National Institutes of Health
Office of Science Policy

CHILDHOOD Hib VACCINES: NEARLY ELIMINATING THE THREAT OF BACTERIAL MENINGITIS

By "teaching" the immune system to defend against infection, vaccines prevent serious illness, disability, and death from dozens of infectious diseases,[1] making vaccines one of the most important public health achievements ever. As a leader in biomedical research, NIH has contributed to the development of many vaccines throughout its history – one standout vaccine has nearly eliminated Haemophilus influenzae type b (Hib) infection in the U.S. Once the leading cause of bacterial meningitis in children, Hib infection can result in serious, long-term disability and death. Today, the near elimination of Hib has had profound benefits throughout the world.[2] NIH, in concert with many other governmental, non-profit, and private organizations, played a key role in making an effective Hib vaccine a reality, resulting in thousands of lives saved.[3]

HAEMOPHILUS INFLUENZAE TYPE B (Hib)

- Bacterial infection spread by direct person-to-person contact as well as coughing and sneezing
- Causes fever, bacterial meningitis, pneumonia, infection of the blood, and swelling of the throat and joints
- Long-term consequences can include deafness, blindness, brain damage, and intellectual disability
- Predominately affects young children, especially infants

Also see Hib information provided by the Centers for Disease Control and Prevention (CDC): http://www.cdc.gov/vaccines/vpd-vac/hib.htm

Hib INFECTIONS: THEN AND NOW

THEN

More than 20,000 cases of Hib were reported in the U.S. each year.[8]

- Antibiotics were not always prescribed at the right time and dose. Even with effective antibiotic treatment, 5 percent of those who contracted the infection died.[4]
- Hib was the **leading cause of bacterial meningitis** and acquired intellectual disability in children – most of whom were under 5 years of age.[6]
- Upwards of **1,000 children died from Hib every year** and 6,000 suffered from deafness, seizures, intellectual disability, or brain damage primarily due to bacterial meningitis.[10]
- **$2 billion per year** in health care costs were attributed to Hib and related illnesses in 1968.[12]

NOW

Cases have dropped by more than 99%, with only around 40 reported in 2009.[9]

- Highly effective Hib vaccines have been in use since the late 1980s.[5]
- More than **90% of children** in the U.S. received a Hib vaccine in 2014.[7]
- The CDC predicts that more than **19,000 cases and 700 Hib-related deaths** will be prevented over the lifespan of the 4 million U.S. children born in 2009 alone.[11]
- For the group of children born in 2009, Hib vaccination is predicted to **save $1.8 billion** in direct costs and **$3.7 billion** in total societal costs.[13]

RESEARCH-TO-PRACTICE MILESTONES FOR THE Hib VACCINE

For more information on the supporting evidence and research sponsors for these milestones, see the Web appendix.

FOUNDATIONAL RESEARCH

1920s

By deactivating disease-causing components of bacteria, vaccines were developed to prevent **tetanus and diphtheria**.[14] These advances would later help enhance the effectiveness of Hib vaccines.

1930s

Hib (*seen below right, in photo*) was found to be the primary cause of bacterial meningitis in children. The bacteria could be distinguished under the microscope by their **unique outer coat**.[15] Later, scientists determined this coat was made up of chains of specific **sugar molecules**.[16]

Because sugar chains typically do not stimulate immune responses as well as proteins, researchers began to look for ways to **link the chains to bacterial proteins** in order to enhance their immunogenicity.[17]

NIH *indicates NIH-funded milestones*

EARLY HIB VACCINE DEVELOPMENT

1968

The **first attempts at developing a Hib vaccine** focused on the sugar chains – researchers worked on isolating, purifying, and preparing these chains for clinical use.[18] NIH

1970s

NIH-funded clinical trials found that these early **Hib vaccines worked well for children** over age 2, but were not as effective in infants.[19] NIH

1977: A young girl receives a vaccination, administered by a public health nursing practitioner

1983

Scientists leading these clinical trials **founded a company**, called Praxis Biologics (now incorporated into Wyeth), to develop and produce vaccines for children, including Hib vaccines.[20]

1985

The Food and Drug Administration (FDA) **approved the first Hib vaccines** (including from Praxis Biologics) for use in children two years of age,[21] while researchers explored ways to make the vaccines more effective in infants.[22]

1985-1989

NIH-funded clinical trials showed that the conjugate vaccine was **safe and effective in infants**.[25] NIH

1987-1993

FDA approved the first **4 conjugate vaccines for use in infants**.[26]

1980

FDA scientists (who later moved to NIH) linked Hib sugar chains to immune-stimulating proteins (e.g., from diphtheria), producing a **"conjugate vaccine."**[23] NIH

1984

NIH and FDA scientists found that this conjugate vaccine triggered immune responses in appropriate **animal models**.[24] NIH

PROTECTING INFANTS WITH A NEXT-GENERATION CONJUGATE VACCINE

1993

The conjugate vaccine developed by NIH-funded scientists was licensed, manufactured, and **commercially distributed**.[27]

CDC included the Hib conjugate vaccine in its **recommended vaccine schedule**.[28]

1995

For their "groundbreaking work and …leadership in the development and commercialization of the [Hib] vaccine," the **Albert and Mary Lasker Foundation** awarded their prestigious Clinical Medical Research Award (often referred to as the "American Nobels") to four NIH-supported scientists.[29] NIH's **National Institute of Allergy and Infectious Diseases** provided grant funding to Drs. Porter Anderson and David Smith. Drs. Rachel Schneerson and John Robbins performed the majority of their research within the intramural laboratories of the ***Eunice Kennedy Shriver* National Institute on Child Health and Human Development**.

IMPACTS OF Hib VACCINES

HEALTH

- First conjugate vaccine approved to treat an infectious disease.[30]
- More than 90% of children in the U.S. receive the Hib vaccine.[31]

Incidence of Hib cases declined more than 99% following availability of the conjugate vaccine.[32]

SOCIETY

- Hospitalization for Hib-meningitis costs upwards of $38,000 depending on the severity of the disease.[36]
- NIH-supported researchers started a company and successfully moved Hib and other experimental vaccines through the full product development pipeline.[37]

For children born in 2009 alone, Hib vaccination saves $3.7 billion, including more than $1.8 billion in direct treatment costs.[35]

KNOWLEDGE

- Hib vaccine research provided fundamental understanding of how the infant immune system works, stimulating new strategies for developing effective vaccines for infants.
- The Hib conjugate vaccine technology has been applied to **create several vaccines against other disease-causing bacteria**, such as pneumococci, meningococci, *Salmonella typhi*, group B streptococci, and *E coli*.[38]

HIB DISEASE NEARLY ELIMINATED IN THE U.S. FOLLOWING THE VACCINE

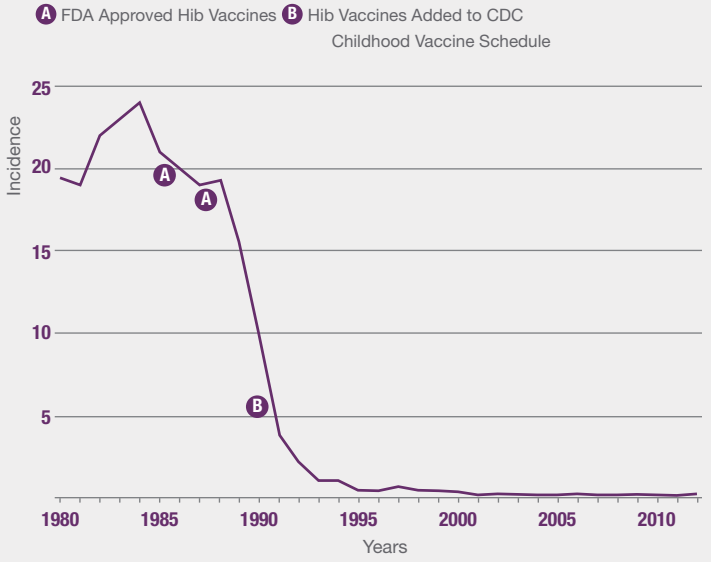

Figure Legend: The CDC-estimated annual incidence of invasive Hib disease (per 100,000 people) is shown here for U.S. children less than five years of age from 1980 to 2012. Once approved and licensed, the use of Hib vaccines resulted in a rapid decline of Hib cases and the disease has been nearly eliminated in the United States.[33]

HEALTH IMPACT OF ROUTINE CHILDHOOD IMMUNIZATION FOR Hib: U.S. 1994-2013[34]

Illnesses Prevented:	Hospitalizations Averted:	Deaths Avoided:
361,000	334,000	13,700

CHILDHOOD VACCINES: OVERALL IMPACT ON SOCIETY

The Hib vaccine success story highlights how continued scientific investment leads to new tools that prevent deadly diseases and improve the lives of people around the world. The Hib vaccine is one of many childhood vaccines, and the CDC projects that over the lifespan of the 4 million U.S. children born in 2009 alone, childhood vaccination overall will:

- save **42,000** lives
- prevent **20 million** cases of disease
- reduce direct health care costs by **$13.5 billion**
- save **$68.8 billion** in indirect costs[39]

For references, supplementary information, and more on the impact of NIH, please visit **http://www.nih.gov/impact**