

Haemophilus influenzae is a bacterium that causes often-severe infections, particularly among infants. It was first described by Richard Pfeiffer in 1892. During an outbreak of influenza, he found *H. influenzae* in patients' sputum and proposed a causal association between this bacterium and the clinical syndrome known as influenza. The organism was given the name *Haemophilus* by Charles-Edward Winslow, et al. in 1920. It was not until 1933 that it was established that influenza was caused by a virus and that *H. influenzae* was a cause of secondary infection.

In the 1930s, Margaret Pittman demonstrated that *H. influenzae* could be isolated in encapsulated (typeable) and unencapsulated (nontypeable) forms. She observed that virtually all isolates from cerebrospinal fluid (CSF) and blood were of the capsular type b.

Before the introduction of effective vaccines, *H. influenzae* type b (Hib) was the leading cause of bacterial meningitis and other invasive bacterial disease, primarily among children younger than age 5 years; approximately one in 200 children in this age group developed invasive Hib disease. Approximately two-thirds of all cases occurred among children younger than age 18 months.

A pure polysaccharide vaccine was licensed for use in the United States in 1985 and was used until 1988. The first Hib conjugate vaccine was licensed in 1987.

Haemophilus influenzae

H. influenzae, a fastidious, pleomorphic, gram-negative coccobacillus, requires hemin (X factor) and nicotinamide-adenine-dinucleotide (NAD, also known as V factor) for in vitro growth. It is generally aerobic, but can grow as an anaerobe under certain conditions.

The outermost structure of encapsulated *H. influenzae* is composed of a polysaccharide, a key virulence factor. Six antigenically and biochemically distinct capsular polysaccharide types have been described; these are designated serotypes a through f. Hib capsule is composed of polyribosyl-ribitol-phosphate (PRP), a polysaccharide used in Hib vaccines. There are currently no vaccines to prevent disease caused by non-b encapsulated or nontypeable strains. In the pre-Hib-vaccine era, type b organisms accounted for 95% of all *H. influenzae* strains that caused invasive disease.

Hib does not survive in the environment on inanimate surfaces.

***Haemophilus influenzae* type b**

- Causes severe bacterial infection, particularly among infants
- During late 19th century believed to cause influenza
- Immunology and microbiology clarified in 1930s
- Leading cause of bacterial meningitis during prevaccine era

Haemophilus influenzae

- Aerobic gram-negative bacteria
- Polysaccharide capsule
- Six different serotypes (a-f) of polysaccharide capsule
- 95% of invasive disease caused by type b during prevaccine era

Hib Pathogenesis

- Enters and colonizes nasopharynx
- May cause an invasive infection—invades bloodstream and infects distant sites in the body
- Incidence is age-dependent; peak occurrence was age 6 to 11 months*
- Most children acquired immunity by age 5 or 6 years*

*Prevaccine era

Pathogenesis

H. influenzae enters the body through the nasopharynx. Organisms colonize the nasopharynx and may remain only transiently or for several months in the absence of symptoms (asymptomatic carrier). In the prevaccine era, Hib could be isolated from the nasopharynx of 0.5% to 3% of healthy infants and children, but was uncommon in adults. Nontypeable strains also frequently inhabit the human respiratory tract.

In some persons, *H. influenzae* causes an invasive infection. The exact mode of invasion of the bloodstream is unknown. A preceding viral or mycoplasma infection of the upper respiratory tract may be a contributing factor. The bacteria spread in the bloodstream to distant sites in the body. Meninges are especially likely to be affected.

Incidence is strikingly age-dependent. In the prevaccine era, up to 60% of invasive disease occurred before age 12 months, although some infants received passive protection from maternal IgG antibodies passed through the placenta and breastfeeding during the first 6 months of life. Peak occurrence was among children age 6 to 11 months.

Antibodies to Hib capsular polysaccharide are protective. The precise level of antibody required for protection against invasive disease is not clearly established. However, a titer of 1 µg/mL 3 weeks postvaccination correlated with protection in studies following vaccination with unconjugated, purified, PRP vaccine and suggested long-term protection from invasive disease.

In the prevaccine era, most children acquired immunity by age 5 or 6 years through asymptomatic nasopharyngeal carriage of Hib bacteria. Since only a relatively small proportion of children carry Hib at any time, it has been assumed exposure to organisms that share common antigenic structures with the capsule of Hib (so-called “cross-reacting organisms”) may also stimulate the development of anticapsular antibodies against Hib. Natural exposure to Hib also induces antibodies to outer membrane proteins, lipopolysaccharides, and other antigens on the surface of the bacterium. The higher the age-specific incidence of Hib disease, the less likely there will be acquisition of both anticapsular and serum bactericidal antibody.

The genetic constitution of the host may also be important in susceptibility to Hib infection. Risk for Hib disease has been associated with a number of genetic markers, but the mechanism of these associations is unknown. No single genetic relationship regulating susceptibility or immune responses to polysaccharide antigens has yet been convincingly demonstrated.

Clinical Features

Hib can affect many organ systems. The most common types of disease are meningitis, bacteremia, epiglottitis, pneumonia, arthritis, and cellulitis.

Meningitis, an infection of the membranes covering the brain and spinal cord, is the most common clinical manifestation of invasive Hib disease, accounting for 50% to 65% of cases in the prevaccine era. Hallmarks of meningitis are fever, decreased mental status, and stiff neck. Hearing impairment or other neurologic sequelae occur in 15% to 30% of survivors. The case fatality ratio is 3% to 6%, despite appropriate antimicrobial therapy.

Epiglottitis is an infection and swelling of the epiglottis, the tissue in the throat that covers and protects the larynx during swallowing. Epiglottitis may cause life-threatening airway obstruction.

Septic arthritis, cellulitis, and pneumonia (which can be mild focal or severe empyema) are common manifestations of invasive Hib disease. Osteomyelitis and pericarditis are less common forms of invasive disease.

Otitis media and acute bronchitis due to *H. influenzae* are generally caused by nontypeable strains. Hib strains account for only 5% to 10% of *H. influenzae* causing otitis media.

Non-type b encapsulated strains can cause invasive disease similar to type b infections. Nontypeable strains are generally less virulent than encapsulated strains among previously healthy individuals, but may cause invasive disease, particularly among neonates and those older than age 65 years.

Laboratory Testing

A Gram stain of an infected body fluid may demonstrate small, gram-negative coccobacilli suggestive of *H. influenzae* disease. CSF, blood, pleural fluid, joint fluid, and middle ear aspirates should be cultured on appropriate media. A positive culture for *H. influenzae* establishes the diagnosis. Detection of antigen or DNA may be used as an adjunct to culture, particularly in diagnosing *H. influenzae* infection in patients who have been partially treated with antimicrobial agents, in which case the organism may not be viable on culture.

All isolates of *H. influenzae* should be serotyped. This is an extremely important laboratory procedure that should be performed on every isolate of *H. influenzae*, especially those obtained from children younger than age 15 years. Two tests are available for serotyping isolates: slide agglutination and serotype-specific, real-time polymerase chain reaction (PCR). Slide agglutination is used to detect Hib capsular polysaccharide antigen in CSF, but a negative test does

Hib Clinical Features

- Most common diseases resulting from Hib infection are meningitis, bacteremia, epiglottitis, pneumonia, arthritis, and cellulitis
- Generally requires hospitalization and 10 days of antimicrobial therapy
- Meningitis accounted for 50% to 65% of cases with a fatality ratio of 3% to 6% (prevaccine era)

not exclude the diagnosis, and false positive tests have been reported. Antigen testing of serum and urine is not recommended because of false positives. Serotype-specific, real-time PCR, currently available to detect the specific target gene of each serotype, can be used for detection of *H. influenzae* in blood, CSF, or other clinical specimens.

Serotype-specific tests, usually done by a state health department or reference laboratory, indicate whether an isolate is type b, the only serotype that is potentially vaccine-preventable.

Medical Management

Invasive Hib disease generally requires hospitalization. Antimicrobial therapy with an effective, third-generation cephalosporin (cefotaxime or ceftriaxone) should be started immediately. Chloramphenicol in combination with ampicillin could be used as an alternative. The treatment course is usually 10 days. 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 therapy.

Epidemiology

Occurrence

Hib disease occurs worldwide.

Reservoir

Humans are the only known reservoir.

Transmission

H. influenzae colonizes the upper respiratory tract of humans and is transmitted person-to-person by inhalation of respiratory droplets or by direct contact with respiratory tract secretions. Neonates can acquire infection by aspiration of amniotic fluid or contact with genital tract secretions during delivery.

Temporal Pattern

Several studies in the prevaccine era described a bimodal seasonal pattern in the United States, with one peak during September through December and a second peak during March through May. The reason for this bimodal pattern is not known.

Communicability

The contagious potential of invasive Hib disease is considered to be limited. However, certain circumstances, particularly close contact with a case-patient (e.g., household, child care, or institutional setting) can lead to outbreaks or direct, secondary transmission of the disease.

Hib Epidemiology

- Reservoir
 - Human
- Transmission
 - Person-to-person through droplet inhalation or direct contact with respiratory tract
 - Neonates can acquire during delivery through amniotic fluid or contact with genital tract secretions
- Temporal pattern
 - Bimodal: peaks in Sept–Dec and March–May
- Communicability
 - Generally limited but higher in some circumstances

Risk Factors

Risk factors for Hib disease include both exposure factors and host factors. Exposure factors include household crowding, large household size, child care attendance, low socioeconomic status, low parental education levels, and school-age siblings. Host factors include age (youngest and oldest ages with elevated risk), race/ethnicity (Native Americans with an elevated risk, possibly confounded by socioeconomic variables associated with both race/ethnicity and Hib disease), and chronic disease (e.g., functional and anatomic asplenia, human immunodeficiency virus [HIV] infection, immunoglobulin deficiency, complement deficiency, receipt of chemotherapy or stem cell transplant). Protective factors (for infants younger than age 6 months) include breastfeeding and passively acquired maternal antibody.

Data are conflicting on the risk for secondary illness among child care contacts, but the risk is thought to be lower than among household contacts. Most studies suggest child care contacts are at relatively low risk for secondary transmission of Hib disease, particularly if contacts are appropriately vaccinated.

Secular Trends in the United States

Before the availability of national reporting data, several areas conducted active surveillance for *H. influenzae* disease, which allowed national estimates of disease. In the early 1980s, it was estimated that about 20,000 cases occurred annually in the United States, primarily among children younger than age 5 years (40 to 50 cases per 100,000 population). The incidence of invasive Hib disease began to decline dramatically in the late 1980s, coinciding with licensure of Hib conjugate vaccines, and has declined by more than 99% since the prevaccine era.

Active Bacterial Core surveillance (ABCs) data includes serotype information on all invasive *H. influenzae* isolates. The number of cases and deaths of invasive *H. influenzae* infections in the United States increased from 3,400 in 1997 to 6,840 in 2018. Approximately 11.8% of cases died. While the rate of invasive *H. influenzae* infections increased from 1.23 per 100,000 population in 1997 to 2.08 per 100,000 population in 2018 in the surveillance areas, the rate of Hib infections decreased from 0.1 per 100,000 population in 1997 to 0.02 per 100,000 population in 2018. Among children younger than age 5 years in 2018, the rate of invasive *H. influenzae* disease was 0.08 per 100,000 population and 38 cases of invasive disease due to Hib were reported in the United States. An additional 9 cases of Hib are estimated to have occurred among the 175 reports of invasive *H. influenzae* infections with an unknown serotype.

Hib Secular Trends in the United States

- About 20,000 cases of Hib annually before vaccine
- Incidence of Hib has declined 99% since the prevaccine era
- From 2009-2018, 36 reported cases of Hib in patients younger than age 5 years
- Secondary cases of Hib are rare (illness occurring 1-60 days following contact with an ill person)

From 2009–2018, 36 Hib cases in patients younger than age 5 years were reported to ABCs. Two (5.6%) were too young to have received Hib vaccine, 12 (33.3%) were unvaccinated, and 14 (38.9%) were undervaccinated (10 of 14 had received the 3-dose primary series but were missing a booster dose at age 12 through 15 months). Eight (22.2%) were age-appropriately vaccinated and had no reported underlying conditions; three of these were 3-month-old infants who had been age-eligible for only the first dose of Hib vaccine.

Secondary cases of Hib disease occur but are rare. Secondary Hib disease is defined as illness occurring 1 to 60 days following contact with an ill person, and accounts for less than 5% of all invasive Hib disease. Secondary attack rates are higher among household contacts younger than age 48 months (2.1%), especially those younger than age 12 months (6%) and younger than age 24 months (3%). In these household contacts, 64% of secondary cases occurred within the first week (excluding the first 24 hours) of disease onset in the index patient, 20% during the second week, and 16% during the third and fourth weeks.

Among children born during 2016–2017, 92.2% had received the Hib vaccine primary series (at least 2 or 3 doses, depending on product) and 79.9% had received the full series (primary series and booster; at least 3 or 4 doses, depending on product type) by age 24 months.

Hib Vaccines

- Three conjugate vaccines
 - PRP-T (ActHIB)
 - PRP-T (Hiberix)
 - PRP-OMP (PedvaxHIB)
- Two combination vaccines containing Hib
 - DTaP-IPV/Hib (Pentacel)
 - DTaP-IPV-Hib-HepB (Vaxelis)

Haemophilus influenzae type b Vaccines

A pure polysaccharide vaccine was licensed for use in the United States in 1985 and was used until 1988. The vaccine had low efficacy and is no longer available in the United States.

The characteristics of the Hib polysaccharide vaccine were similar to other polysaccharide vaccines. The response to the vaccine was typical of a T-independent antigen, most notably an age-dependent immune response and poor immunogenicity in children age 2 years or younger. In addition, no boost in antibody titer was observed with repeated doses, the antibody that was produced was relatively low-affinity IgM, and switching to IgG production was minimal.

The first Hib conjugate vaccine was licensed in 1987. Conjugation is the process of chemically bonding a polysaccharide to a more effective protein carrier. This process changes the polysaccharide from a T-independent to a T-dependent antigen and greatly improves immunogenicity, particularly in young children. In addition, repeat doses of conjugate vaccines elicit booster responses and allow maturation of class-specific immunity with predominance of IgG antibody. The conjugates also cause carrier priming and elicit antibody to “useful” carrier protein.

Three monovalent Hib polysaccharide-protein conjugate vaccines (ActHIB, PedvaxHIB, and Hiberix) are currently licensed for use in the United States.

Two combination vaccines containing Hib are currently licensed for use, DTaP-IPV/Hib (Pentacel) and DTaP-IPV-Hib-HepB (Vaxelis).

Characteristics

Hib (PRP-T [ActHIB, Hiberix]) use a tetanus toxoid carrier protein, while Hib (PRP-OMP [PedvaxHIB]) uses a meningococcal outer membrane protein. DTaP-IPV/Hib (Pentacel) contains Hib (PRP-T) and DTaP-IPV-Hib-HepB (Vaxelis) contains Hib (PRP-OMP). Hib vaccines are administered by intramuscular injection. Each dose of Hib (PRP-OMP [PedvaxHIB]) vaccine contains aluminum as an adjuvant. Monovalent Hib vaccines contain no antibiotic or preservative. Specific ingredients to combination vaccines containing Hib vaccine differ.

Vaccination Schedule and Use

All infants should receive a primary series of Hib conjugate vaccine (monovalent or combination vaccine) beginning at age 2 months. The number of doses in the primary series depends on the type of vaccine used. A primary series of Hib (PRP-T) requires 3 doses, whereas Hib (PRP-OMP) requires 2 doses. A booster dose is recommended at age 12 through 15 months, regardless of which vaccine is used for the primary series. The recommended age for dose 4 of DTaP-IPV/Hib is age 15 through 18 months, but it can be administered as early as age 12 months, provided at least 6 months have elapsed since dose 3.

Hib Vaccine Characteristics

- PRP-T use a tetanus toxoid carrier protein
- PRP-OMP uses a meningococcal outer membrane protein
- Administered by intramuscular injection
- PRP-OMP doses contain aluminum adjuvant

Haemophilus influenzae type B

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Hib Vaccination Schedule (Monovalent Vaccines)

- PRP-T (ActHIB and Hiberix) 3-dose primary series at age 2, 4, and 6 months
- PRP-OMP (PedvaxHIB) 2-dose primary series at age 2 and 4 months
- Booster dose at age 12 through 15 months
- Recommended interval between primary series doses is 8 weeks and minimum interval is 4 weeks
- Minimum age for dose 1 is 6 weeks
- Catch-up recommendations depend on child's age
- Vaccines are interchangeable and should follow a 3-dose schedule if more than 1 brand is used

Haemophilus influenzae type b (Hib) Routine Vaccination Schedule

Vaccine type	Vaccine Trade Names	2 months	4 months	6 months	12–15 months
PRP-T	ActHIB	Dose 1	Dose 2	Dose 3	Booster
	Pentacel	Dose 1	Dose 2	Dose 3	Booster*
	Hiberix	Dose 1	Dose 2	Dose 3	Booster†
PRP-OMP	PedvaxHIB	Dose 1	Dose 2	—	Booster
	Vaxelis	Dose 1	Dose 2	Dose 3 [§]	Not indicated

* The recommended age for dose 4 of DTaP-IPV/Hib (Pentacel) is age 15 through 18 months, but it can be administered as early as 12 months, provided at least 6 months have elapsed since dose 3.

† The recommended age for dose 4 of Hib (PRP-T) (Hiberix) is age 15 months, but to facilitate timely booster vaccination, it may be administered as early as age 12 months.

§ The recommended minimum age for dose 3 of DTaP-IPV-Hib-HepB (Vaxelis) is 24 weeks, the minimum age for completion of the hepatitis B vaccine series.

The recommended interval between doses in the primary series is 8 weeks, with a minimum interval of 4 weeks. At least 8 weeks should separate the booster dose from the previous (2nd or 3rd) dose. If DTaP-IPV/Hib is administered for the booster dose, at least 6 months need to have elapsed since dose 3.

Hib vaccines should be given at the same visit as other recommended vaccines.

Limited data suggest Hib conjugate vaccines administered before age 6 weeks can induce immunologic tolerance, reducing the response to subsequent doses of Hib vaccine. Therefore, Hib vaccines, including combination vaccines containing Hib conjugate vaccine, should never be administered to a child younger than age 6 weeks.

The monovalent Hib conjugate vaccines are interchangeable. A series that includes vaccine of more than one brand will induce a protective antibody level. If a child receives different brands of Hib vaccine at age 2 and 4 months, a 3rd dose of any brand should be administered at age 6 months to complete the primary series. Any of these vaccines may be used for the booster dose, regardless of which vaccines were administered for the primary series. Data on the interchangeability of Hib combination vaccine with monovalent vaccines are limited. Whenever feasible, the same combination vaccine should be used for the subsequent doses.

Unvaccinated children age 7 months or older may not require a full series of 3 or 4 doses. The number of doses a child needs to complete the series depends on the child's current age.

Haemophilus influenzae type b Vaccine Schedule for Previously Unvaccinated Children

Vaccine	Age at 1st Dose (months)	Primary series	Booster
PRP-T	2–6	3 doses, each dose 8 weeks apart	12–15 months
	7–11	2 doses, 4 weeks apart	12–15 months
	12–14	1 dose	8 weeks later
	15–59	1 dose	--
PRP-OMP	2–6	2 doses, 8 weeks apart	12–15 months
	7–11	2 doses, 4 weeks apart	12–15 months
	12–14	1 dose	8 weeks later
	15–59	1 dose	—

PRP-T (ActHIB, Hiberix)

Unvaccinated infants age 2 through 6 months should receive 3 doses of vaccine, administered 2 months apart. The primary series should be followed by a booster dose at age 12 through 15 months, administered at least 8 weeks after the last dose. A booster dose is only needed if 2 or 3 primary doses were administered before age 12 months. Unvaccinated children age 7 through 11 months should receive 2 doses of vaccine, 4 weeks apart. Those 2 doses should be followed by a booster dose at age 12 through 15 months, administered at least 8 weeks after the last dose. Unvaccinated children age 12 through 14 months should receive 1 dose of vaccine, followed by a booster dose at least 8 weeks later. Any previously unvaccinated child age 15 through 59 months should receive a single dose of vaccine.

PRP-OMP (PedvaxHIB)

Unvaccinated infants age 2 through 6 months should receive 2 doses of vaccine, administered 2 months apart. Those 2 doses should be followed by a booster dose at age 12 through 15 months, administered at least 8 weeks after the last dose. Unvaccinated children age 7 through 11 months should receive 2 doses of vaccine, 4 weeks apart, followed by a booster dose at age 12 through 15 months. The booster should be administered

at least 8 weeks after the last dose. Unvaccinated children age 12 through 14 months should receive 1 dose of vaccine, followed by a booster at least 8 weeks later. Any previously unvaccinated child age 15 through 59 months should receive a single dose of vaccine.

DTaP-IPV/Hib (Pentacel)

DTaP-IPV/Hib vaccine is approved for use as a 4-dose series for children age 6 weeks through 4 years. It is administered to infants at age 2, 4, 6, and 15 through 18 months. The minimum intervals for DTaP-IPV/Hib vaccine are determined by the DTaP component. The first 3 doses must be separated by at least 4 weeks between doses. Dose 4 must be separated from dose 3 by at least 6 months, and should not be administered before age 12 months. When DTaP-IPV/Hib vaccine is used to provide 4 doses at age 2, 4, 6, and between 15 through 18 months (based on the DTaP and Hib schedules), an additional booster dose with IPV-stand alone or DTaP-IPV vaccine should be administered at age 4 through 6 years. This will result in a 5-dose IPV vaccine series, which is acceptable.

DTaP-IPV-Hib-HepB (Vaxelis)

DTaP-IPV-Hib-HepB is approved for use as a 3-dose series for children age 6 weeks through 4 years. It is administered to infants at age 2, 4, and 6 months. The minimum intervals for DTaP-IPV-Hib-HepB vaccine are determined by the DTaP component. The 3 doses must be separated by at least 4 weeks between doses. Because the minimum age for the first dose of DTaP-IPV-Hib-HepB vaccine is 6 weeks, this vaccine cannot be used for the birth dose of hepatitis B (HepB) vaccine. The final dose of DTaP-IPV-Hib-HepB vaccine should be administered at age 24 weeks or older, the minimum age for completion of the hepatitis B vaccine series. When DTaP-IPV-Hib-HepB vaccine is used to provide 3 doses at age 2, 4, and 6 months (based on the DTaP and IPV schedules), this will result in a 4-dose HepB vaccine series, which is acceptable.

While single antigen PRP-OMP Hib vaccines are licensed as a 2-dose primary series at age 2 and 4 months, DTaP-IPV-Hib-HepB is licensed as a 3-dose primary series. Therefore, three doses of a Hib conjugate-containing vaccine are needed to complete the primary series if DTaP-IPV-Hib-HepB is used for any doses. DTaP-IPV-Hib-HepB should not be used for the booster dose (given after completion of the 3-dose primary series). Any Hib conjugate vaccine licensed for a booster dose can be used. If DTaP-IPV-Hib-HepB is inadvertently given for the booster dose, the dose does not need to be repeated with another Hib-containing vaccine, if the proper spacing of prior doses is maintained.

Vaccination of Special Populations and Older Children

Children younger than age 24 months who develop invasive Hib disease should be considered susceptible and should receive Hib vaccine. Vaccination of these children should start as soon as possible during the convalescent phase of the illness. A complete series as recommended for the child's age should be administered.

Children age 12 through 59 months who are at increased risk for Hib disease, including chemotherapy recipients and those with anatomic and functional asplenia (including sickle-cell disease), HIV infection, immunoglobulin deficiency, or early complement component deficiency, who have received either no doses or only 1 dose of Hib vaccine before age 12 months, should receive 2 additional doses of Hib vaccine, 8 weeks apart. Children who received 2 or more doses of Hib vaccine before age 12 months should receive 1 additional dose.

If a child younger than age 5 years undergoing chemotherapy or radiation treatment received a Hib vaccine dose(s) within 14 days of starting therapy or during therapy, they should receive a repeat dose(s) at least 3 months following therapy completion.

In general, Hib vaccination of persons older than age 59 months is not recommended. The majority of older children are immune to Hib, probably from asymptomatic infection as infants. However, some older children and adults are at increased risk for invasive Hib disease and may be vaccinated if they were not vaccinated in childhood. A single dose of any Hib-containing vaccine should be administered to persons age 15 months or older undergoing an elective splenectomy if they are considered unimmunized. "Unimmunized" means they have not received a primary series and booster dose or at least 1 dose of Hib vaccine after age 14 months. If possible, the vaccine should be administered at least 14 days before the procedure. Hib vaccine should be administered to children age 5 years or older and adults who have anatomic or functional asplenia if they are considered unimmunized. Hib vaccine should be administered to children and adolescents age 5 through 18 years if they have HIV and are considered unimmunized. Adults with HIV do not need a dose of Hib vaccine. Hematopoietic stem cell transplant recipients of any age should receive 3 doses of Hib vaccine at least 4 weeks apart, beginning 6 to 12 months post-transplant, regardless of Hib vaccination history.

For American Indians/Alaska Natives (AI/AN), the Advisory Committee on Immunization Practices (ACIP) recommends Hib (PRP-OMP) as the preferred vaccine for the primary series doses. Hib meningitis incidence peaks at a younger age among AI/AN infants, and Hib (PRP-OMP) produces a protective antibody response after the first dose, providing early protection.

Hib Vaccination of Special Populations and Older Children

- Children younger than age 24 months who develop invasive Hib
 - Vaccinate as soon as possible during convalescent phase
 - Administer complete series for age
- Children age 12 through 59 months at increased risk (chemotherapy, anatomic and functional asplenia, HIV infection, immunoglobulin deficiency, early complement component deficiency)
 - If child received 0 or 1 dose before age 12 months, administer 2 doses, 8 weeks apart
 - If child received 2 or more doses before age 12 months, administer 1 dose
- Unimmunized persons age 15 months or older undergoing an elective splenectomy
 - Administer 1 dose at least 14 days before procedure
- Unimmunized persons age 5 years or older with anatomic or functional asplenia
 - Administer 1 dose
- Unimmunized children and adolescents age 5 through 18 years with HIV
 - Administer 1 dose
- Hematopoietic stem cell transplant recipients of any age
 - Administer 3 doses at least 4 weeks apart, beginning 6 to 12 months post-transplant
- American Indians/Alaska Natives
 - Administer PRP-OMP as preferred vaccine

Hib Vaccine Efficacy

- Highly immunogenic
- More than 95% of infants develop protective antibody levels after a primary series

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Hib Vaccine Contraindications and Precautions

- Contraindication
 - Severe allergic reaction to a vaccine component or following a prior dose of vaccine
 - Children younger than age 6 weeks
- Precaution
 - Moderate or severe acute illness

Hib Vaccine Safety

- Adverse reactions uncommon
- Swelling, redness, or pain
 - 5%–30%
- Fever
 - 31%
- Crying
 - 11%
- Injection site erythema
 - 11%
- Irritability
 - 10%
- Rash
 - 9%

Immunogenicity and Vaccine Efficacy

Hib conjugate vaccines are highly immunogenic. More than 95% of infants develop protective antibody levels after a primary series. Clinical efficacy has been estimated at 95% to 100%. Invasive Hib disease is uncommon in children who are fully vaccinated.

Hib vaccine is also immunogenic in patients at increased risk for invasive disease, such as those with sickle-cell disease, leukemia, or those who have had a splenectomy. In persons with HIV infection, immunogenicity varies with stage of infection and degree of immunocompromise. Efficacy studies have not been performed in populations with increased risk of invasive disease.

Contraindications and Precautions to Vaccination

As with other vaccines, a history of a severe allergic reaction (anaphylaxis) to a vaccine component or following a prior dose is a contraindication to further doses. Moderate or severe acute illness with or without fever in a patient is considered a precaution to vaccination, although persons with minor illness may be vaccinated.

Hib conjugate vaccines are contraindicated for children younger than age 6 weeks because of the potential for development of immunologic tolerance.

Contraindications to combination vaccines that contain Hib include the contraindications to the individual component vaccines, but specific ingredients might differ.

Vaccine Safety

Adverse reactions following Hib conjugate vaccines are not common. Swelling, redness, or pain have been reported in 5% to 30% of recipients and usually resolve within 12 to 24 hours. Systemic reactions such as fever and irritability are infrequent.

Among reports to the Vaccine Adverse Event Reporting System (VAERS) following Hib vaccination, the most frequently reported adverse events were fever (31%), crying (11%), injection site erythema (11%), irritability (10%), and rash (9%). The median time from vaccination to onset of an adverse event was 1 day. The adverse event reporting frequencies for Hib vaccines are similar to those of other childhood vaccines; no unusual or unexpected safety concerns were observed in VAERS data for Hib vaccines.

In an observational study conducted by the Vaccine Safety Datalink of DTaP-IPV/Hib, children age 1 to 2 years who received DTaP-IPV/Hib had an elevated risk of fever compared to children who received DTaP-containing control vaccine (i.e., without Hib vaccine). DTaP-IPV/Hib was not associated with any other medically-attended adverse health event.

Vaccine Storage and Handling

Hib vaccines should be maintained at refrigerator temperature between 2°C and 8°C (36°F and 46°F). Manufacturer package inserts contain additional information. For complete information on best practices and recommendations for vaccine storage and handling, please refer to CDC's *Vaccine Storage and Handling Toolkit*, www.cdc.gov/vaccines/hcp/admin/storage/toolkit/storage-handling-toolkit.pdf.

Surveillance and Reporting of Hib Disease

Reporting of *H. influenzae* varies by state. Invasive *H. influenzae* infections became nationally notifiable in 1991. Reporting of serotype information continues to be incomplete. For information on the case definition and guidance on case and contact investigations, please consult the Manual for the Surveillance of Vaccine-Preventable Diseases, www.cdc.gov/vaccines/pubs/surv-manual/index.html.

