no cases reported in that age group in 1993. Rates in one to four year olds were also very low (three cases) in 1993. Fewer than 10 cases were reported annually from 1993 to 1997.

From 1998 to 2002 a total of 17 cases of invasive Hib disease were reported. Eight were in children less than five years of age, however, most were not old enough to have received a full series of vaccine. Three cases were in children from five to 14 years of age. One case was identified as a vaccine failure.

Key Investigation

Single Case/Household Cluster (9)

- Verify the diagnosis with the physician.
- Verify serotype with lab. Once growth on the culture media has occurred, serotyping for type b will take approximately 24 hours. (K Kowalewska-Grochowska, personal communication, July 2002)
- Determine immunization status of the case. This will assist with determining the likelihood of Hib infection i.e., if the case has completed a full series of vaccine it is less likely to be Hib.
- Identify contacts and obtain the ages, immunization status, and weights (if the contact is less than 12 years of age). Contacts include:
  - all persons living in the household and
  - any individual (household or non-household) who has had four or more hours of contact with the case for five of the seven days prior to the onset of illness regardless of the age of the case
  - AND one of the following lives in the same household as the case:
    - at least one unvaccinated child younger than 48 months, and/or
    - a child younger than 12 months (who has not received a primary series i.e., three doses of vaccine), and/or
    - an immunocompromised child of any age (regardless of the child's immunization status).
- Determine attendance in a childcare centre or nursery school. Obtain the ages, immunization status, and weights (if less than 12 years of age) of attendees.
  - All staff and children attending childcare centres (daycare or dayhome) or nursery schools are considered contacts when two or more cases of invasive Hib have occurred within 60 days and unimmunized or incompletely immunized children attend.

Control

Management of a Case

- Follow up is only done if the responsible organism is *Haemophilus influenzae* type b and the disease is invasive i.e., fits the case definition.
- Routine practices and droplet precautions until the completion of 24 hours of appropriate antibiotic therapy.

- Vaccine failures should be investigated. Serum antibody responses occur 1-2 weeks after immunization hence, vaccine recipients may not be protected during this period. Vaccine failures have been reported in Canada. From 1991 to 1995, 8-12 vaccine failures were reported annually and from 1996 to 1999, three to four annually.(10;11) The US reports approximately 15 cases of invasive Hib disease annually in children less than five years of age who have previously received the primary Hib vaccine series.

Treatment of a Case

- Treat with cefotaxime, ceftriaxone or chloramphenicol, or ampicillin/ chloramphenicol combination. Approximately 30% of strains are ampicillin resistant.
- Rifampin is also recommended if the case was treated with chloramphenicol or ampicillin and this should be initiated during hospitalization. Rifampin can be given up to seven days following the completion of therapy. It is not indicated in those treated with cefotaxime or ceftriaxone as these drugs eradicate Hib from the nasopharynx.

Management of Contacts (12)

- Obtain the age, Hib immunization status and weight (if less than 12 years of age) of all household and childcare/nursery school contacts.
- Educate parents regarding the risk of secondary cases in contacts less than five years old, especially infants, and the need for prompt evaluation and treatment if fever or stiff neck develops.
- Monitor for one full incubation period (10 days) contacts who are children under the age of six years (especially infants, including those in the household, childcare settings, and nursery schools) for signs of illness, especially fever.
- Prophylaxis
  - Prophylaxis should be offered to contacts up to seven days preceding the date of onset (illness) or hospitalization of the index case. Prophylaxis can be considered for up to 10 days after last contact with an untreated case.(13) (A Singh, personal communication, October 15, 2003)
  - In cases where the decision is made to provide prophylaxis to contacts in the household, childcare setting or nursery school, prophylaxis must be offered to all persons in that setting, regardless of age or immunization status.(12)
  - Rifampin prophylaxis** is provided free of charge by AHW. The dosage is based on weight for children under the age of 12 years.
- Household and non-household contacts.
  - Rifampin** is recommended for:
    - all contacts regardless of age or immunization status who have had contact or reside with at least one unvaccinated or incompletely vaccinated contact younger than 48 months of age,
    - all contacts of a fully immunized but immunocompromised child, regardless of age, and
    - all contacts of an unimmunized or incompletely immunized child younger than 12 months of age.
  - Children in the household who are unimmunized or incompletely immunized should be referred to public health for Hib vaccine as soon as possible.
  - Complete immunization is defined as having at least one dose of Hib conjugate vaccine at 15 months of age or older; two doses between 12 and 14 months of age; or a two or three dose primary series when younger than 12 months, with a booster dose at 12 to 18 months of age. Refer to the current Alberta Immunization Manual.

- Childcare and nursery school contacts:
  - When two or more cases have occurred within 60 days and children who have incomplete or absent immunization history attend, administration of Rifampin** to all attendees and personnel is indicated.
  - Those children who are unimmunized or incompletely immunized should receive Hib vaccine as soon as possible.

****Rifampin Dosage for Treatment of Contacts:**

Adults/Children ≥ 12 years:	600 mg orally once daily for 4 days.
Children < 12 years:	20 mg/kg (maximum 600 mg) orally once daily for 4 days.
Infants younger than 1 month:	10mg/kg orally once daily for 4 days.

NOTE: Rifampin is available for order by regions through the Provincial Vaccine Depot and is given to contacts of *Haemophilus influenzae* Type b disease at no charge.

Preventive Measures (12)

- Immunize with a vaccine containing Hib at two, four, six, and 18 months of age as per the current Alberta Immunization Manual. Antibody response develops in more than 93% individuals receiving vaccine.
- One dose of Hib vaccine may be provided to asplenic patients five years of age or older as per the current Alberta Immunization Manual.
- Children age two to 59 months who are approved for cochlear implant surgery as well as past implant recipients should receive Hib conjugate vaccine as outlined in the current Alberta Immunization Manual. Persons five years of age or older need not receive vaccine.
- Children who develop invasive Hib disease before 24 months of age should receive vaccine as recommended, since natural disease may not induce protection.
- Children who develop invasive Hib disease after complete or partial immunization should be referred to a pediatrician for an immunologic assessment.
- Careful observation of exposed unimmunized or incompletely immunized household, non-household, childcare or nursery contacts is vital. Exposed children who develop a febrile illness should receive prompt medical attention and, if indicated, appropriate antimicrobial therapy should be initiated.

References

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(12) Alberta Health and Wellness, Disease Control and Prevention. *Alberta Immunization Manual – Haemophilus influenza type b.* January 2001.

(13) *Regional Policy – Haemophilus B. Influenza infection: HIB (Invasive).* Health Authority 5. Policy number CDC-6B-60 Section H: October 2002

