



# Haemophilus Influenzae Type b (Hib) and Hib Vaccines

## Frequently Asked Questions (FAQ)

These questions and answers are designed to provide concise but comprehensive information on *Haemophilus influenzae* type b, bacteria which can cause serious childhood diseases, and the vaccine that protects against it.

**What is *Haemophilus influenzae* type b disease?** *Haemophilus influenzae* type b, or Hib disease refers to diseases (mainly pneumonia and meningitis) caused by the Hib bacterium. The World Health Organization (WHO) estimates that Hib is responsible for approximately 3 million serious illnesses and an estimated 400,000 deaths per year, mainly in the developing world. Almost all victims are children under the age of five years; those between the ages of 4-18 months are especially vulnerable.

Although influenzae is part of the name, it is unrelated to the virus that is commonly referred to as the "flu."

**How is Hib spread?** Hib bacteria normally establish themselves in the nose or upper throat (medically referred to as the nasopharynx). The bacteria are spread through respiratory droplets, which occur during sneezing, coughing, or speaking closely with an infected person. Children often carry Hib bacteria without showing any signs or symptoms (asymptomatic carriage); however, they are still able to infect others.

**How many types of *Haemophilus influenzae* exist?** *Haemophilus influenzae* bacteria fall into two groups: some surrounded by a protective capsule and others without this capsule. Within the encapsulated group, there are 6 serotypes (groups of related microorganisms distinguished by a common set of antigens) of *Haemophilus influenzae*, named a through f, that have been classified. It is estimated that *Haemophilus influenzae* type b serotype accounts for 95% of all invasive disease caused by *Haemophilus influenzae* where no vaccine is used. The non-encapsulated organism is commonly referred to as non-typhable.

**What does Hib cause?** **Hib pneumonia:** A chest x-ray is sometimes used to help diagnose pneumonia. Chest x-rays with a distinct area of infection, also known as 'consolidation', are often associated with bacterial infection. However, Hib pneumonia cannot be distinguished from other forms of pneumonia by x-ray. The only way to diagnose it is by isolating the organism from the blood or pleural (lung) fluid of a patient with pneumonia.

**Hib Meningitis:** Diagnosis of Hib meningitis requires the organism to be identified from fluid from the spine, (cerebrospinal fluid or CSF). CSF can only be obtained by performing a lumbar puncture, a procedure during which a needle is inserted into the spinal canal.

**Other severe infections:** More rarely, Hib is responsible for other life-threatening complications in young children, such as septic arthritis (inflammation of the joints) and septicemia (blood poisoning), both of which can have other causes. Hib may also lead to epiglottitis (a life-threatening inflammation of the flexible cartilage that covers the gap in the vocal cords during swallowing). Body fluid samples such as joint fluid, blood or secretions from the respiratory tract can help to identify the organism in these various conditions.

What are the symptoms of Hib disease?

Symptoms of Hib infection depend on the disease that the individual has, and can range from those of mild respiratory illness to life-threatening illness. Children with meningitis often exhibit classical symptoms such as high fever, stiff neck, and headache. Pneumonia is usually characterized by cough, rapid breathing or shortness of breath, and with severe disease, chest retractions.

How is Hib disease diagnosed?

Diagnosis of Hib can be quite challenging for a number of reasons. Prior antibiotic use, use of inappropriate lab materials or failure to obtain samples or improper handling, can all impact the ability to diagnose the disease. In addition, it is often not feasible to diagnose Hib pneumonia because extracting fluid from the lungs is an invasive procedure that is usually not done by most physicians.

Aside from technical difficulties with diagnosis, there are issues with the misdiagnosis and recognition of Hib pneumonia.

## Epidemiology of Disease

Can a child have no symptoms but still carry the bacteria?

The WHO estimates that, in developing countries, up to 15% of children are asymptomatic carriers of Hib, never developing symptoms, yet remaining a risk to other children to whom they may transmit bacteria. Only a minority of Hib carriers will develop Hib disease. Preschool aged children usually have the highest prevalence of Hib carriage. Higher prevalence of carriage has also been shown in certain ethnic groups.

What factors increase the risk of Hib diseases?

There are a number of factors that can increase the risk of invasive Hib disease. Young age (less than 2 years) is the major risk factor. Other risk factors include certain races/ethnicities, as well as medical conditions resulting in immunodeficiency and immunosuppression (e.g. HIV/AIDS). Socio-demographic factors may also play a role, including large household size, low levels of education, and crowding.

Are HIV positive children at greater risk for Hib disease?

Yes. When compared to children who are HIV-negative, it is documented that HIV-positive children have higher rates of severe Hib disease, including more severe illness and higher rates of death.

## Vaccine and Formulations

What formulations are available for Hib vaccine?

The following Hib vaccines are currently available:

- Pentavalent DTP-HepB-Hib combination (all-liquid or liquid DTP-Hep B + lyophilized Hib)
- Tetravalent DTP-Hib combination
- Monovalent Hib

Pentavalent (a vaccine formulation that protects against 5 diseases) is the most popular in GAVI-eligible countries, as no additional vaccinations are added to the immunization schedule. Other formulations, including vaccines containing acellular pertussis and other antigens, are also available within private markets and national programs in developed countries.

What is the manufacturing supply situation regarding Hib combination vaccines?

There are currently five WHO prequalified pentavalent vaccines (DTP-HepB/Hib) from 4 manufacturers. Because two of the pentavalent vaccines have recently been prequalified, it may take a bit of extra time in the short run for UNICEF to be sure there is a secure supply of these two vaccines. Countries looking to introduce the vaccines will have a choice between all-liquid and lyophilized vaccines until the supply situation becomes more stable. Additional all-liquid formulations are expected in the 2009/2010 time frame.

## Vaccine Effectiveness

How effective is the Hib vaccine?

In clinical trials, Hib conjugate vaccines have been shown to have between 90-100% efficacy against invasive Hib disease. Since the introduction of Hib vaccine, rates of invasive disease have declined significantly in several developing countries including Uruguay, the Gambia, Kenya and Malawi, as well as middle-income countries such as Chile.

Several countries such as Bangladesh, Malawi, Rwanda, and Uganda have demonstrated the vaccine's effectiveness through case-control studies.

Is Hib vaccine effective in HIV positive children?

Yes, however, the effectiveness is likely to be reduced. A study in South Africa did show reduced effectiveness of Hib vaccine in HIV infected children when compared with uninfected children. Despite this, the vaccine is still considered an important preventive tool for all children, regardless of HIV status. A study in Malawi demonstrated that the effectiveness of Hib vaccine in preventing Hib meningitis among HIV infected Malawian children with more than two doses of the vaccine compared to no doses was 100% when adjusted for age and residence.

## Vaccine Safety

What are the side effects of the vaccine?

Adverse side effects are uncommon with Hib conjugate vaccine although mild local reactions (e.g. redness, slight swelling or warmth) at the injection site or fever may occur. Vaccination with Hib conjugate vaccine is contraindicated for persons known to have experienced a severe allergic reaction (anaphylaxis) to a vaccine component or following a prior dose of that vaccine. Vaccination should be delayed for children with moderate or severe acute illnesses; however, minor illnesses are not contraindications to vaccination. Hib conjugate vaccines should not be given to children younger than 6 weeks.

Can Hib vaccine cause Hib disease?

No. There have been no known cases of Hib disease caused by the vaccine.

## Hib Vaccine in National Immunization Programmes

If Hib vaccine is so effective, why don't more children receive it?

Although Hib vaccines have been used routinely in developed countries for more than 18 years, children in developing countries continue to have limited access to the vaccine. Hib vaccine has been extremely effective in countries where it has been introduced as a part of the national immunization program, also known as the Expanded Program on Immunization (EPI), even in situations with interruptions in vaccine supply or usage. Primary barriers to the adoption of Hib vaccine include lack of awareness on the burden of disease, financial considerations, and competing priorities. However, the situation is rapidly changing in the 72 poorest countries of the world. These countries are eligible for funding from the GAVI Alliance, a public/private global health partnership committed to saving lives and protecting health through the widespread use of vaccines.

Is it necessary to vaccinate older children?

The World Health Organization states that the vaccine is not generally required for children over the age of 24 months due to the limited burden of Hib disease among children older than that age.

When should a child begin the series of doses?

Hib vaccine is administered on the same infant immunization schedule that exists for DTP. Children in developing countries generally receive Hib vaccine at 6, 10 and 14 weeks or 2, 4 and 6 months of age. Schedules may vary by country or depend on the particular manufacturer of the Hib vaccine.

Do children need a booster dose?

In some countries, mostly developed countries, a booster dose is offered between 12 and 18 months of age. WHO recommends a three dose infant schedule and states that the need for and timing of a booster dose of Hib vaccine in developing countries requires further study. Continued surveillance is ongoing in order to monitor disease trends among older age groups and to provide evidence on the need for a booster dose in different settings.

Instead of Hib vaccine, is it just as beneficial to use antibiotics once Hib is diagnosed?

In general, prevention is better than treatment. There are many difficulties in properly diagnosing and treating Hib, including inequities in access to care and the difficulty of isolating Hib in the laboratory. In addition, antibiotic resistance is becoming increasingly prevalent and there is potential for severe outcomes even when treatment is received. Considering the availability of safe and effective vaccines against Hib, prevention is preferable.

Which GAVI-eligible countries<sup>1</sup> have introduced the vaccine?

As of June 2008, 28 of 72 (39%) GAVI eligible countries have introduced Hib vaccine into their EPI schedule. By 2009 it is expected that 52 (72%) GAVI eligible countries will have introduced the vaccine. The following countries have already introduced, or have been approved by the GAVI Alliance to introduce Hib vaccine by 2009 (\*) and have received new vaccine support from GAVI:

**Africa:**

Angola	Congo DRC*	Guinea Bissau*	Mozambique*	Uganda
Benin	Congo Rep*	Kenya	Niger*	Zambia
Burkina Faso	Cote d'Ivoire*	Lesotho*	Rwanda	Zimbabwe
Burundi	Eritrea*	Liberia	Sao Tome & Principe*	
Cameroon*	Ethiopia	Madagascar*	Senegal	
CAR*	Gambia	Malawi	Sierra Leone	
Chad*	Ghana	Mali	Tanzania*	
Comoros*	Guinea*	Mauritania*	Togo	

**Eastern Mediterranean:**

Afghanistan\*  
Djibouti  
Pakistan\*

Sudan  
Yemen

**Central and Eastern Europe:**

Moldova\*  
Tajikistan\*  
Ukraine  
Uzbekistan\*

**South-East Asia:**

Bangladesh\*  
Nepal\*

Sri Lanka

**Western Pacific:**

Kiribati\*  
Mongolia  
Papa New Guinea  
Solomon Islands\*

**Pan-America (adopted outside of or with partial GAVI support):**

Bolivia  
Cuba  
Guyana  
Honduras  
Nicaragua

## Vaccine Price and Financing

What is the price per dose for a combination vaccine?

The price paid by each country varies. The 72 countries eligible to receive funding from the GAVI Alliance are required to pay a small portion of the price of the vaccine. For all Hib containing vaccines, including pentavalent, co-payments range from \$0.15 for fragile states to a minimum of \$0.30 for the least poor countries. The least poor countries are expected to scale up co-financing by 15% annually.

GAVI will conduct an evaluation of the co-financing policy in 2009. Based on the outcomes of the evaluation, current co-financing levels, country groupings and eligibility criteria are expected to be revised in 2010. This price will be based on what UNICEF is able to procure from manufacturers. Already, based on declines in prices seen for DTP-Hep B combinations, the prices for pentavalent combinations look promising if demand, capacity and competition materialize.

In private markets, prices are negotiated directly with manufacturers. In addition, governments in high and middle-income countries may directly negotiate prices with manufacturers.

<sup>1</sup> Countries eligible for support is determined initially by national income and includes countries with a Gross National Income (GNI) per capita below US\$1,000 in 2003 – currently there are 72 eligible countries.

Is this vaccine cost-effective?

Hib vaccine has been shown to be cost-effective in a number of countries, including developing countries, where Hib vaccine is routinely used. Studies conducted in Indonesia and Kenya have shown a marked increase in the total treatment costs saved due to Hib vaccination. Every successful intervention requires some investment for each life saved. With GAVI support there is a decrease in vaccine and equipment costs for individual countries, making the vaccine more affordable. As the cost of the vaccine decreases over time, cost-effectiveness will continue to improve.

If my country cannot afford all the new vaccines it will need, why adopt Hib vaccine?

This is a question that concerns many countries. Other vaccines may be available, which could provide similar or better protection against diseases for children as compared to Hib vaccine. However, it is important to recognize that addressing the child health priorities in a country will require multiple interventions. Hib vaccine is an important tool for reaching the 2015 Millennium Development Goal of reducing child mortality. There is a cost for delaying introduction and we encourage countries to adopt all feasible, cost-effective options as soon as they are able. The Hib Initiative aims to guide countries in making informed decisions regarding the introduction of Hib vaccine in the context of other health problems and can offer technical assistance and support for countries during their decision making process.

What about pneumococcal vaccine as an option for combating childhood pneumonia?

It is important to note that pneumonia is the leading killer of children under the age of 5. Hib and *Streptococcus pneumoniae* (pneumococcus) are both major causes of pneumonia among children. The GAVI Alliance now funds Hib and pneumococcal vaccines and encourages all countries to implement both vaccines as soon as possible. A significant reduction in pneumonia requires a multifaceted approach including vaccines, improved nutrition, indoor air pollution control, case management, and breastfeeding. It is important for countries to use every intervention possible.

## Decision Making

Many of our neighboring countries with similar burden of disease have not implemented Hib vaccine, why should we?

There are many reasons why countries have not adopted the Hib vaccine. Each country must assess their individual situation when considering adopting Hib vaccine. WHO has recommended global implementation of Hib vaccination with the following statement:

*"In view of their demonstrated safety and efficacy, conjugate Hib vaccines should be included in all routine infant immunization programs. Lack of local surveillance data should not delay the introduction of these vaccines, especially in countries where regional evidence indicates there is a high burden of disease."*

It is important that each country assess their data, as well as data from the region, and make practical decisions regarding the health of their children. The Hib Initiative, along with their partners, is eager to work with countries in identifying possible solutions for overcoming barriers to allow for greater protection of children. By working together to eliminate difficult obstacles, countries can reach the critical Millennium Development Goal of reducing under-five mortality by two-thirds by the year 2015.

## Disease Burden

What are the consequences if my country does not introduce this vaccine?

For reasons previously mentioned, Hib disease is often difficult to detect and diagnose, causing routine surveillance to significantly underestimate Hib disease burden.

There are a number of potential concerns, including illness leading to permanent disability or death, as well as increased poverty for families trying to provide care for a sick child. There can also be broader economic consequences of treating the children of families that cannot otherwise afford medical care. Other impacts may include an overall decline in a child's educational outcomes or productivity. Hib vaccine offers a cost-effective option for the prevention of childhood disease, which can provide benefits reaching far beyond the individual child.

## How many deaths will be prevented with Hib vaccine?

The number of deaths prevented with Hib vaccine included in the national immunization programme depends on the disease burden and vaccine coverage in your country. It has been estimated that Hib vaccine prevents 4% of under 5 child mortality on a global basis; but, again, these results may vary between countries.

## Resources

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## The Hib Initiative

- The Hib Initiative aims to guide countries in making informed decisions regarding introduction or continuation of Hib vaccine programs in the context of other health problems and offers technical assistance and support for GAVI-eligible countries.
- The Hib Initiative unites experts from Johns Hopkins Bloomberg School of Public Health, the London School of Hygiene and Tropical Medicine, the World Health Organization, and the Centers for Disease Control and Prevention (CDC) and is supported by a 4-year grant from the GAVI Alliance [www.gavialliance.org](http://www.gavialliance.org).

Visit the Hib Initiative at [www.HibAction.org](http://www.HibAction.org)

