

# VACCINES

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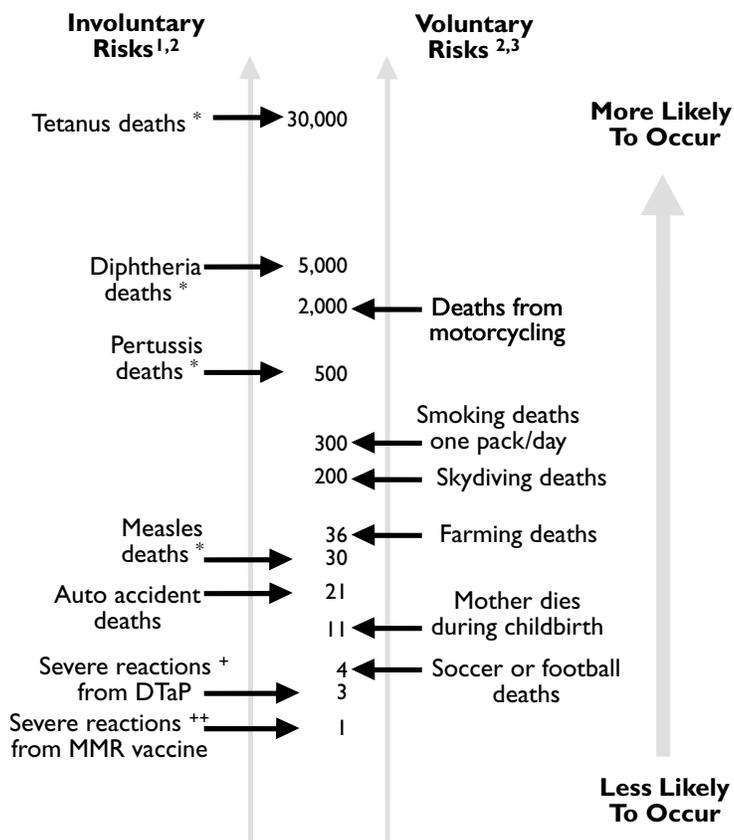
# VACCINES

## Safety Assessment

Most dictionaries define safety as freedom from harm. So in order for something to be 100% safe, it would have to be completely devoid of any and all chance of harm. As the following examples indicate, nothing we do nor experience fits this qualification. We can slip and fall as we get out of bed, become ill or choke on our food as we eat, get hit by a car as we cross the street, turn an ankle or bump into something as we walk or inhale dangerous chemicals, smoke or viruses as we breathe. Therefore, we must analyze the risks and benefits of a situation in order to decide the course of action we will take. Although the risks described exist, they need to be balanced against the benefits of taking each risk. We must get up out of bed in order to move on with our day, eat food to nourish ourselves, cross the street to continue our journey, walk to move forward and breathe to stay alive.

## Likelihood of Death or Serious Injury Associated with Disease, Vaccination and Various Activities

(Values are expressed as the number of affected persons per 100,000 people at risk each year in the United States.)



\* Risk of death from this disease once disease has been contracted.  
 + Includes breathing difficulty and shock and severe brain reactions such as long seizures, coma or lowered consciousness.  
 ++ Includes temporary bleeding problems, seizures related to high fever, lowered consciousness or coma.

Physicians, public health officials and individuals share an interest in understanding the health and safety implications associated with vaccine usage. As noted in the section *Importance of Immunizations*, vaccines play an significant role in protecting both individuals and the community at large from infectious diseases. In the absence of such protection, diseases such as measles, mumps, polio and hepatitis can cause injury and death. This is illustrated in the accompanying figure. For example, in the absence of a vaccine against tetanus, out of every 100,000 persons in the US infected

## GLOSSARY TERMS

Adverse events	Mumps
Advisory Committee on Immunization Practices	Pertussis
Anthrax	Risk
Cases	Rubella
Diphtheria	Smallpox
Disease	Tetanus
Encephalitis	Vaccine
Measles	Virus

## ACRONYMS

DTaP	Diphtheria, tetanus, acellular pertussis vaccine
MMR	Measles, mumps, rubella
NIH	National Institutes of Health

## WEB RESOURCES

- Centers for Disease Control and Prevention (CDC), National Immunization Program**  
<http://www.cdc.gov/nip/vacsafe/#risk>
- Harvard Center for Risk Analysis**  
<http://www.hcra.harvard.edu>
- Johns Hopkins School of Public Health, Risk Sciences and Public Policy Institute**  
<http://www.jhsph.edu/research/centers/rsppi>
- Society for Risk Analysis**  
<http://www.sra.org>

with the tetanus-causing bacterium, 30,000 would die. Similarly, if there was no diphtheria vaccine, 5,000 out of every 100,000 infected children would die on an annual basis. In contrast, out of every 100,000 people who smoke one pack of cigarettes a day, 300 deaths would be expected each year.

As pointed out in the above diagram, absolute safety cannot be guaranteed; everything carries some risk. The section *Federal Regulation, Surveillance and Evaluation of Vaccines* describes the strong commitment of the government, researchers, public health officials, advisory committees and vaccine manufacturers to provide the public with the safest vaccines possible.

Despite these efforts, because no two people are identical, different persons may vary in how they will respond to a vaccine. Most will quickly develop an effective, protective immunity to the disease agent without complications, some (a very small minority) will not develop immunity for a variety of medical reasons and rarely, responders and non-responders will develop a severe adverse reaction. Current scientific knowledge cannot identify how individuals will react to a vaccine.

The diagram above places the health risks associated with vaccinating or not vaccinating in context with the risk of injury or death associated with other activities. One in 100,000 children given the MMR vaccine will have a serious adverse reaction; 30 in 100,000 unvaccinated children who develop measles will die of complications brought on by the infection.

Recent events provide an example of how fear can alter a person's ability to make rational decisions, weighing both the benefits of acting against the risks of not. Following the anthrax attacks in October and November 2001, heightened concern has been raised across the country about the potential use of smallpox virus as a bioterrorism weapon. As a result, a National Institutes of Health (NIH) study was launched in October 2001 to determine if existing smallpox vaccine stocks could be diluted to be used for more people. In addition, US officials signed a \$428 million contract with Acambis and Baxter International to fast-track delivery of 155 million smallpox vaccine doses by the end of 2002.<sup>4</sup> Continued speculation that terrorists might use smallpox virus as a weapon has resulted in mounting pressure in the US to provide widespread, or even universal, smallpox vaccination. A poll in May 2002 found that 59% of Americans would get a smallpox vaccination if the vaccine were made available.<sup>5</sup> And, during recent Congressional hearings, Congress members' views often echoed that of US Senator Arlen Specter (R-PA)

who said that it is just "common sense" to make smallpox vaccine available to everyone who wants it.<sup>6</sup>

But how much sense does it really make? Smallpox has not been seen since 1977 and has been eradicated worldwide. Other than through a criminal act, the risk of developing smallpox is zero. But the risk of serious and life-threatening adverse events is greater with the smallpox vaccine than with any other recommended vaccine.<sup>7</sup> Approximately one in every 300,000 persons who receive a dose of this vaccine will develop encephalitis, which can lead to permanent neurological damage; and between one and three in every million persons who receive the vaccine will die. If the smallpox vaccine was made available to the general public, approximately 25% of the US population would be excluded from receiving the vaccine because they would be at high risk of developing adverse events or because they are close contacts of a high-risk individual. After excluding this group of people, a recent study found that vaccination of all persons one to 65 years of age in the US would result in approximately 4,600 serious adverse events and 285 deaths.<sup>7</sup>

At the June 2002 Advisory Committee on Immunization Practices (ACIP) meeting, members decided that under current circumstances that include no cases of confirmed smallpox and a low risk of a bioterrorism attack using smallpox, vaccination should not be recommended for the general population, as the potential benefits of vaccination would not outweigh the risks of vaccine adverse reactions. However, smallpox vaccination is recommended for persons pre-designated by the appropriate bioterrorism and public health authorities to conduct investigation and follow-up of initial smallpox cases that would necessitate direct patient contact.<sup>6</sup>

The example of smallpox demonstrates how widespread fears and misinterpretation can cloud one's judgement about the necessity and safety of vaccines. For this reason, public health officials scrutinize in great detail all of the risks and benefits before they make decisions about the licensure and use of vaccines for the general population. Providing the public with safe vaccines is the point of the testing, evaluation and review that each vaccine undergoes before licensing, and why surveillance and other follow-up studies continue long after the vaccine is marketed. Scientists in government, industry and academic laboratories are committed to assuring and improving the safety of current vaccines, and making the next generation of vaccines even safer.

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# DIPHTHERIA, TETANUS, ACELLULAR PERTUSSIS (DTaP) VACCINE

## General Disease Information

Diphtheria is a serious respiratory disease caused by the bacterium *Corynebacterium diphtheriae*. These bacteria infect the throat, tonsils, skin and nose and can cause a sore throat and cough. In some cases, a characteristic thin gray membrane coats the tonsils and throat and may block the patient's airway. If diphtheria is not treated, the disease can lead to pneumonia, heart failure, paralysis and death.<sup>1,2</sup>

Tetanus, a disease of the nervous system, is caused by the bacterium *Clostridium tetani*, which can be found in dirt, gravel and on objects associated with these such as rusty metal. The bacteria enter the body through a break in the skin and release a toxin, or poison, that causes the muscles to spasm. The toxin first attacks jaw muscles and may cause them to "lock" (this disease characteristic has led to tetanus also being referred to as lockjaw). Tetanus can go on to affect other muscles, leading to abdominal rigidity and generalized painful muscle spasms; death may result.<sup>1-3</sup>

Pertussis, or whooping cough, is a highly contagious respiratory disease caused by the bacterium *Bordetella pertussis*. The disease can last for up to two months and produces a severe "barking" cough followed by an inspiratory "whoop" lasting up to two months and often occurring in spasms that can make it difficult to eat, drink or sleep. Complications of pertussis can result in pneumonia, encephalopathy, seizures and death. Young infants are at the greatest risk for acquiring pertussis and for pertussis-associated complications.<sup>1-3</sup>

## Benefits from Vaccination

Completion of the full DTaP vaccine series is over 95% effective in preventing children from contracting the diseases of diphtheria, tetanus and pertussis. Prior to the availability of vaccine, the number of cases and deaths for diphtheria, tetanus and pertussis were significant. More than 175,000 cases of diphtheria, 1,300 cases of tetanus and 140,000 cases of pertussis were reported per year before the introduction of the vaccine.<sup>4</sup> Up to 10% of diphtheria cases<sup>5</sup>, 11% of tetanus cases<sup>6</sup> and 0.2% of pertussis cases<sup>6</sup> die from the respective disease. In 2000, 7,867 cases of pertussis, 35 cases of tetanus and one case of diphtheria were reported in the United States.<sup>4</sup>

## Risk of Vaccine Adverse Events

Most children experience no adverse reactions to DTaP. Some 1% to 5% of children vaccinated with DTaP develop mild adverse events such as injection site tenderness, swelling and redness as well as fretfulness, drowsiness, vomiting and minor fevers. About 1% of children experience moderate reactions such as prolonged crying, high fever, seizure or the child becomes limp, pale or less alert. Less than three serious adverse events (breathing difficulty and shock, prolonged seizure, coma or lowered consciousness) are reported per 100,000 children vaccinated.<sup>3</sup>

## Cost-Benefit Analysis

An economic analysis of diphtheria, tetanus, pertussis vaccine use in the United States has calculated a societal net savings of over \$22 million for DTaP and \$22.62 million for diphtheria, tetanus, whole cell pertussis vaccine (DTP). The benefits of DTaP exceeded the costs by 27:1 for indirect costs and 9:1 for direct health care costs.<sup>7</sup>

## Safety Studies

- When DTP was first licensed in the late 1940s, it contained whole killed pertussis organisms. Following the release of two reports by the Institute of Medicine (IOM), which found evidence that supported a causal relationship between DTP immunization and rare severe adverse events,<sup>8</sup> a new vaccine was developed. The pertussis

## GLOSSARY TERMS

Adverse events	Heart failure
Advisory Committee on Immunization Practices	Immunization
Bacteria	Pertussis
Booster	Pneumonia
<i>Bordetella pertussis</i>	Protein
Cases	Risk
<i>Clostridium tetani</i>	Seizure
Coma	Spasm
Combination vaccine	Sudden Infant Death Syndrome
<i>Corynebacterium diphtheriae</i>	Tetanus
Diphtheria	Tonsil
Disease	Toxin
Encephalopathy	Vaccine
	Whooping cough

## ACRONYMS

DTaP	Diphtheria, tetanus, acellular pertussis vaccine
DTP	Diphtheria, tetanus, whole cell pertussis vaccine
IOM	Institute of Medicine
SIDS	Sudden Infant Death Syndrome
VAERS	Vaccine Adverse Events Reporting System

## WEB RESOURCES

### DIPHTHERIA:

**National Partnership for Immunization**  
<http://www.partnersforimmunization.org/diphtheria.html>

**Centers for Disease Control and Prevention's Epidemiology and Prevention of Vaccine-Preventable Diseases (The Pink Book)**  
<http://www.cdc.gov/nip/publications/pink/dip.pdf>

**National Network for Immunization Information**  
<http://www.immunizationinfo.org/database/index.cfm>

**Vaccine Education Center at The Children's Hospital of Philadelphia**  
[http://www.vaccine.chop.edu/each\\_vaccine2.shtml#name01](http://www.vaccine.chop.edu/each_vaccine2.shtml#name01)

**Immunization Action Coalition**  
<http://www.immunize.org/diphtheria>

### TETANUS:

**National Partnership for Immunization**  
<http://www.partnersforimmunization.org/diphtheria.html>

**Centers for Disease Control and Prevention's Epidemiology and Prevention of Vaccine-Preventable Diseases (The Pink Book)**  
<http://www.cdc.gov/nip/publications/pink/tetanus.pdf>

**National Network for Immunization Information**  
<http://www.immunizationinfo.org/database/index.cfm>

**Vaccine Education Center at The Children's Hospital of Philadelphia**  
[http://www.vaccine.chop.edu/each\\_vaccine2.shtml#name02](http://www.vaccine.chop.edu/each_vaccine2.shtml#name02)

**Immunization Action Coalition**  
<http://www.immunize.org/tetanus>

### PERTUSSIS:

**National Partnership for Immunization**  
<http://www.partnersforimmunization.org/diphtheria.html#pertussis>

(continued)

component of this new acellular vaccine (DTaP) contained only the specific parts of pertussis bacteria necessary to establish protective immunity. Pre- and post-licensure studies have shown that adverse events occurred less frequently among infants vaccinated with acellular pertussis combination vaccine (DTaP) than among those vaccinated with whole-cell pertussis combination vaccine (DTP).<sup>1, 5, 7, 9-17</sup>

- A study involving 22,505 subjects who were given a total of 67,000 doses of DTaP found that incidences of sudden infant death syndrome (SIDS), infantile spasms and seizures without fever following vaccination did not exceed those estimated for the general population.<sup>18</sup>
- An analysis of all VAERS data from the first two years of DTaP use found that the annual number of reported adverse events following vaccination with all pertussis-containing vaccines declined after the introduction of DTaP. No clear DTaP safety concerns were identified during this period.<sup>9</sup>
- Review of post-licensure Vaccine Adverse Event Reporting System (VAERS) reports after five million doses of DTaP had been distributed showed that all reported adverse events, seizures and hospitalizations for DTaP were approximately one-third of those reported to be associated with whole-cell pertussis-containing vaccines.<sup>19</sup>

**Centers for Disease Control and Prevention's  
Epidemiology and Prevention of Vaccine-  
Preventable Diseases (The Pink Book)**

<http://www.cdc.gov/nip/publications/pink/pert.pdf>

**National Network for Immunization  
Information**

<http://www.immunizationinfo.org/database/index.cfm>

**Vaccine Education Center at the Children's  
Hospital of Philadelphia**

[http://www.vaccine.chop.edu/each\\_vaccine2.shtml#name03](http://www.vaccine.chop.edu/each_vaccine2.shtml#name03)

**Immunization Action Coalition**

<http://www.immunize.org/pertussis>

**DTaP VACCINE:**

**National Partnership for Immunization**

<http://www.partnersforimmunization.org/diphtheria.html#pertussis>

**Recommendations of the Advisory Committee  
on Immunization Practices (ACIP)**

<http://www.cdc.gov/mmwr/preview/mmwrhtml/rr4913a1.htm>

<http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5102a1.htm>

**DTaP Vaccine Information Statement**

<http://www.cdc.gov/nip/publications/vis/vis-dtp.pdf>

**Tetanus-Diphtheria Vaccine Information  
Statement**

<http://www.cdc.gov/nip/publications/vis/vis-td.pdf>

**VACCINE MANUFACTURERS:**

**Aventis Pasteur**

<http://www.us.aventispasteur.com/vaccines/tetanus/main.htm>

**GlaxoSmithKline**

<http://www.worldwidevaccines.com/public/diseas/diphth.toc.asp>

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## HAEMOPHILUS INFLUENZAE TYPE B (HIB) VACCINE

### General Disease Information

The bacteria *Haemophilus influenzae* type b (Hib) can cause a severe infection in infants and young children. Invasive disease caused by these bacteria can spread to many organ systems and cause meningitis, epiglottitis, pneumonia, arthritis and cellulitis, and is spread by contact with secretions, coughing and sneezing. Invasive Hib disease is uncommon beyond five years of age, presumably because the immune system matures with age thus resulting in greater levels of protection from this disease.<sup>1,2</sup>

### Benefits from Vaccination

Vaccination prevents children from contracting meningitis, epiglottitis, pneumonia, arthritis and skin infections. Because Hib bacteria can live in the throats of healthy people, the potential for unprotected children to contract this disease is high.<sup>3</sup> Before the introduction of the vaccine, about 20,000 cases occurred annually in the United States, primarily among children younger than five years of age (approximately one in 200 children in this age group).<sup>4</sup> Hib was also the leading cause of bacterial meningitis and other invasive bacterial disease among children less than five years old. Five percent of children who developed Hib meningitis died, and 10% to 30% of survivors had permanent brain damage.<sup>5</sup>

Surveillance has shown that the introduction of Hib vaccine in the United States coincided with steep declines in Hib disease in infants less than one year old. Public health officials have largely attributed the rapid reduction in the number of disease cases to the vaccine's ability to reduce carriage of Hib among the vaccinated population, which likely reduced exposure and infection even in those persons who were not immunized.<sup>6,7</sup> The Centers for Disease Control and Prevention (CDC) data suggest that the number of cases of disease that have occurred since the vaccine was first licensed has significantly decreased. In 2000, 1,398 such cases were reported.<sup>5,8</sup>

This trend has also been seen in other countries. In Finland, large-scale immunization against Hib began in 1986 and, since 1988, Hib has disappeared, eliminating one-third of Finland's cases of childhood septic arthritis. This resulted in a reduction in the amount, cost and variety of medication needed to treat children with this disease.<sup>9</sup>

### Risk of Vaccine Adverse Events

More than 70% of children who receive this vaccine will experience no adverse events.<sup>3</sup> Mild reactions that have been reported include injection site tenderness, swelling and redness as well as mild to moderate fever.<sup>3</sup> Hib vaccine is not known to cause serious adverse events.<sup>10</sup>

### Safety Studies

- The safety and immunogenicity of the vaccine were evaluated in a study of 61,080 children ages six weeks to six months in the Kaiser Permanente Medical Care Program of Northern California. The rate of sudden infant death syndrome (SIDS) following vaccine administration did not differ significantly from that of unvaccinated children of the same ages and was lower than that observed for the Kaiser Permanente Medical Care Program as a whole.<sup>11</sup>
- The Institute of Medicine (IOM) reviewed the safety of many childhood vaccines and did not find any serious adverse events linked to Hib vaccines.<sup>12,13</sup>

## GLOSSARY TERMS

Adverse events	<i>Haemophilus influenzae</i> type b
Advisory Committee on Immunization Practices	Hib vaccine
Arthritis	Immunization
Bacteria	Influenza
Bacterial meningitis	Invasive
Cases	Pneumonia
Cellulitis	Risk
Disease	Septic arthritis
Epiglottitis	Sudden Infant Death Syndrome Vaccine

## ACRONYMS

CDC	Centers for Disease Control and Prevention
Hib	<i>Haemophilus influenzae</i> type b
IOM	Institute of Medicine
SIDS	Sudden Infant Death Syndrome

## WEB RESOURCES

### HIB VACCINE:

#### National Partnership for Immunization

<http://www.partnersforimmunization.org/haemophilus.html>

#### Centers for Disease Control and Prevention's *Epidemiology and Prevention of Vaccine-Preventable Diseases (The Pink Book)*

<http://www.cdc.gov/nip/publications/pink/hib.pdf>

#### National Network for Immunization Information

<http://www.immunizationinfo.org/database/index.cfm>

#### Vaccine Education Center at The Children's Hospital of Philadelphia

[http://www.vaccine.chop.edu/each\\_vaccine2.shtml#name05](http://www.vaccine.chop.edu/each_vaccine2.shtml#name05)

#### Immunization Action Coalition

<http://www.immunize.org/hib>

#### Recommendations of the Advisory Committee on Immunization Practices (ACIP)

<http://www.cdc.gov/mmwr/preview/mmwrhtml/00022926.htm>

#### Vaccine Information Statement

<http://www.cdc.gov/nip/publications/vis/vis-hib.pdf>

### VACCINE MANUFACTURERS:

#### Aventis Pasteur

<http://www.us.aventispasteur.com/vaccines/hib/main.htm>

#### Merck Vaccine Division

<http://www.mercksharpdohme.com/disease/preventable/hib>

#### Wyeth Vaccines

<http://www.vaccineworld.com>

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## HEPATITIS A VACCINE

### General Disease Information

Hepatitis A, caused by the hepatitis A virus (HAV), is the most common type of viral hepatitis reported in the United States. Hepatitis A virus is extremely hardy; it can live for long periods of time outside of its host and cannot be destroyed by bleach or freezing temperatures. The virus is transmitted from person-to-person between household contacts or sex partners, or by contaminated food or water. In rare cases, Hepatitis A can be transmitted as a blood-borne pathogen, much like hepatitis B and C. This disease can cause jaundice, fatigue, abdominal pain, anorexia, fever and nausea. This disease can result in sudden, severe liver failure and claims over 100 lives each year. The vaccine is recommended for travelers to countries with high or intermediate rates of HAV infection, children two years of age and older in communities with consistently high rates of hepatitis A, men who have sex with men, illegal drug users, persons with chronic liver disease, persons with clotting-factor disorders and persons who work with HAV-infected primates or with HAV in a research laboratory setting.<sup>1-3</sup>

### Benefit from Vaccination

Hepatitis A vaccine can provide long-term protection against HAV infection for persons two years of age and older. Approximately 10 cases of hepatitis A are reported per 100,000 population each year. However, hepatitis A occurs in epidemics both nationwide and in communities every five to 10 years when rates of disease have been as high as 700 cases per 100,000 persons. This disease leads to about 100 deaths in the United States per year. Patients with hepatitis A suffer substantial morbidity and require hospital care in 11% to 22% of cases. Children play an important role in transmission of this disease and serve as both a source and reservoir of infection for others. Because most children have unrecognized infections and some appear asymptomatic,<sup>3</sup> this disease is often underreported. In 2000, 13,397 cases of this disease were reported.<sup>4</sup> However, a recent scientific model has predicted that the actual incidence of hepatitis A is 7.4 to 13.9 times the number of cases that are reported.<sup>5</sup>

Hepatitis A vaccine is of particular importance in communities with high rates of hepatitis A disease. For example, vaccination offered to children ages two to 12 years from January 1995 through December 2000 in a California community with elevated rates of the disease reduced the number of hepatitis A cases reported in the entire county by 93.5%.<sup>6</sup> Communities with consistently high rates of hepatitis A disease typically have epidemics every 5-10 years, with each episode lasting several years. In the late 1990s, however, hepatitis A vaccine was more widely used, and the number of cases reached historic lows.<sup>3</sup>

Each month, about 20 out of 1,000 travelers to foreign countries become infected with HAV.<sup>7</sup> Only travelers to North America (except Mexico and Central America), western Europe, Japan, Australia and New Zealand are at no increased risk for hepatitis A.<sup>3</sup>

HAV infection causes great concern to food service establishments. Food handlers infected with HAV can potentially expose thousands of people. In such cases, one infected food handler can damage the name and reputation of the establishment, decrease sales, accrue significant medical costs, reduce productivity, consume corporate time and prompt litigation. Reported sales losses can be up to 80% and, in some instances, businesses have been forced to close.<sup>8</sup> During these outbreaks, the resources of the overtaxed public health departments charged with managing the predicament are considerably drained. Extra nursing staff is needed to handle the influx of patients, disease education and vaccination. Extra time, effort and more people are necessary to investigate the cause of the outbreak and identify all persons who may have been exposed.

### Risk of Vaccine Adverse Events

About half of the adults and children who receive the hepatitis A vaccine will experience no adverse events.<sup>2</sup> Mild reactions such as injection site tenderness, pain or swelling has been reported in 20% to 50% of recipients. Less than 10% of vaccinees

## GLOSSARY TERMS

Acute	Hepatitis A
Adverse events	Immunization
Advisory Committee on Immunization Practices	Jaundice
Anorexia	Liver failure
Background incidence	Morbidity
Cases	Nausea
Chronic	Risk
Coverage	Systemic
Disease	Vaccine
Efficacy	Vaccine Adverse Events Reporting System
Epidemic	Virus
Hepatitis	

## ACRONYMS

HAV	Hepatitis A virus
HAVRIX®	Hepatitis A vaccine (GlaxoSmithKline)
VAERS	Vaccine Adverse Events Reporting System
VAQTA®	Hepatitis A vaccine (Merck & Co.)

## WEB RESOURCES

### HEPATITIS A:

**National Partnership for Immunization**  
<http://www.partnersforimmunization.org/hepatitisa.html>

**Centers for Disease Control and Prevention's Epidemiology and Prevention of Vaccine-Preventable Diseases (The Pink Book)**  
<http://www.cdc.gov/nip/publications/pink/hepa.pdf>

**National Center for Infectious Diseases**  
<http://www.cdc.gov/ncidod/diseases/hepatitis/a/index.htm>

**Hepatitis Foundation International**  
<http://www.hepfi.org>

**National Network for Immunization Information**  
<http://www.immunizationinfo.org/database.index.cfm>

**Vaccine Education Center at The Children's Hospital of Philadelphia**  
[http://www.vaccine.chop.edu/each\\_vaccine2.shtml#name18](http://www.vaccine.chop.edu/each_vaccine2.shtml#name18)

**Immunization Action Coalition**  
<http://www.immunize.org/hepa>

### HEPATITIS A VACCINE:

**National Partnership for Immunization**  
<http://www.partnersforimmunization.org/hepatitisa.html>

**Centers for Disease Control and Prevention's Epidemiology and Prevention of Vaccine-Preventable Diseases (The Pink Book)**  
<http://www.cdc.gov/nip/publications/pink/hepa.pdf>

**Recommendations of the Advisory Committee on Immunization Practices (ACIP)**  
<http://www.cdc.gov/mmwr/preview/mmwrhtml/rr4812a.htm>

**Vaccine Information Statement**  
<http://www.cdc.gov/nip/publications/vis/vis-hep-a.pdf>

**Immunization Action Coalition**  
<http://www.immunize.org/catg.d/2081ab.htm>

### VACCINE MANUFACTURER:

**GlaxoSmithKline**  
<http://www.worldwidevaccines.com/public/diseases/hepatoc.asp>

**Merck Vaccine Division**  
<http://www.mercksharpdohme.com/disease/preventable/hepa>

report mild systemic complaints, fatigue and low grade fever.<sup>1</sup> No serious adverse reactions to this vaccine have been reported.<sup>1,3</sup>

### Cost-Benefit Analysis

Adults who become ill with hepatitis A lose an average of 27 work-days per illness and health departments treat about 11 potentially exposed contacts per one infected person. The average direct and indirect costs of hepatitis A disease range from \$1,817 to \$2,459 per adult case and \$433 to \$1,492 per pediatric case.<sup>8</sup> In a 1996 hepatitis A outbreak in Colorado involving 43 persons, the estimated total cost was \$800,000.<sup>9</sup> When 65% to 80% vaccination rates of preschool and school-age children are achieved and routine vaccination is sustained, ongoing outbreaks of hepatitis A are effectively interrupted, a sustained reduction in disease incidence has been observed and subsequent outbreaks prevented.<sup>10-14</sup>

### Safety Studies

- A two-year safety review of the Vaccine Adverse Events Reporting System (VAERS) hepatitis A safety data revealed that following distribution of more than six million doses, 19 persons (approximately three events per one million doses used) reported unexpected vaccine-associated events.<sup>15</sup>
- A study involving the vaccination of 29,789 children ages two to 12 years reported no serious adverse events following

vaccination. Reported adverse reactions were generally mild and included reactions at the site of injection, fever and rash.<sup>6</sup>

- The safety of hepatitis A vaccination was evaluated in 37 vaccinated liver transplant patients who were compared to 45 unvaccinated control patients. (Liver transplant patients frequently suffer from chronic liver disease related to tissue rejection, recurrence of pretransplantation disease or complications following transplantation that put them at increased risk for liver failure associated with acute hepatitis A infection.) Although hepatitis A vaccine efficacy was found to be low in these patients, immunization was found to be safe and well tolerated. Headache was the most frequent side effect reported by the patients involved in this study.<sup>16</sup>
- Protective efficacy studies of approximately 50,000 persons given the hepatitis A vaccine, HAVRIX<sup>®</sup> did not attribute any reported adverse events to the vaccine.<sup>17</sup> Likewise, studies on the newer hepatitis A vaccine, VAQTA<sup>®</sup> followed 9,200 persons and found no adverse events related to the vaccine.<sup>18</sup>
- An estimated 1.3 million persons had been vaccinated with HAVRIX<sup>®</sup> by 1999. The rates of serious adverse events for these persons for which background incidence data are known are not higher than would be expected for an unvaccinated population. An estimated 20,000 persons had been administered VAQTA<sup>®</sup> by 1999, and no adverse events had been reported.<sup>3</sup>

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## HEPATITIS B VACCINE

### General Disease Information

Hepatitis B is a liver disease caused by hepatitis B virus (HBV). HBV is transmitted from individuals with acute or chronic infection, through contact with their blood or bodily fluids containing blood. This can occur through direct blood-to-blood contact, unprotected sex, illicit drug use, unsterile needles or from an infected woman to her newborn during the delivery process. In certain circumstances hepatitis B can be considered a sexually transmitted disease.

Acute hepatitis B disease can cause liver failure and lead to death. Chronic hepatitis B disease can cause long-term liver damage, including cirrhosis and liver cancer. Groups at risk for HBV infection include: persons with multiple sex partners or who have a diagnosis of a sexually transmitted disease, men who have sex with men, sexual contacts of infected persons, injection drug users, household contacts of chronically infected persons, infants born to infected mothers, infants or children of immigrants from areas with high rates of HBV infection, health care and public safety workers, individuals living or working in institutional settings such as prisons and group homes, and hemodialysis patients.<sup>1,2</sup>

### Benefit from Vaccination

Hepatitis B vaccination is the best protection against acquiring HBV infection. The number of new infections per year has declined from an average of 450,000 in the 1980s when the hepatitis B vaccine was first introduced to about 180,000 in 1998. The greatest decline occurred among children and adolescents and is a result of routine hepatitis B vaccination.

However, one out of every 20 persons (or about 12.5 million persons) has been infected with hepatitis B during their lifetime, an estimated 1.25 million Americans have chronic, lifelong hepatitis B infection and 4,000–5,500 deaths occur each year in the US from hepatitis B-related chronic liver disease such as cirrhosis and liver cancer.<sup>2</sup> More widespread use of currently available vaccine could prevent up to one million deaths worldwide due to hepatitis B-associated liver cirrhosis and liver cancer.<sup>4</sup>

High vaccine coverage levels need to be maintained to prevent transmission of HBV from infected individuals to susceptible contacts. Approximately 10% of all acute HBV infections progress to chronic infection (the risk of chronic infection decreases as age increases). Of the chronic cases of hepatitis B, 20% to 30% acquired their infection in childhood. These persons are a reservoir for transmission to others.<sup>5</sup>

The risk of chronic hepatitis B infection decreases as age increases. As many as 90% of infants exposed to hepatitis B from their mothers at birth become carriers. Thirty to fifty percent of affected children between one and five years of age become carriers. But by adulthood, the risk of becoming a carrier is 6% to 10%.<sup>1</sup>

### Risk of Vaccine Adverse Events

More than 65% of children who receive the hepatitis B vaccine will experience no adverse events. The adverse events that do occur are primarily mild reactions such as injection site tenderness or mild fever.<sup>6</sup> A rare side effect of hepatitis B vaccine is anaphylaxis, a type of allergic reaction. This reaction occurs in about one case per 600,000 doses given. Recent studies have shown no association between hepatitis B vaccination and multiple sclerosis.<sup>7</sup> (See *Vaccine Safety Issues* on page 97.) No deaths from hepatitis B vaccination have been reported.

### Cost-Benefit Analysis

The cost of acute and chronic hepatitis B disease in the US is estimated at \$658 million in 1992 dollars.<sup>8</sup> A cost analysis of hepatitis B vaccination was conducted in Iowa, a state where the annual attack rate is low—approximately one-sixth that of national levels. This study found that routine infant immunization would prevent 45.7 cases

## GLOSSARY TERMS

Acute	Guillain-Barré syndrome
Adverse events	Hemodialysis
Advisory Committee on Immunization Practices	Hepatitis
Anaphylaxis	Hepatitis B
Association	Immunization
Cases	Liver failure
Chronic	Placebo
Cirrhosis	Risk
Coverage	Seizure
Disease	Vaccine
	Virus

## ACRONYMS

HBV	Hepatitis B Virus
VAERS	Vaccine Adverse Events Reporting System

## WEB RESOURCES

### HEPATITIS B:

#### National Partnership for Immunization

<http://www.partnersforimmunization.org/hepatitisb.html>

#### Centers for Disease Control and Prevention's *Epidemiology and Prevention of Vaccine-Preventable Diseases (The Pink Book)*

<http://www.cdc.gov/nip/publications/pink/hepb.pdf>

#### National Center for Infectious Diseases

<http://www.cdc.gov/ncidod/diseases/hepatitis/b/index.htm>

#### Hepatitis Foundation International

<http://www.hepfi.org>

#### National Network for Immunization Information

<http://www.immunizationinfo.org/database/index.cfm>

#### Vaccine Education Center at The Children's Hospital of Philadelphia

[http://www.vaccine.chop.edu/each\\_vaccine2.shtml#name10](http://www.vaccine.chop.edu/each_vaccine2.shtml#name10)

#### Immunization Action Coalition

<http://www.immunize.org/hepb>

### HEPATITIS B VACCINE:

#### National Partnership for Immunization

<http://www.partnersforimmunization.org/hepatitisb.html>

#### Recommendations of the Advisory Committee on Immunization Practices (ACIP)

<http://www.cdc.gov/mmwr/preview/mmwrhtml/00056293.htm>

#### Vaccine Information Statement

<http://www.cdc.gov/nip/publications/vis/vis-hep-b.pdf>

#### National Center for Infectious Diseases

<http://www.cdc.gov/ncidod/diseases/hepatitis/b/index.htm>

### VACCINE MANUFACTURERS:

#### Merck Vaccine Division

<http://www.mercksharpdohme.com/disease/preventable/hepb>

#### GlaxoSmithKline

<http://www.worldwidevaccines.com/public/diseas/hepbtc.asp>

of infection per 10,000 newborns, and save a total of 52 years of life per year. A proposal to immunize all Iowans as teenagers (except individuals born to mothers known to be infected with HBV, who would continue to be immunized at birth), was found to be more costly and would prevent less disease than would be achieved by immunizing all newborns.<sup>9</sup>

### Safety Studies

- Safety studies have shown that the most frequently reported adverse events of hepatitis B vaccination are pain at the site of injection (3% to 29%) and fever (1% to 6%),<sup>10,11</sup> but that these effects occurred no more frequently among people receiving the vaccine than among those receiving a placebo.<sup>12,13</sup>

- In Taiwan, Alaska and New Zealand, large-scale infant immunization programs have not detected an association between hepatitis B vaccination and the occurrence of severe adverse events, including seizures, Guillain-Barré syndrome or anaphylaxis.<sup>14,15</sup>
- A review of Vaccine Adverse Event Reporting System (VAERS) case reports from 1991-1994 concluded that no unexpected adverse events occurred after more than 12 million doses of vaccine were given to infants.<sup>16</sup>
- A Canadian study evaluating health problems occurring one month before and one month after vaccination with the hepatitis B vaccine in 1,130 children (all about nine years of age) found only a minimal increase in the incidence of adverse events after vaccination.<sup>17</sup>

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# INACTIVATED POLIOVIRUS (IPV) VACCINE

## General Disease Information

Polio is remembered by many people as a frightening viral disease that was epidemic during the 1950s. Poliomyelitis affects the lymphatic and nervous system and is spread by contact with an infected person or their stool. Polio symptoms begin with fever, sore throat, headache and stiff neck and can quickly progress to paralysis of the limbs and chest, making walking and breathing difficult to impossible. There is no cure for this disease.<sup>1-3</sup>

## Benefit from Vaccination

Vaccination with inactivated poliovirus (IPV) vaccine prevents children from becoming infected with poliovirus. In 1952, more than 20,000 people—mostly children—were diagnosed with polio. Before the polio vaccine was introduced in the US, 13,000 to 20,000 people became paralyzed from this disease and 1,000 people died each year.<sup>4</sup> IPV vaccine was licensed in 1955 and was used extensively until the early 1960s. In 1963, oral poliovirus (OPV) vaccine was licensed and largely replaced IPV vaccine because this live-attenuated vaccine was more effective at producing community immunity. Nearly exclusive use of OPV led to elimination of wild-type poliovirus from the US in less than 20 years.<sup>1</sup> Today due to high population coverage rates and safety considerations (see Safety Studies below) we have returned to using IPV.

## Risk-Benefit Analysis

The last case of natural or “wild-type” poliovirus infection in the United States was in 1979, and global polio eradication is currently underway. According to provisional data from the Centers for Disease Control and Prevention (CDC), the number of cases of paralytic polio in the US has been reduced from an average of 16,316 cases each year during the course of the twentieth century to zero cases in 2000.<sup>5</sup> Outbreaks of polio continue to occur in Africa and Asia. The virus could be imported to the US via international travelers if vaccine coverage levels are not maintained. Until polio is eradicated worldwide, people in the US remain at risk. The US can remain free of poliomyelitis by continuing to vaccinate children with IPV to reduce the risk that importation of poliovirus will result in outbreaks of polio.<sup>1</sup>

## Risk of Vaccine Adverse Events

Most children experience no adverse events after IPV immunization. Some children experience mild reactions such as tenderness at the injection site. IPV vaccine has caused no serious adverse events.<sup>6</sup>

## Cost-Benefit Analysis

The Poliomyelitis Eradication Initiative examined the net costs and benefits of polio vaccination during the period 1986-2040. The model assumed different vaccine delivery costs in industrialized and developing countries, and ignored all benefits aside from reductions in direct costs for treatment and rehabilitation. The model predicted that the benefits will exceed the costs during 2007, with a cumulative savings of \$13,600 million by the year 2040.<sup>7</sup>

## Safety Studies

- During the period of OPV use, approximately one case of vaccine-associated paralytic polio was observed for every 2.4 million doses administered.<sup>8</sup> In order to reduce the occurrence of vaccine-associated paralytic polio, the Advisory Committee on Immunization Practices (ACIP) recommended an increase in the use of IPV vaccine through a sequential schedule of IPV vaccine followed by OPV vaccine. As of January 1, 2000, ACIP recommends that IPV vaccine be used exclusively in

## GLOSSARY TERMS

Adverse events	Lymphatic system
Advisory Committee on Immunization Practices	Nervous system
Cases	Oral poliovirus vaccine
Community immunity	Poliomyelitis Eradication Initiative
Coverage	Risk
Disease	Vaccine
Epidemic	Virus
Immunization	Wild-type
Inactivated poliovirus vaccine	

## ACRONYMS

ACIP	Advisory Committee on Immunization Practices
CDC	Centers for Disease Control and Prevention
IOM	Institute of Medicine
IPV	Inactivated poliovirus
OPV	Oral poliovirus

## WEB RESOURCES

### POLIO:

**National Partnership for Immunization**  
<http://www.partnersforimmunization.org/polio.html>

**Centers for Disease Control and Prevention's Epidemiology and Prevention of Vaccine-Preventable Diseases (The Pink Book)**  
<http://www.cdc.gov/nip/publications/pink/polio.pdf>

**National Network for Immunization Information**  
<http://www.immunizationinfo.org/database/index.cfm>

**Vaccine Education Center at The Children's Hospital of Philadelphia**  
[http://www.vaccine.chop.edu/each\\_vaccine2.shtml#name04](http://www.vaccine.chop.edu/each_vaccine2.shtml#name04)

**Immunization Action Coalition**  
<http://www.immunize.org/polio>

### INACTIVATED POLIO VACCINE:

**National Partnership for Immunization**  
<http://www.partnersforimmunization.org/polio.html>

**Recommendations of the Advisory Committee on Immunization Practices (ACIP)**  
<ftp://ftp.cdc.gov/pub/Publications/mmwr/rr/rr4905.pdf>

**Recommendations of the American Academy of Pediatrics (AAP)**  
<http://www.aap.org/policy/re9949.html>

**Vaccine Information Statement**  
<http://www.cdc.gov/nip/publications/vis/vis-ipv.pdf>

### VACCINE MANUFACTURER:

**Aventis Pasteur**  
<http://www.us.aventispasteur.com/vaccines/polio/main.htm>

the US. Unlike OPV, IPV cannot replicate in the intestine of a vaccinated person. Therefore, IPV cannot be shed by a vaccinated person into the environment and possibly infect others with poliovirus.<sup>1</sup>

- Beginning in 1954, a total of 1,829,916 children from all parts of the US took part in the largest experiment of its kind up to that time to test the IPV vaccine. The vaccine was found to be safe and effective and was licensed within a few days after the announcement of the results of the field trial.<sup>9</sup>
- According to CDC, no serious adverse events related to IPV have been documented since IPV vaccine use was expanded in 1996.<sup>10</sup>
- An Institute of Medicine (IOM) Safety Committee found no serious adverse events associated with the use of IPV vaccine in countries relying on all-IPV childhood immunization schedules.<sup>11</sup>

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## INFLUENZA VACCINE

### General Disease Information

Influenza (flu) is a highly contagious viral infection which affects the nose, throat and lungs. Influenza is spread easily from person to person via droplets, primarily when an infected person coughs or sneezes. It may lead to hospitalization or even death, especially among the elderly. In 1918-1919, the “Spanish flu” pandemic caused an estimated 21 million deaths worldwide.<sup>1</sup>

### Benefit from Vaccination

Influenza vaccine prevents up to 40% of people who are exposed to the highly contagious disease of influenza from becoming ill.<sup>2</sup> In the average year, influenza is associated with over 20,000 deaths and 114,000 hospitalizations nationwide.<sup>3</sup> During most influenza seasons, approximately 10% to 20% of the population is infected with the influenza virus, although rates of infection vary among different age groups and from one season to another.<sup>1</sup>

The primary objective of preventing influenza is to reduce the incidence of severe illness and premature death in groups at increased risk of severe disease and, as a consequence, reduce the need for specialized health care services and pharmaceutical supplies, in particular antiviral drugs and antibiotics.<sup>4</sup> Influenza can lead to bacterial pneumonia, viral pneumonia or exacerbation of underlying medical conditions, e.g., chronic obstructive pulmonary disease, congestive heart failure.<sup>1</sup> Serious complications of influenza resulting in hospitalization or death most often occur in persons over 65 years of age, high-risk children or children younger than four years.<sup>5</sup>

The burden of influenza illness is greatest among children with asthma and other chronic medical conditions. During months when the influenza virus is circulating, this group experiences high rates of hospitalization and outpatient morbidity.<sup>6-9</sup> Among elderly persons, the vaccine is 50% to 60% effective in preventing hospitalization and 80% effective in preventing death.<sup>10</sup> A recent study assessed the outcomes of 259,627 persons age 65 years or older who were offered influenza and pneumococcal vaccines. Researchers found that the incidence of hospital treatment for influenza, pneumonia, pneumococcal pneumonia and invasive pneumococcal disease was significantly lower in the vaccinated group as compared to the unvaccinated group and that total mortality was 57% lower among vaccinated individuals.<sup>11</sup> The influenza vaccine is up to 90% effective in preventing illness among persons less than 65 years of age when the type of vaccine used is similar to the circulating influenza virus.<sup>12</sup>

Influenza vaccination of Japanese children from 1962 to 1987 prevented about 37,000 to 49,000 deaths in Japanese persons across all age groups per year, or about one death for every 420 children vaccinated. As the vaccination of schoolchildren was discontinued, the flu-related mortality rates of the general population in Japan increased.<sup>13</sup>

### Risk of Vaccine Adverse Events

About 80% of people who receive the influenza vaccine will experience no adverse events.<sup>7</sup> Fifteen to twenty percent of vaccines will have minor adverse events such as tenderness or redness at the injection site.<sup>3</sup> Fever, muscle aches or malaise lasting one to two days occurs in less than 1% of people who receive the influenza vaccine. In rare instances, an immediate allergic reaction, which can include hives, asthma, swelling of the throat, low blood pressure or shock occurs. Persons allergic to egg proteins are at an increased risk for such an allergic reaction and should follow published protocols regarding influenza vaccination.<sup>2, 14</sup>

### Cost-Benefit Analysis

The 1918-1919 influenza pandemic is believed to have resulted in the death of 550,000 Americans and 21 million people worldwide.<sup>2</sup> Analysts forecast that today a

## GLOSSARY TERMS

Acute	Immunization
Adverse events	Influenza
Advisory Committee on Immunization Practices	Invasive
Antibiotic	Morbidity
Asthma	Pandemic
Background incidence	Placebo
Chronic	Pneumococcal disease
Chronic obstructive pulmonary disease	Pneumonia
Congestive heart failure	Protein
Disease	Risk
Epidemic	Spanish flu
Guillain-Barré syndrome	Systemic
Heart failure	Vaccine
	Virus

## WEB RESOURCES

### INFLUENZA:

#### National Partnership for Immunization

<http://www.partnersforimmunization.org/influenza.html>

#### Centers for Disease Control and Prevention

<http://www.cdc.gov/ncidod/diseases/flu/fluvirus.htm>

#### National Foundation for Infectious Diseases

<http://www.nfid.org/library/influenza>

#### Centers for Disease Control and Prevention's *Epidemiology and Prevention of Vaccine-Preventable Diseases (The Pink Book)*

<http://www.cdc.gov/nip/publications/pink/flu.pdf>

#### National Network for Immunization Information

<http://www.immunizationinfo.org/database/index.cfm>

#### Vaccine Education Center at The Children's Hospital of Philadelphia

[http://www.vaccine.chop.edu/each\\_vaccine2.shtml#name13](http://www.vaccine.chop.edu/each_vaccine2.shtml#name13)

#### Immunization Action Coalition

<http://www.immunize.org/influenza>

### INFLUENZA VACCINE:

#### National Partnership for Immunization

<http://www.partnersforimmunization.org/influenza.html>

#### Recommendations of the Advisory Committee on Immunization Practices (ACIP)

<http://www.cdc.gov/mmwr/preview/mmwrhtml/rr4903al.htm>

#### Vaccine Information Statement

<http://www.cdc.gov/nip/publications/vis/vis-flu.pdf>

### VACCINE MANUFACTURERS:

#### Aventis Pasteur

<http://www.us.aventispasteur.com/vaccines/flu/main.htm>

#### Wyeth Vaccines

<http://www.wyeth.com/products/flushield.asp>

similar influenza pandemic could lead to up to 207,000 deaths in the US.<sup>15</sup> During a regular flu season in the US, influenza accounts for \$1-3 billion in direct medical costs; indirect costs, including lost earnings due to illness and lost future earnings due to death, are in the range of \$10-15 billion a year.<sup>16</sup>

Along with pneumococcal vaccine, the influenza vaccine appears to be more cost-effective than any other medical intervention commonly used in the care of the elderly (this includes mammograms, bypass surgery and hypertension screening).<sup>17</sup> A study of six cohorts, each including more than 20,000 persons over 64 years of age, reported a direct medical care cost savings per year averaging \$73 per person vaccinated. Vaccination was also associated with a 50% reduction in mortality from pneumonia, influenza, all acute and chronic respiratory conditions and congestive heart failure during the three influenza seasons studied.<sup>18</sup>

Influenza vaccination of healthy working adults aged 18 to 64 years has also been found to be cost saving. Taking into account both direct and indirect cost savings resulting from vaccination, this population saved an average of \$13.66 per person vaccinated.<sup>19</sup>

### Safety Studies

- Reports have described exacerbations of asthma following influenza vaccination. However, the vaccine is administered at the time of year when the background incidence of asthma activity is high. A causal relationship between influenza vaccine and the development of asthma has not been established<sup>20</sup>

and results from a recent study show that influenza vaccination does not result in exacerbation of asthma in children.<sup>21</sup>

- A study of two influenza seasons has shown that the increased risk of developing Guillain-Barré syndrome in the vaccinated population is approximately one case per one million influenza vaccinations.<sup>22</sup> Guillain-Barré syndrome is a rare neurological disease that is characterized by loss of reflexes and temporary paralysis. Even if Guillain-Barré syndrome was a side effect of influenza vaccination, the estimated risk for this disease would be substantially less than the risk of developing severe influenza in the absence of vaccination.<sup>23</sup>
- A study evaluating the usefulness of administering influenza immunization to hospitalized patients noted that 74% of reported side effects were reported to be not significant. The most common side effect reported was soreness at the site of vaccine injection (12%).<sup>24</sup>
- A trial was performed in the UK using 729 healthy individuals with a median age of 68.9 years who received either the influenza vaccine or a placebo. No significant difference in reported systemic symptoms (fever, aching limbs, fatigue, rash, cough, runny nose, headache and sore throat) between vaccine and placebo groups was found. Only local side effects occurred with a significantly increased incidence following influenza vaccination in healthy older people when compared to placebo. No individual had to seek medical advice because of side effects and participants did not inform researchers of any severe reactions following vaccination.<sup>25</sup>

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# MEASLES, MUMPS, RUBELLA (MMR) VACCINE

## General Disease Information

Measles is a highly contagious respiratory disease caused by a virus. Symptoms of measles last for about a week and include rash, high fever, cough, runny nose and red, watery eyes. More severe complications include pneumonia, encephalitis, seizures and death. The most common causes of measles-associated death are pneumonia in children and acute encephalitis in adults. During pregnancy, measles illness results in an increased risk of premature labor, spontaneous abortion and low birthweight infants. Measles in immunosuppressed persons may be severe and prolonged.<sup>1-3</sup>

Mumps is a viral disease that usually begins with swollen salivary glands. Serious complications of mumps include swelling of the testicles in adolescents and adults, deafness, aseptic meningitis and death. Women who develop mumps during the first trimester of pregnancy have an increased risk for fetal death.<sup>3-6</sup>

Rubella, also called German measles, is often a mild rash illness when contracted by adult males and children. However, arthritis or arthralgia has been reported in up to 70% of women who contract this disease but is rare in children and adult males.<sup>7</sup> Infection of a pregnant woman can cause devastating birth defects to the developing child and could be followed by a disease called congenital rubella syndrome (CRS), which may lead to fetal death or premature delivery, deafness, cataracts, heart defects, abnormalities of the nervous system, mental retardation, bone alterations, and liver and spleen damage. Fifty percent of infected people will have no disease symptoms.<sup>3,5</sup>

## Benefits from Vaccination

Measles, mumps and rubella (MMR) vaccination prevents the diseases of measles, mumps and rubella. Before MMR vaccine was introduced, approximately 500,000 cases of measles<sup>8</sup> and 500 measles-associated deaths were reported annually with epidemics occurring every 2-3 years.<sup>9</sup> Following licensure of a vaccine in 1963, the incidence of measles decreased by more than 98% and epidemic cycles no longer occurred. The Centers for Disease Control and Prevention (CDC) reports that the number of measles cases has been reduced from an average of 503,282 cases per year during the pre-vaccine era to 86 cases in 2000.<sup>8</sup>

Measles virus outbreaks still occur in the US. Therefore, decreased use of the measles vaccine would likely result in the resurgence of measles.<sup>10</sup> Discontinuing measles vaccination in the US and the eventual loss of community immunity would result in an eventual return to pre-vaccine era rates of disease that include three million to four million cases of measles each year and more than 1,800 deaths, 1,000 cases of encephalitis and 80,000 cases of pneumonia.<sup>11</sup>

The impact of decreased immunization coverage was demonstrated between 1989 and 1991 when low vaccination rates caused a rise in the number of measles cases.<sup>5</sup> During these three years, a total of 55,467 measles cases and 136 measles-associated deaths were reported.<sup>12</sup> Reported cases of measles declined rapidly thereafter due primarily to intensive efforts to vaccinate preschool-aged children.<sup>5</sup>

Mumps and rubella outbreaks have also occurred but the number of reported cases of these diseases has significantly declined since MMR vaccine was introduced.<sup>13</sup> The US is on the verge of eliminating rubella, but the 31 outbreaks of rubella that have been reported in the US since 1993 serve as a reminder that this disease continues to occur. In 1964, a rubella outbreak in the US resulted in 12.5 million cases of rubella infection and 20,000 newborns with CRS.<sup>5</sup> The most prominent outbreak setting has been worksites, followed by communities and correctional facilities.<sup>14</sup> Like measles, mumps has been reduced from 152,209 cases in the pre-vaccine era to 338 cases in 2000.<sup>7</sup> Similarly, the number of cases of rubella fell from 47,745 cases to 176 cases in 2000.<sup>7</sup>

## GLOSSARY TERMS

Acute	Encephalitis
Adverse events	Encephalopathy
Advisory Committee on Immunization Practices	Epidemic
Arthralgia	German measles
Arthritis	Guillain-Barré syndrome
Aseptic meningitis	Immunization
Association	Measles
Autism	MMR vaccine
Cases	Mumps
Cataracts	Placebo
Chronic	Pneumonia
Coma	Risk
Community immunity	Rubella
Congenital rubella syndrome	Salivary glands
Coverage	Seizure
Crohn's disease	Testicles
Disease	Vaccine
Efficacy	Vaccine Safety Datalink Project
	Virus

## ACRONYMS

CDC	Centers for Disease Control and Prevention
CRS	Congenital rubella syndrome
MMR	Measles, mumps, rubella
PAHO	Pan American Health Organization

## WEB RESOURCES

### MEASLES:

#### National Partnership for Immunization

<http://www.partnersforimmunization.org/mmr.html>

#### Centers for Disease Control and Prevention's *Epidemiology and Prevention of Vaccine-Preventable Diseases (The Pink Book)*

<http://www.cdc.gov/nip/publications/pink/meas.pdf>

#### National Network for Immunization Information

<http://www.immunizationinfo.org/database/index.cfm>

#### Vaccine Education Center at The Children's Hospital of Philadelphia

[http://www.vaccine.chop.edu/each\\_vaccine2.shtml#name07](http://www.vaccine.chop.edu/each_vaccine2.shtml#name07)

#### Immunization Action Coalition

<http://www.immunize.org/measles>

### MUMPS:

#### National Partnership for Immunization

<http://www.partnersforimmunization.org/mmr.html>

#### Centers for Disease Control and Prevention's *Epidemiology and Prevention of Vaccine-Preventable Diseases (The Pink Book)*

<http://www.cdc.gov/nip/publications/pink/mumps.pdf>

#### National Network for Immunization Information

<http://www.immunizationinfo.org/database/index.cfm>

#### Vaccine Education Center at The Children's Hospital of Philadelphia

[http://www.vaccine.chop.edu/each\\_vaccine2.shtml#name08](http://www.vaccine.chop.edu/each_vaccine2.shtml#name08)

#### Immunization Action Coalition

<http://www.immunize.org/mumps>

### RUBELLA:

(continued)

## Risk of Vaccine Adverse Events

More than 80% of children who receive this vaccine will experience no adverse events. The majority of adverse events that do occur will be mild and include tenderness, redness or swelling at the injection site, rash, fever, swelling of the lymph glands and temporary joint pain, stiffness or swelling. In about three cases out of 10,000 injections given, high fever will result in a seizure. In very rare cases of one case out of 100,000 injections, MMR vaccine may cause a temporary bleeding problem or seizures related to high fever, lowered consciousness or coma.<sup>6</sup>

## Cost-Benefit Analysis

A childhood measles, mumps and rubella immunization program using MMR vaccine in the United States was found to have prevented 3,322,128 cases of measles, 2,067,150 cases of mumps and 1,496,184 cases of rubella. The cost-benefit ratio calculated from this study found that for every \$1 spent on the MMR immunization program \$14 were saved.<sup>15</sup> According to the CDC, the estimated cost of the 1964 rubella epidemic that resulted in 20,000 cases of CRS was \$840 million. Today, the lifetime cost of one case of CRS is estimated to be in excess of \$200,000.<sup>7</sup>

## Safety Studies

- It has been postulated that use of the MMR vaccine may be associated with the development of inflammatory bowel disease and/or autism.<sup>16</sup> The available scientific evidence does not support this hypothesis, but these issues are discussed in greater detail in the section *Vaccine Safety Issues*.
- 1.8 million Finnish children immunized with nine million doses of MMR vaccine were followed by researchers from the time MMR vaccine was first introduced in Finland in 1982 until 1996. No cases of autism or Crohn's disease were reported. A safety analysis determined that serious events related to MMR vaccine were rare and were greatly outweighed by the risks of the diseases the vaccine prevents.<sup>17</sup>
- A study was conducted on 1,162 identical and fraternal twins at 14 to 83 months of age, each receiving a placebo and then the vaccine, or vice versa, three weeks apart. The study population was followed for three weeks after each injection. No difference was found in reported minor reactions between vaccine and placebo recipients.<sup>18</sup>
- A study of the relationship between vaccination with a measles-containing vaccine and the development of acute encephalopathy in persons who were previously healthy found no increase in the risk of this disease or other nervous system problems after measles vaccination.<sup>19</sup>
- A study assessing the risk of hospitalization for aseptic meningitis within 30 days of MMR vaccination followed 300,000 vaccine doses and did not identify a single case of encephalopathy or encephalitis.<sup>18</sup>
- Analysis of 2,296 reported cases of Guillain-Barré syndrome identified no difference in the number of cases following measles vaccination compared with the number of expected cases during that time period.<sup>19</sup>
- Although a 1991 review by the Institute of Medicine found a possible association between rubella vaccination and chronic arthritis among women,<sup>20</sup> a later retrospective cohort study utilizing the Vaccine Safety Datalink Project reviewed the records of 4,884 women and found no evidence of an increased risk of the onset of chronic arthralgia, arthritis or neurologic conditions in women who were vaccinated against rubella.<sup>21</sup>
- A recent review of MMR vaccine safety data suggested that MMR vaccine pre-licensure safety studies were inadequate because only a few pre-licensure studies were conducted and because these studies had very short periods of follow-up observation of study participants.<sup>22</sup> The United Kingdom's Medicines Control Agency and Department of Health responded to this study by reassuring the

### National Partnership for Immunization

<http://www.partnersforimmunization.org/mmr.html>

### Centers for Disease Control and Prevention's *Epidemiology and Prevention of Vaccine-Preventable Diseases (The Pink Book)*

<http://www.cdc.gov/nip/publications/pink/rubella.pdf>

### National Network for Immunization Information

<http://www.immunizationinfo.org/database/index.cfm>

### Vaccine Education Center at The Children's Hospital of Philadelphia

[http://www.vaccine.chop.edu/each\\_vaccine2.shtml#name09](http://www.vaccine.chop.edu/each_vaccine2.shtml#name09)

### Immunization Action Coalition

<http://www.immunize.org/rubella>

### MMR VACCINE:

#### National Partnership for Immunization

<http://www.partnersforimmunization.org/mmr.html>

#### Recommendations of the Advisory Committee on Immunization Practices (ACIP)

<http://www.cdc.gov/mmwr/preview/mmwrhtml/00053391.htm>

#### Vaccine Information Statement

<http://www.cdc.gov/nip/publications/vis/vis-mmr.pdf>

### VACCINE MANUFACTURER:

#### Merck Vaccine Division

<http://www.mercksharpdohme.com/disease/preventable/mmr>

public that the licensing process for MMR was adequate to establish the safety, quality and efficacy of the vaccines. They noted that 30 research studies have been published that

examined combined measles, mumps and rubella vaccines with follow ups of study participants extending up to 10 years.<sup>23</sup>

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# MENINGOCOCCAL VACCINE

## General Disease Information

*Neisseria meningitidis* bacteria are a leading cause of bacterial meningitis and sepsis in older children and young adults in the US. During 1991-1998, the highest rate of meningococcal disease occurred among infants under one year of age; however, the rate among persons ages 18-23 years was also higher than that for the general population. Certain medical conditions, household crowding, chronic illness and smoking increase the risk for developing meningococcal disease.<sup>1</sup>

## Benefits from Vaccination

Meningococcal vaccine helps prevent meningococcal disease in persons age two years and older. This highly contagious disease can cause epidemics in child care centers, schools and universities.<sup>2</sup> Meningococcal vaccine protects against disease caused by four serotypes of *Neisseria meningitidis* bacteria; A, C, Y and W-135. Most outbreaks of meningococcal disease are caused by serotype C.<sup>1</sup>

Each year in the US, 2,400-3,000 cases of meningococcal disease occur at a rate of 0.8-1.3 cases per 100,000 population.<sup>3-5</sup> Although many antibiotics are very effective against *Neisseria meningitidis*,<sup>6</sup> 10% of people who contract meningococcal disease will die.<sup>4</sup> From January 1990 through December 1999, 25% of meningococcal infection cases among persons ages 15 through 24 years in Maryland were fatal.<sup>7</sup> Eleven to nineteen percent of persons who survive this disease will suffer from permanent neurologic disability, limb loss and hearing loss.<sup>8,9</sup>

In the US, African Americans, persons of low socioeconomic status, military recruits living in barracks and college students living in dormitories are at increased risk for meningococcal disease. A US Army field study found an 89.5% reduction in the rate of meningococcal disease in serotype C-vaccinated recruits compared to unvaccinated recruits.<sup>10,11</sup> As a result of this report, in October 1971, the US Army began requiring that all new recruits be vaccinated with this vaccine.<sup>1,12</sup> A recent study of college students found that the overall incidence rate for undergraduates was 0.7 per 100,000 compared to an incidence of meningitis of 1.4 per 100,000 for the general population of 18- to 23-year-old non-students. However, freshmen living in dormitories had the highest incidence rate at 5.1 per 100,000. Of the 79 cases for whom information was available, 54 (68%) had illness due to vaccine-preventable meningococcal serotypes.<sup>13</sup>

## Risk of Vaccine Adverse Events

More than 50% of those receiving the meningococcal vaccine will have no adverse events. Up to 40% of people will experience mild reactions such as pain and redness at the injection site. Fever, the most common adverse reaction reported to the Vaccine Adverse Event Reporting System (VAERS),<sup>14</sup> may last one to two days. Approximately three people per 1,000,000 doses given can experience a serious allergic reaction resulting in breathing difficulties.<sup>15</sup> From July 1990 through October 1999, during which more than six million doses of meningococcal vaccine were distributed, 110 adverse events were reported to VAERS. The most common events reported were fever, headache and dizziness.<sup>14</sup>

## Cost-Benefit Analysis

A cost-benefit analysis projected that a program to vaccinate all college freshmen living in dormitories would require the administration of 300,000-500,000 doses of vaccine per year. This program would prevent 15 to 30 cases of meningococcal disease and one to three deaths. The cost of the program per case prevented was found to be between \$600,000 and \$1.8 million and the cost per death prevented varied between \$7 million and \$20 million.<sup>1</sup>

## GLOSSARY TERMS

Adverse events	Disease
Advisory Committee on Immunization Practices	Epidemic
Antibiotic	Meningitis
Association	Meningococcal disease
Bacteria	<i>Neisseria meningitidis</i>
Bacterial meningitis	Polysaccharide
Cases	Risk
Chronic	Sepsis
Clinical trials	Serotype
	Vaccine

## ACRONYMS

VAERS	Vaccine Adverse Event Reporting System
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## WEB RESOURCES

### MENINGOCOCCAL DISEASE:

**National Partnership for Immunization**  
<http://www.partnersforimmunization.org/mening.html>

**Center for Disease Control and Prevention's Division of Bacterial and Mycotic Diseases**  
[http://www.cdc.gov/ncidod/dbmd/diseaseinfo/meningococcal\\_g.htm](http://www.cdc.gov/ncidod/dbmd/diseaseinfo/meningococcal_g.htm)

**National Foundation for Infectious Diseases**  
<http://www.nfid.org/library/meningococcal>

**American College Health Association**  
<http://www.acha.org/special-prj/mem.htm>

**National Network for Immunization Information**  
<http://www.immunizationinfo.org/database/index.cfm>

**Vaccine Education Center at The Children's Hospital of Philadelphia**  
[http://www.vaccine.chop.edu/each\\_vaccine2.shtml#name15](http://www.vaccine.chop.edu/each_vaccine2.shtml#name15)

**Immunization Action Coalition**  
<http://www.immunize.org/mening>

### MENINGOCOCCAL VACCINE:

**National Partnership for Immunization Information**  
<http://www.partnersforimmunization.org/mening.html>

**Recommendations of the Advisory Committee on Immunization Practices (ACIP)**  
<http://www.cdc.gov/mmwr/preview/mmwrhtml/rr4907a.htm>

**Recommendations of the American Academy of Pediatrics (AAP)**  
<http://www.aap.org/policy/re0035.html>

**Vaccine Information Statement**  
<http://www.cdc.gov/nip/publications/vis/vis-mening.pdf>

### VACCINE MANUFACTURER:

**Aventis Pasteur**  
<http://www.us.aventispasteur.com/vaccines/meningitis/main.htm>

## Safety Studies

- Clinical trials of the group C vaccine in over 28,000 infants, children and young adults in the US, United Kingdom, Canada and Holland found that the vaccine was well-tolerated and caused no serious adverse events.<sup>16</sup>
- Between 1991 and 1998, a total of 4,568,572 doses of meningococcal vaccine were distributed in the US and 222 adverse events reported for a rate of 49 adverse events per one million doses given; no deaths were reported.<sup>1</sup>

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# PNEUMOCOCCAL CONJUGATE VACCINE

## General Disease Information

Worldwide, *Streptococcus pneumoniae* bacteria are a leading cause of serious illness among young children and are the most frequent cause of bacteremia, meningitis, pneumonia, sinusitis and severe ear infections. The highest rates of these diseases occur among young children, especially those under two years of age.<sup>1</sup> Higher rates of disease occur among African Americans, Alaskan Natives and specific Native American populations, compared with whites.<sup>2</sup> The highest rates of invasive disease occur among Navajo and Apache American Indian children with incidence rates of 557 to 2,396 cases per 100,000 children between the ages of one and two.<sup>3</sup>

## Benefits from Vaccination

Pneumococcal conjugate vaccine protects children under five years of age from developing pneumonia, meningitis, sepsis, ear infections and sinusitis from pneumococcal disease. Annually, pneumococcal disease causes approximately 17,000 cases of invasive disease among children under age five years, resulting in 700 cases of meningitis and 200 deaths. Treatment of pneumococcal disease among young children is complicated by the emergence of disease strains that are resistant to penicillin and other antibiotics. Although a 23-valent polysaccharide vaccine is available to prevent pneumococcal disease, this vaccine is not effective in children under two years of age. A new vaccine was developed and licensed in 2000 that is able to prevent pneumococcal disease in children two years old and younger. This new conjugate vaccine contains polysaccharides from the seven most common serotypes of *Streptococcus pneumoniae* that cause 80% of pneumococcal infections in children less than six years old.<sup>2</sup>

Each year in the US, routine pneumococcal conjugate vaccination is estimated to prevent approximately 12,000 cases of pneumococcal meningitis and bacteremia, 53,000 cases of pneumococcal pneumonia, more than one million episodes of clinically diagnosed ear infections and 116 deaths due to pneumococcal infection.<sup>4</sup> Approximately 15 million hospital/doctor's office visits for ear infections and more than 500,000 ear tube placements occur in children each year in the US. Widespread use of pneumococcal conjugate vaccine could greatly decrease visits for ear infections.<sup>5</sup> A study of 1,662 infants enrolled in a randomized, double-blind efficacy trial found that the pneumococcal conjugate vaccine reduced the number of episodes of acute ear infection from any cause by 6%, culture-confirmed pneumococcal episodes by 34%, and the number of episodes due to the serotypes contained in the vaccine by 57%.<sup>6</sup>

Because of the prevalence of pneumococcal disease in the US, antibiotic therapy is commonly prescribed to resolve cases of pneumonia and ear infection.<sup>4</sup> Since antibiotic therapy was first introduced, disease-causing strains of *Streptococcus* have gradually acquired resistance to the antibacterial effects of many of the commonly used antibiotics.<sup>4</sup> Up to one-third of all pneumococcal bacteria isolated in patients in the US now demonstrate moderate to high-level resistance to penicillin and multiple antibiotics.<sup>7-12</sup> This resistance limits the therapeutic value of these medications, resulting in the potential for more serious and/or more persistent disease.<sup>4</sup> The acquisition of resistance has been attributed to the widespread use and misuse of antibiotics in clinical practice as well as to non-clinical uses of these agents.<sup>13</sup> As disease causing organisms acquire resistance to various medications, newer, more powerful broad-spectrum antibiotics must be used to treat infected patients. Already, evidence is accruing that *Streptococcus* is acquiring resistance to state-of-the-art antibiotics.<sup>14</sup> The potential loss of sensitivity to these drugs has profound implications for public health. Because pneumococcal diseases can be prevented through the use of the conjugate vaccine, increased usage of the vaccine could reduce disease prevalence.<sup>4</sup> This would reduce the use of antibiotics and thus impede the development of antibiotic resistance by these deadly pathogens.<sup>5</sup>

## GLOSSARY TERMS

Acute	Penicillin
Acute otitis media	Pneumococcal disease
Adverse events	Pneumonia
Advisory Committee on Immunization Practices	Polysaccharide
Antibiotic	Polysaccharide vaccine
Bacteremia	Prevalence
Bacteria	Risk
Cases	Sepsis
Conjugate vaccine	Serotype
Disease	Sinusitis
Efficacy	<i>Streptococcus pneumoniae</i>
Immunization	Sudden Infant Death Syndrome
Invasive	Systemic
Meningitis	Vaccine
Pathogens	Valent

## ACRONYMS

SIDS	Sudden Infant Death Syndrome
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## WEB RESOURCES

### PNEUMOCOCCAL DISEASE:

#### National Partnership for Immunization

<http://www.partnersforimmunization.org/pneumo.html>

#### National Foundation for Infectious Diseases

<http://www.nfid.org/library/pneumococcal>

#### Centers for Disease Control and Prevention's Epidemiology and Prevention of Vaccine-Preventable Diseases (The Pink Book)

<http://www.cdc.gov/nip/publications/pink/pneumo.pdf>

#### National Network for Immunization Information

<http://www.immunizationinfo.org/database/index.cfm>

#### Vaccine Education Center at The Children's Hospital of Philadelphia

[http://www.vaccine.chop.edu/each\\_vaccine2.shtml#name06](http://www.vaccine.chop.edu/each_vaccine2.shtml#name06)

#### Immunization Action Coalition

<http://www.immunize.org/pneumoconj>

### PNEUMOCOCCAL CONJUGATE VACCINE:

#### National Partnership for Immunization

<http://www.partnersforimmunization.org/pneumo.html>

#### Recommendations of the Advisory Committee on Immunization Practices (ACIP)

<http://www.cdc.gov/mmwr/pdf/rr/rr4909.pdf>

#### Vaccine Information Statement

<http://www.cdc.gov/nip/publications/vis/vis-PneumoConjugate.pdf>

### VACCINE MANUFACTURER:

#### Wyeth Vaccines

<http://www.prevnar.com>

## Risk of Adverse Events

Mild reactions such as injection site redness, tenderness or swelling will occur in 10% to 20% of children vaccinated with pneumococcal conjugate vaccine.<sup>16</sup> Moderate reactions, including fever, irritability and drowsiness occur in up to 40% of children vaccinated. No serious adverse events have been reported in large, pre-licensure studies.<sup>7</sup>

## Cost-Benefit Analysis

A recent publication estimated that infant immunization would cost society \$80,000 per year of life saved, \$160 per case of ear infection prevented, \$3,200 per case of pneumonia prevented, \$15,000 per case of bacteremia prevented and \$280,000 per episode of meningitis prevented.<sup>17</sup>

## Safety Studies

- A large efficacy study in 23 medical centers within the Kaiser Permanente Medical Care Program of Northern California compared vaccinated and unvaccinated children in a total study population of 37,868 children. The study did not reveal any severe adverse events related to vaccination resulting in hospitalization or emergency room or clinic visits. Local and systemic reactions observed generally were mild and more severe local and systemic reactions were uncommon. The rate of sudden infant death syndrome (SIDS) observed in the study population was less than the rate observed in the state of California during 1996 and 1997, prior to use of this vaccine.<sup>5</sup>

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# PNEUMOCOCCAL POLYSACCHARIDE VACCINE

## General Disease Information

*Streptococcus pneumoniae* bacteria can cause bacteremia, pneumonia, sinusitis and meningitis. Pneumococcal disease is most common in children less than two years of age and adults over 40 years of age, and occurs more often in males than in females at all ages. Higher rates of disease occur among African Americans, Alaska Natives and specific Native American populations, compared with whites. Mortality rates are greatest among persons 65 years of age and older; mortality is also associated with higher frequency of complications of respiratory infections.<sup>1</sup>

## Benefit from Vaccination

Pneumococcal polysaccharide vaccine protects persons older than two years of age from pneumonia, bacteremia and meningitis. Each year, pneumococcal disease causes approximately 175,000 hospitalized cases of pneumonia, more than 50,000 cases of bacteremia and 3,000 to 6,000 cases of meningitis. Five to seven percent of cases of pneumonia, about 20% of bacteremia cases and about 30% of meningitis cases will die from the disease. The death rate among persons suffering from these diseases increases significantly in elderly populations.<sup>4</sup> A recent study assessed the outcomes of 259,627 persons age 65 years or older who were offered influenza and pneumococcal vaccines. The incidence of hospital treatment for influenza, pneumonia, pneumococcal pneumonia and invasive pneumococcal disease was significantly lower in the vaccinated group as compared to the unvaccinated group, and total mortality was 57% lower in vaccinated individuals.<sup>2</sup> Efficacy estimations of the pneumococcal polysaccharide vaccine range from 56% to 81%, and immunity has been shown to last for at least six years.<sup>3,4</sup>

## Risk of Adverse Events

About half of the people who receive this vaccine will have no adverse events. Thirty to fifty percent will experience mild reactions such as injection site tenderness or redness usually lasting less than 48 hours and less than 1% will experience fever, chills or malaise. Very rare cases (less than one person per 10,000) will experience a serious reaction such as breathing difficulties, hives, paleness, weakness, increased heart rate or dizziness.<sup>5</sup>

## Cost-Benefit Analysis

Along with the influenza vaccine, pneumococcal vaccine appears to be more cost-effective than any other medical intervention commonly used in the care of the elderly (this includes mammograms, bypass surgery and hypertension screening).<sup>6</sup> One study of persons aged 65 years and older in three geographic areas (Atlanta, GA; Franklin County, OH; and Monroe County, NY) estimated that 23 million elderly people unvaccinated in 1993 would have gained about 78,000 years of healthy life and saved \$194 million if they had been vaccinated with pneumococcal polysaccharide vaccine. The results also suggested that pneumococcal vaccination is likely to be even more cost saving for African Americans than for the general population. African Americans have rates of pneumococcal bacteremia more than twice those of whites, but vaccination rates are only about half as high.<sup>7</sup>

An observational study assessing the effectiveness of implementing an emergency department-based pneumococcal vaccination program found that doing so would result in overall cost savings ranging from \$168,940 to \$427,380 per year.<sup>8</sup>

## Safety Studies

- Severe systemic adverse effects have rarely been reported after administration of pneumococcal polysaccharide vaccine, and no neurologic disorders have been associated with the vaccine.<sup>1</sup>

## GLOSSARY TERMS

Adverse events	Invasive
Advisory Committee on Immunization Practices	Neurologic disorder
Anaphylaxis	Pneumococcal disease
Bacteremia	Pneumococcal polysaccharide
Bacteria	Pneumonia
Cases	Polysaccharide
Disease	Polysaccharide vaccine
Efficacy	Risk
Immunization	Sinusitis
Immunocompetent	<i>Streptococcus pneumoniae</i>
Immunosuppressed	Systemic
	Vaccine

## WEB RESOURCES

### PNEUMOCOCCAL DISEASE:

#### National Partnership for Immunization

<http://www.partnersforimmunization.org/pneumo.html>

#### National Foundation for Infectious Diseases

<http://www.nfid.org/library/pneumococcal>

#### Centers for Disease Control and Prevention's *Epidemiology and Prevention of Vaccine-Preventable Diseases (The Pink Book)*

<http://www.cdc.gov/nip/publications/pink/pneumo.pdf>

#### National Network for Immunization Information

<http://www.immunizationinfo.org/database/index.cfm>

#### Immunization Action Coalition

<http://www.immunize.org/pneumopoly>

### PNEUMOCOCCAL POLYSACCHARIDE VACCINE:

#### National Partnership for Immunization

<http://www.partnersforimmunization.org/pneumo.html>

#### Recommendations of the Advisory Committee of Immunization Practices (ACIP)

<http://www.cdc.gov/mmwr/pdf/rr/rr4608.pdf>

#### Vaccine Information Statement

<http://www.cdc.gov/nip/publications/vis/vis-ppv.pdf>

### VACCINE MANUFACTURERS:

#### Merck Vaccine Division

<http://www.mercksharpdohme.com/disease/preventable/pneu>

#### Wyeth Vaccines

<http://www.vaccineworld.com>

- Analysis of nine randomized controlled trials of pneumococcal vaccine efficacy found that local, minor reactions were observed in one-third or fewer of 7,531 patients receiving the vaccine. No reports of severe fever or anaphylaxis were reported.<sup>9</sup>
- Revaccination with pneumococcal polysaccharide vaccine has not been associated with severe adverse reactions. Mild localized reactions have been associated with higher levels of circulating

anti-pneumococcal antibodies. Therefore, a larger proportion of immunocompetent persons have reported local reactions such as redness, stiffness and pain at the injection site, than immunosuppressed persons. Mild to moderate fever was the most common systemic reaction reported by re-vaccinees and first-time vaccinees. Elevated temperatures did not last more than two days.<sup>10</sup>

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## VARICELLA VACCINE

### General Disease Information

Varicella, or chickenpox, is a highly contagious disease caused by varicella zoster virus that is transmitted by airborne droplets and direct contact with lesions. In the pre-vaccine era, the majority of cases of chickenpox (more than 90%) occurred among children under 15 years of age. Varicella complications include bacterial infection of skin lesions and dehydration; more serious complications that may result in hospitalization and death<sup>1,2</sup> include invasive group A streptococcus infections, hemorrhagic complications, encephalitis and pneumonia. Herpes zoster or shingles is caused by reactivation of the chickenpox virus and develops most frequently among immunocompromised persons and the elderly. In children, chickenpox generally lasts four to five days and usually involves between 250 to 500 lesions.<sup>1</sup>

### Benefits from Vaccination

Before the varicella vaccine became available, approximately four million cases occurred annually in the US, resulting in 11,000 hospitalizations and 105 deaths.<sup>3</sup> Chickenpox is a more severe disease in adults, pregnant women, immunosuppressed individuals and children less than one year of age.<sup>4</sup> The risk of complications and death attributable to varicella can be up to 10- to 20- times higher for adults than for children.<sup>5</sup>

During the years (1990-1994) immediately preceding introduction of the vaccine, more than 90% of the infections, two-thirds of varicella-related hospitalizations and almost half of varicella-related deaths in the US occurred in children.<sup>6</sup> Post-licensure vaccine effectiveness studies have shown that the vaccine is highly effective in preventing severe disease and is 70% to 87% effective in preventing all disease.<sup>7,8</sup> Since introduction of varicella vaccine in the US in 1995, varicella cases and hospitalizations have declined approximately 80% in areas of the country where active surveillance for varicella is being conducted and where vaccine coverage reached 70% to 80% in 2000. Varicella cases declined in all age groups, including infants and adults with the greatest decline occurring among children one to four years of age. In the combined three surveillance areas, hospitalizations due to varicella declined from a range of 2.7 to 4.2 per 100,000 population in 1995 through 1998 to 0.6 and 1.5 per 100,000 population in 1999 and 2000, respectively.<sup>9</sup>

### Risk of Vaccine Adverse Events

The majority of children who receive the varicella vaccine will have no adverse events. Adverse events that do occur are typically mild reactions such as injection site tenderness or swelling, fever and mild rash. Local reactions have been reported by 19% of children and by 24% of adolescents and adults.<sup>10</sup> Two cases out of 100,000 shots given may experience a serious reaction consisting of seizure caused by fever and pneumonia.<sup>11</sup>

A mild form of chickenpox may occur among vaccinees. Most of these cases occur in children and all cases have been without complications. The risk of developing disease from natural wild virus is four to five times higher than developing the disease from the vaccine.<sup>10</sup>

### Cost-Benefit Analysis

A cost-effectiveness study, modeling the projected impact of vaccination and current direct and indirect costs, found a savings of \$5.40 for every dollar spent on routine vaccination of preschool-age children. This is equivalent to a savings of \$400 million in healthcare costs annually in the US.<sup>12</sup> Another model, using data from the National Health Interview Survey, the National Hospital Discharge Survey and the National Medical Expenditure Survey, determined the net economic benefit of varicella vaccination to be \$6.6 million.<sup>13</sup> These studies found that the cost of a varicella vaccination program was equal to, or greater than, the direct medical cost of treating the disease if

## GLOSSARY TERMS

Adverse events	Immunocompromised
Advisory Committee on Immunization Practices	Immunosuppressed
Bacteria	Invasive
Breakthrough cases	Pneumonia
Cases	Risk
Chickenpox	Seizure
Coverage	Shingles
Disease	Vaccine
Encephalitis	Vaccine Adverse Events Reporting System
Group A streptococcus	Vaccinees
Hemorrhagic	Varicella
Herpes zoster	Virus
Immunization	

## ACRONYMS

VAERS Vaccine Adverse Events Reporting System

## WEB RESOURCES

### VARICELLA:

**National Partnership for Immunization**  
<http://www.partnersforimmunization.org/chickenpox.html>

**Centers for Disease Control and Prevention's Epidemiology and Prevention of Vaccine-Preventable Diseases (The Pink Book)**  
<http://www.cdc.gov/nip/publications/pink/varicella.pdf>

**National Center for Infectious Diseases**  
[http://www.cdc.gov/ncidod/diseases/list\\_varid.htm](http://www.cdc.gov/ncidod/diseases/list_varid.htm)

**National Network for Immunization Information**  
<http://www.immunizationinfo.org/database/index.cfm>

**Vaccine Education Center at The Children's Hospital of Philadelphia**  
[http://www.vaccine.chop.edu/each\\_vaccine2a.shtml#name11](http://www.vaccine.chop.edu/each_vaccine2a.shtml#name11)

**Immunization Action Coalition**  
<http://www.immunize.org/varicella>

### VARICELLA VACCINE:

**National Partnership for Immunization**  
<http://www.partnersforimmunization.org/chickenpox.html>

**Recommendations of the Advisory Committee on Immunization Practices (ACIP)**  
<http://www.cdc.gov/mmwr/preview/mmwrhtml/rr4806a1.htm>

**Vaccine Information Statement**  
<http://www.cdc.gov/nip/publications/vis/vis-varicella.pdf>

### VACCINE MANUFACTURER:

**Merck Vaccine Division**  
<http://www.mercksharpdohme.com/disease/preventable/cpox>

indirect costs associated with the disease were not included in the analysis. Savings came from the difference in lost wages from parents caring for ill children as fewer children would contract varicella after immunization. Therefore, fewer parents would need to stay home to care for them.<sup>14</sup>

### Safety Studies

- A study evaluated the vaccination of 89,753 children and adults for possible rare medical events associated with vaccination. The varicella vaccine was shown to display a favorable safety profile, free of serious side effects. In addition, rates of varicella-like rash were low, consisting of approximately 2.5 breakthrough cases per year.<sup>15</sup>
- Analyses of reports to the Vaccine Adverse Events Reporting System (VAERS) from March 17, 1995 through July 25, 1998 found that the vast majority of reported cases of vaccine reactions were not serious. VAERS received 6,574 case reports of adverse events in recipients of varicella vaccine, a rate of 67.5 reports per 100,000 doses. Approximately 4% of the reports described serious adverse events, including 14 deaths.<sup>16</sup>
- Mathematical models predict that if varicella vaccine coverage in children is more than 90%, a greater proportion of cases will occur at older ages, but the overall varicella disease burden will decrease for children and adults. However, if immunization rates for young children vaccinated with varicella vaccine remain relatively low, the number of children who become susceptible adults will increase as will the opportunities for susceptible adults to contract varicella from unimmunized children.<sup>2</sup>
- Fourteen pre-licensure studies were conducted on a total of 12,323 subjects aged six months to 17 years. Mild adverse events reported in these studies included injection site pain and redness, rashes and increased body temperature. Moderate events included rash, fever and swelling. The only reported serious adverse event attributed to the vaccine was herpes zoster or shingles.<sup>12</sup>

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## VACCINES FOR SPECIAL RISK GROUPS AND TRAVELERS TO SELECTED GEOGRAPHICAL AREAS

Vaccines recommended for use by the general public are not the only vaccines currently available to help prevent the spread of infectious diseases worldwide. Many vaccines have been and are being developed for use by specific groups of people who, because of their health, working or living environment, travels or genetic background, are at increased risk of developing a particular disease. This section includes a discussion of vaccines available for some of these groups. As these vaccines have not been recommended for general use, weighing the benefits and risks of their use becomes especially important in evaluating their use in particular individuals.

Because of recent increased concern about the use of anthrax and smallpox as biological weapons, information on these diseases and the vaccines currently available to prevent them have been included. Neither vaccine is currently available for general use by the public in the US. Anthrax vaccine is available for use by military personnel and was made available to anthrax-exposed civilians during 2001-2002. In the absence of a confirmed case of smallpox and with the presumption that the risk of bioterrorist attack with smallpox is low, smallpox vaccine has been recommended for persons in the US predesignated by the appropriate bioterrorism and public health authorities to conduct investigation and follow-up of initial smallpox cases. Under these same circumstances, smallpox vaccine has also been recommended for some US healthcare personnel at risk of exposure to initial cases of smallpox in facilities that are predesignated to receive these patients.<sup>1</sup>

### GLOSSARY TERMS

Anthrax  
Cases  
Disease

Risk  
Smallpox  
Vaccine

# ANTHRAX

## General Disease Information

Anthrax is an acute infectious disease caused by the large, spore-forming bacterium *Bacillus anthracis*. Anthrax spores are extremely resistant and can survive for 40 years in soil<sup>2</sup> and 80 years in a vial.<sup>3</sup> But more commonly, when significant microbial competition exists in the soil, anthrax contamination usually lasts only a few months and rarely for more than three or four years.<sup>4</sup> In infected animals or humans, *Bacillus anthracis* can replicate and release an endotoxin that causes the symptoms of anthrax. Animals are infected with anthrax when they ingest or inhale spores while grazing,<sup>5</sup> thus the disease is most common in herbivores, which become infected by ingesting spores from the soil.<sup>6</sup>

Naturally occurring disease in humans is acquired by skin contact, ingestion or inhalation of *Bacillus anthracis* spores from infected animal products or from inhalation of spores from the environment.<sup>5</sup> Anthrax is not contagious and therefore cannot be transmitted from one person to another. In humans, three types of anthrax infection can occur:

1. **Cutaneous anthrax:** Up to 2,000 cases of cutaneous anthrax occur worldwide in humans each year.<sup>6</sup> Most of these infections (about 95%) occur when the bacterium enters a cut or abrasion on the skin.<sup>7</sup> Infections begin as a raised itchy bump resembling an insect bite and progress to a fluid-filled blister with a black area in the center. Lymph glands may swell in the areas surrounding the blister.<sup>8</sup> While approximately 5% to 20% of untreated cases will result in death, such deaths are rare (<1%) when the infection is treated with the appropriate antimicrobial therapy. Only two cases of cutaneous anthrax arising from direct contact have been reported.<sup>5</sup>
2. **Gastrointestinal anthrax:** Although outbreaks have been reported in Africa and Asia, this form of anthrax is very uncommon. Gastrointestinal anthrax occurs when a person ingests insufficiently cooked, contaminated meat.<sup>6</sup> Infection results in an acute inflammation of the intestinal tract. Symptoms include nausea, vomiting, loss of appetite and fever followed by abdominal pain, vomiting of blood and severe diarrhea. The death rate for this form of anthrax is unknown but has been estimated to be between 25% and 60% of cases.<sup>5</sup>
3. **Inhalational anthrax:** This form of anthrax is acquired from environmental sources and occurs when 8,000 to 50,000 anthrax bacteria spores enter the body through the airways. After an incubation period of one to seven days, mild symptoms of fever, malaise, fatigue, cough and mild chest discomfort may develop. Mild symptoms will rapidly progress to respiratory distress and shock in another two to four days and is then followed by more severe symptoms, including breathing difficulty and exhaustion. Human-to-human transmission of inhalational anthrax has never been reported.<sup>7</sup> Before recent events, no case of inhalational anthrax had been reported in the US since 1978.<sup>6</sup> The case fatality rate of inhalational anthrax cases in 2001 with the use of intensive antibiotic and other therapy was 45%.<sup>5</sup>

Prior to September 11, 2001, the annual incidence of anthrax in the US had declined from 127 cases per year in the early years of the twentieth century to less than one case per year in the last 20 years.<sup>8</sup> The mortality rate of these cases of anthrax in the US was 89%, but the majority of cases occurred before the development of critical care units and, in some cases, before the introduction of antibiotics.<sup>6</sup>

Research on anthrax as a biological weapon began more than 80 years ago and today at least 17 nations are believed to have offensive biological weapons programs. It is uncertain how many of these countries are working with anthrax.<sup>6</sup> Inhalational anthrax is considered to be a bioweapon of interest to terrorists and one that is highly feared by civilians. Rough estimates of the potential effects of an attack suggest that the release of 100 kg (220 pounds) of anthrax spores by aerosol from a single airplane

## GLOSSARY TERMS

Acute	Gastrointestinal anthrax
Allergic reaction	Immunization
Anthrax	Induration
Antibiotic	Inhalational anthrax
<i>Bacillus anthracis</i>	Malaise
Bacteria	Nodules
Booster	Penicillin
Cases	Placebo
Clinical trials	Prevalence
Cutaneous anthrax	Reactogenicity
Disease	Risk
Endemic	Scarification
Endotoxin	Systemic
Erythema	Vaccine

## ACRONYMS

CDC	Centers for Disease Control and Prevention
FDA	Food and Drug Administration

## WEB RESOURCES

### Advisory Committee on Immunization Practices

<http://www.cdc.gov/mmwr/preview/mmwrhtml/rr4915a1.htm>

### Centers for Civilian Biodefense Strategies

<http://www.bt.cdc.gov/agent/anthrax/anthraxgen.asp>

### Center for Disease Control and Prevention

<http://www.bt.cdc.gov/agent/anthrax/anthraxgen.asp>

### Department of Defense

<http://www.anthrax.osd.mil/>

### University of Alabama at Birmingham's Bioterrorism Web Site

<http://www.bioterrorism.uab.edu>

### VACCINE MANUFACTURER:

#### Bioport

<http://www.bioport.com>

could cause from one to three million casualties in a city the size of Washington, DC.<sup>9</sup> Other estimates have suggested the potential for 50% fatalities to occur as far as 160 km (100 miles) downwind from an aerosol release.<sup>10</sup> However, most experts agree that individuals or groups without access to advanced biotechnology would not be able to manufacture a lethal anthrax aerosol that could be inhaled.<sup>6</sup>

On October 4, 2001, the threat of anthrax as a biological weapon became a reality when a man in Boca Raton, Florida was diagnosed with and later died of inhalational anthrax. An additional four US citizens fell victim, and a total of 18 contracted either the inhalational or cutaneous form. The Centers for Disease Control and Prevention (CDC) has recommended ciprofloxacin and doxycycline as the preferred post-exposure treatment for cutaneous anthrax and combination therapy with more than one active agent against *Bacillus anthracis* for inhalational anthrax.<sup>5</sup> And since the first case of anthrax was diagnosed, an estimated 30,000 people (mainly federal employees) have received prophylactic antibiotics.<sup>11</sup>

### Risk-Benefit Analysis of Vaccination

Anthrax vaccine was first licensed in the US in 1970 and is produced by Bioport Corporation in Lansing, Michigan (formerly Michigan Biologic Products Institute). The vaccine is a cell-free filtrate that is produced from a form of anthrax that does not cause disease.<sup>6</sup> Since its licensure, the anthrax vaccine has been safely administered to at-risk wool mill workers, veterinarians, laboratory workers, livestock handlers and the US military. The duration of protection from disease following vaccination is unknown. The US Army's anthrax vaccine program alone has inoculated more than 150,000 soldiers.<sup>11</sup>

A controlled clinical trial was conducted in a susceptible population working in four mills in the northeastern US where raw imported goat hair contaminated with *Bacillus anthracis* was used. The vaccine used was similar to the currently licensed US vaccine and was found to be 92.5% effective in protecting the population against cutaneous anthrax as compared with a placebo. No assessment of the effectiveness of the vaccine against inhalational anthrax could be made because there were too few cases.<sup>8</sup>

Approximately 30% of vaccinated men and 60% of vaccinated women will experience temporary reactions such as soreness, redness, itching, swelling and lumps at the site of injection. Muscle aches, joint aches, headaches, rash, chills, fever, nausea, loss of appetite, malaise or related symptoms will occur in 5% to 35% of persons vaccinated. Severe allergic reactions may occur in one out of 100,000 doses administered, and rare, serious events such as those requiring hospitalization occur once per 200,000 doses.<sup>11</sup>

Because of limited production capacity, the anthrax vaccine is not currently available for the general public. The only people currently receiving the anthrax vaccine are designated military units and personnel involved in anthrax research.

### Treatment of Anthrax Infection

Anthrax is susceptible to antibiotics, including penicillin, tetracycline and oral fluoroquinolones (ciprofloxacin and ofloxacin). The Federal Drug Administration (FDA) has

approved quinolone ciprofloxacin (Bayer Corporation, West Haven, CT) and tetracycline doxycycline (Pfizer, Inc., New York, NY) as treatment options for anthrax. The antibiotics do not kill the bacteria but prevent them from replicating and releasing the deadly endotoxins that are the primary cause of death.<sup>9</sup> Prophylactic treatment with these antibiotics should be given to exposed individuals regardless of their anthrax vaccination status.<sup>8</sup>

### Safety Studies

- In the former Union of Soviet Socialist Republics (USSR), 3,500 volunteers were vaccinated with anthrax vaccine from 1943 to 1950. Complete safety and a lack of local side effects were reported.<sup>12</sup>
- From 1951 to 1952, a field trial was conducted in 14 anthrax-endemic rural districts in the former USSR. A total of 141,663 individuals were vaccinated (92,150 by scarification and 49,513 by injection under the skin). Among those individuals who were vaccinated by injection under the skin, 5,402 experienced a rise in body temperature and local erythema. A slight induration at the site of injection occurred in 14 cases.<sup>12</sup>
- Follow-up of 110 US military personnel who had received the anthrax vaccine found that the prevalence of adverse reactions following immunization was 40%, which was higher than expected.<sup>13</sup>
- A study conducted to determine whether receipt of anthrax vaccination by reproductive-age women had an effect on pregnancy rates followed 385 pregnancies occurring after at least one anthrax vaccination in 3,136 women and 130 pregnancies in 962 unvaccinated women. Women who received the anthrax vaccine were 1.2 times as likely to give birth as unvaccinated women.<sup>14</sup>
- Studies on the safety of four lots of anthrax vaccine, including approximately 16,000 doses administered to approximately 7,000 participants, found that mild local reactions were reported in 3% to 20% of all doses, moderate reactions were reported in 1% to 3% of all doses and severe reactions in less than 1% of all doses.<sup>7</sup>
- From 1973 to 1999, 1,590 individuals working in the US Army Medical Research Institute of Infectious Diseases received 10,451 doses of anthrax vaccine. Under a passive reporting system, 4% of these doses produced a local reaction consisting of erythema, induration, itching and swelling at the site of injection. Systemic reactions consisting of fever, chills, malaise, muscle aches or joint aches occurred following 0.5% of doses. All local and systemic reactions resolved without any lost time from work or long-term effects.<sup>5</sup>
- Investigators from the US Army Medical Research Institute of Infectious Diseases assessed vaccine safety in previously vaccinated soldiers who were given a booster of anthrax vaccine as part of an actively monitored study. Of 486 subjects who received the anthrax vaccine, 21% had local erythema and/or induration. In 5%, the erythema and/or induration was 5 cm or more. No reaction caused lost time from work and all resolved.<sup>5</sup>

- A study of anthrax vaccine reactogenicity, conducted by the Canadian Armed Forces in 547 individuals who received the anthrax vaccine revealed mild local reactions after 10.1% of doses, moderate local reaction after 0.5% and systemic reactions occurred in 1.5%. No long-term effects nor serious local reactions were reported except for one individual reporting a persistent nodule at the local site and multiple nodules at several distant sites.<sup>15</sup>

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# JAPANESE ENCEPHALITIS

## General Disease Information

Japanese encephalitis (JE) is a viral infection transmitted mainly by the bites of a particular type of mosquito. JE is the leading cause of childhood encephalitis in Asia with approximately 35,000 cases and 10,000 deaths reported annually. Because the disease is often found in remote locations that are not conducting routine surveillance for JE, and because the great majority of infections are asymptomatic, official reports likely underestimate the true number of cases.<sup>1</sup> In endemic areas, children are at the greatest risk for developing this disease. Only one in 250 infections results in clinical disease such as encephalitis, high fever, headache, seizures and gastrointestinal symptoms. JE will lead to severe encephalitis in one in 20 to 1,000 cases. Of those who develop encephalitis, death occurs in up to 30% of cases.<sup>2</sup>

## Risk-Benefit Analysis of Vaccination

The JE vaccine is 91% effective in preventing this disease and has been effective in reducing the number of cases of disease in Beijing and other parts of China where high JE immunization rates are maintained.<sup>1,3</sup> The risk of JE for short-term international travelers and for those who confine their travel to urban areas is very low.<sup>2</sup> Between 1981 and 1992 only 11 US residents became infected with JE virus; eight were military personnel or their dependents.<sup>3</sup> Expatriates and travelers who live in rural areas where JE is endemic or epidemic for prolonged periods are at the greatest risk for developing this disease. In addition, travelers with extensive outdoor and evening exposure in these areas might be at an increased risk of disease even if their trip is brief.<sup>2</sup>

No association has been found between this vaccine and serious vaccine-related neurological complications during the more than 30 years that the vaccine has been used. Approximately 20% of vaccinees will experience local tenderness, redness or swelling at the site of injection. Mild systemic symptoms, chiefly headache, low-grade fever, myalgias, malaise and gastrointestinal symptoms are reported in 10% to 30% of vaccinees.<sup>1</sup> However, information contained in the product insert for this vaccine warns that vaccinated persons should remain within access of prompt medical care for 10 days following immunization because of the rare but real possibility of a severe reaction.

## Safety Studies

- After an outbreak of JE on Okinawa, Japan in 1945, 53,000 American soldiers stationed there received this vaccine. Eight neurological reactions were observed. However, similar cases were reported concurrently in nonvaccinated individuals, and it is unclear whether the illnesses were vaccine-related.<sup>4</sup>
- One case of Guillain-Barré syndrome, temporally related to JE immunization, was observed following immunization of approximately 20,000 American soldiers with the vaccine prior to US licensure.<sup>1</sup>
- Several anecdotal reports of severe neurological side effects following vaccination have been reported in Japan, Korea and Denmark, but no positive association between these reports and the vaccine have been made.<sup>1</sup>
- An early prospective study in Japan to detect vaccine-associated adverse events found no neurological complications occurring within a month after vaccination in 38,384 subjects receiving crude or purified vaccine.<sup>5</sup>
- A country-wide study in Japan to detect neurological complications found 26 temporally related cases between 1957 and 1966. Rates and comparisons with nonimmunized controls were not available.<sup>1</sup>

## GLOSSARY TERMS

Advisory Committee on Immunization Practices	Immunization
Association	Japanese encephalitis
Cases	Malaise
Controls	Myalgia
Disease	Risk
Encephalitis	Seizure
Endemic	Systemic
Epidemic	Vaccine
Guillain-Barré syndrome	Vaccinees
	Virus

## ACRONYMS

JE Japanese encephalitis

## WEB RESOURCES

### Advisory Committee on Immunization Practices Recommendations

<http://www.cdc.gov/mmwr/preview/mmwrhtml/00020599.htm>

### Children's Vaccine Center

[http://www.childrevaccine.org/html/v\\_enceph\\_qf.htm](http://www.childrevaccine.org/html/v_enceph_qf.htm)

### McKinley Health Center – University of Illinois at Urbana-Champaign

<http://www.mckinley.uiuc.edu/health-info/dis-cond/vacimmun/jap-ence.html>

### National Center for Infectious Diseases

<http://www.cdc.gov/travel/jenceph.htm>

### VACCINE MANUFACTURER:

#### Aventis Pasteur

<http://www.aventispasteur.com>

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## RABIES

### General Disease Information

Rabies is a viral infection transmitted to humans by a scratch or a bite of an infected animal or the transfer of the infected animal's saliva to a human mucous membrane (lining of nose or mouth, open wound, etc.).<sup>1</sup> Disease occurs after the rabies virus invades the victim's central nervous system, causing inflammation of the brain and spinal cord and rapid progression to paralysis, coma and death.<sup>1</sup> The disease is almost always fatal.<sup>2</sup> Worldwide at least 50,000 deaths occur each year.<sup>3</sup>

Rabies is found on all continents except Antarctica<sup>1</sup> and more than 2.5 billion people live in regions where rabies is endemic.<sup>3</sup> Although human rabies can be found in all age groups, cases are most common in persons younger than 15 years. The majority of rabies victims are male<sup>4</sup> and globally every year more than 10 million people receive post-exposure vaccination against this disease.<sup>3</sup> Almost one million emergency room visits for animal bites occur each year in the US (mostly from dogs and cats) and each case has to be evaluated as a possible rabies exposure.<sup>5-7</sup>

In the 1940s and 1950s, a marked decrease in the number of rabies cases among US domestic animals resulted in a substantial decrease in the incidence of rabies among humans in the US. In 1950, 4,979 cases of rabies were reported among dogs, and 18 cases were reported among humans. But between 1980 and 1997, only 95 to 247 rabies cases were reported each year among dogs and on average only two human cases were reported each year.<sup>8</sup> During this same period, 12 cases of human rabies in the US resulted from dog bites that were inflicted outside of the US ("imported cases").<sup>9</sup>

Meanwhile, rabies among wildlife—especially raccoons, skunks and bats—has become more prevalent since the 1960s, accounting for more than 90% of all cases of animal rabies reported to the Centers for Disease Control and Prevention (CDC) each year. Rabies among wildlife occurs throughout the continental US; only Hawaii remains consistently rabies-free.<sup>10</sup>

Since 1990, bats have become the major source of rabies transmission to humans in the US. Between 1990 and 2000, 32 cases of rabies in humans were reported. Seventy-five percent of these cases were caused by rabies virus transmitted by bats. Recognizing the significant role of bats in rabies transmission, the CDC has recommended that post-exposure treatment might be appropriate if the bat cannot be tested even if a bite, scratch or mucous membrane exposure from the bat is not apparent.<sup>2</sup> Cavers are considered to be at higher risk for rabies exposure than the general public due to their potential contact with bats and have been recommended since the 1960s to receive pre-exposure prophylaxis.<sup>11</sup>

### Risk-Benefit Analysis of Vaccination

Rabies vaccine can be given either pre- or post-exposure. Pre-exposure vaccination eliminates the need for rabies immune globulin (RIG) and reduces the post-exposure vaccine regimen. It can protect against unapparent exposures, such as in children<sup>12</sup> or when treatment is delayed.<sup>2</sup> The vaccine induces an active immune response (rabies neutralizing antibodies) after seven to 10 days that usually lasts for two or more years. Because rabies exposures are rare and are always episodic, the general US population does not require pre-exposure vaccination.<sup>2</sup>

RIG is also a component of post-exposure treatment. RIG provides a rapid, passive immunity that persists for only a short time.<sup>2</sup> However, RIG is expensive. One proven rabid cat in New Hampshire in 1994 resulted in an expenditure of \$1.1 million to provide at least 665 individuals with post-exposure treatment.<sup>13</sup> And although rabies among humans is rare in the US, approximately 16,000 to 39,000 persons receive post-exposure prophylaxis each year.<sup>14</sup>

## GLOSSARY TERMS

Cases	Meningitis
Coma	Multiple sclerosis
Disease	Prophylaxis
Eczema	Rabies
Encephalitis	Rabies immune globulin
Endemic	Risk
Erythema	Steroids
Guillain-Barré syndrome	Systemic
Immunization	Vaccine
Imported cases	Vaccinees
Malaise	Virus

## ACRONYMS

CDC	Centers for Disease Control and Prevention
RIG	Rabies immune globulin

## WEB RESOURCES

### Advisory Committee on Immunization Practices Recommendations

<http://www.cdc.gov/travel/diseases/rabies.htm>

### National Center for Infectious Diseases

<http://www.cdc.gov/ncidod/dvrd/rabies/>

### National Center for Infectious Diseases Travelers' Health

<http://www.cdc.gov/travel/diseases/rabies.htm>

### National Institute of Allergy and Infectious Disease

<http://www.niaid.nih.gov/factsheets/rabies.htm>

### VACCINE MANUFACTURER:

#### Aventis Pasteur

<http://www.us.aventispasteur.com/vaccines/rabies/main.htm>

#### Chiron

<http://www.chiron.com>

RabAvert® and Imovax® rabies vaccines are equally effective in providing protection from rabies disease and are generally well-tolerated. In studies with Imovax®, 30% to 74% of rabies vaccinees experienced local reactions, such as pain, erythema and swelling or itching at the site of injection. Systemic reactions, such as headache, nausea, abdominal pain, muscle aches and dizziness have been reported among 5% to 40% of Imovax® recipients.<sup>15</sup>

Severe and life-threatening neurological adverse events are rare after receiving RabAvert® or Imovax® rabies vaccines. For instance, against a background of 11.8 million doses of RabAvert® rabies vaccine distributed worldwide, 10 cases of encephalitis or meningitis, seven cases of temporary paralysis, including two cases of Guillain-Barré syndrome, one case of myelitis, one case of neurologic disease and two cases of suspected multiple sclerosis were temporally associated with the rabies vaccine RabAvert®.<sup>16</sup> Three cases of neurological illness resembling Guillain-Barré syndrome that resolved without secondary problems in 12 weeks, and a focal subacute central nervous system disorder temporally associated with Imovax® have been reported.<sup>15</sup>

### Cost-Benefit Analysis

A pharmaco-economic study on pre-exposure rabies immunization indicated that the CDC's recommendation to serologically test for rabies following possible exposure coupled with the use of

vaccine will yield a cost savings for those who should maintain an adequate rabies antibody level due to their vocation or activities.<sup>17</sup>

According to existing documented economic evaluations in the US, only two individuals per 1,000 exposed persons need to be at risk of contracting bat rabies for it to be economical to give post-exposure prophylaxis to all of the exposed persons.<sup>18</sup>

### Safety Studies

- In a Phase III post-exposure (1,252 patients) and pre-exposure (37 patients) clinical study in India from 1985 to 1993, RabAvert® vaccine was well-tolerated in all age groups among the 1,289 vaccinees. Forty patients (3.2%) complained of mild to moderate pain or tenderness at the site of injection that lasted for one to two days. Six (0.5%) patients developed mild temperatures lasting 12 to 24 hours. Two (0.2%) patients developed a mild rash lasting 24 to 28 hours and two (0.2%) patients developed a generalized eczema that was controlled using steroids.<sup>19</sup>
- In a pre-exposure study of normal volunteers who were vaccinated against rabies using the two human rabies vaccines available in the US (RabAvert® and Imovax®), pain at the site of injection was the most common local adverse reaction (34% and 45%, respectively) and the most common systemic adverse reactions were malaise (15% and 25%, respectively), headache (10% and 20%, respectively) and dizziness (15% and 10%, respectively).<sup>16</sup>

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## SMALLPOX

### General Disease Information

Smallpox is an acute infectious disease caused by the variola virus. This disease spreads most easily during cool, dry winter months but can be transmitted in any climate and in any part of the world.<sup>1</sup> Initial symptoms of high fever of 101 degrees Fahrenheit or higher, chills, abdominal pain, vomiting, fatigue and head and back aches usually appear about 12 days after exposure to the virus. A characteristic rash, usually seen on the face, arms and legs, develops one to four days later. The rash then develops into pus-filled lesions that eventually scab and fall off after three to four weeks.<sup>2</sup>

Smallpox is contagious and spreads from person to person by infected saliva droplets. Before vaccine became available, almost everyone throughout the world contracted smallpox, including George Washington<sup>3</sup> and Abraham Lincoln.<sup>4</sup> Spread of smallpox throughout the population was generally slower than for other infectious diseases such as measles or chickenpox. Because smallpox is not contagious until immediately before the appearance of a rash on the infected person, the disease was spread primarily to household members and friends, and large outbreaks were uncommon. Infected persons are most contagious during the first week following the onset of rash.<sup>5</sup>

Two major forms of the disease, variola major and variola minor, exist. Variola major is the more severe form of smallpox and consists of four main clinical presentations. These include ordinary, modified, flat and hemorrhagic. Ordinary smallpox occurs among 90% or more of the unvaccinated persons who contract smallpox. Modified smallpox is a less severe form of disease that occurs mostly in previously vaccinated persons. This form of smallpox disease is rarely fatal. Flat smallpox is characterized by flat lesions and severe disease. Hemorrhagic smallpox is a severe yet uncommon form of smallpox disease that is accompanied with extensive internal bleeding. Most cases of flat and hemorrhagic smallpox are fatal.<sup>2</sup>

While the majority of patients who were infected with smallpox recovered, variola major epidemics resulted in death rates of 30% of infected, unvaccinated persons. Epidemics of the milder variola minor form of smallpox resulted in death rates of 1% or less of infected, unvaccinated persons.<sup>2</sup>

Smallpox was probably first used as a biological weapon during the French and Indian Wars of 1754-1767 when British forces in North America distributed blankets that had been used by smallpox patients to Native Americans collaborating with the French. As many as 50% of those exposed are believed to have died.<sup>6</sup> Development of a smallpox vaccine by Edward Jenner in 1796 ultimately led to the World Health Organization's (WHO) declaration of worldwide smallpox eradication in 1977 and elimination of the threat of natural infection by the smallpox virus.<sup>6</sup>

Routine vaccination of children in the US was discontinued in 1971 with the recognition that the risks of vaccination complications exceeded the essentially zero risk of acquiring smallpox. In 1980, the World Health Assembly recommended that all countries cease smallpox vaccination. WHO also recommended that all laboratories destroy their stocks of smallpox virus or transfer them to one of two WHO reference laboratories - the Institute of Virus Preparations in Moscow, Russia, or the Centers for Disease Control and Prevention (CDC) in Atlanta, Georgia, US. All countries reported compliance.<sup>2</sup>

The eradication of smallpox cost approximately US \$313 million over 10 years, an investment which has been paid back many times over in savings in vaccines and medical care and the suspension of international surveillance activities.<sup>7</sup> The savings, as a result of the cessation of vaccination and quarantine measures, was estimated to be in excess of \$1 billion annually.<sup>8</sup>

Currently, there is no evidence of smallpox transmission anywhere in the world. It is not known what type of materials may have been produced by bioweapons laboratories that worked with smallpox virus prior to or after 1980, or if smallpox

## GLOSSARY TERMS

Acute	Epidemic
Adverse events	Immunization
Advisory Committee on Immunization Practices	Immunocompromised
Blood serum	Placebo
Cases	Risk
Case series	Serum
Chickenpox	Smallpox
Clinical trials	Systemic
Controls	Vaccine
Disease	Vaccinees
Eczema	Vaccinia virus
Efficacy	Variola virus
Encephalitis	Virus

## ACRONYMS

ACIP	Advisory Committee on Immunization Practices
AIDS	Acquired Immune Deficiency Syndrome
CDC	Centers for Disease Control and Prevention
HIV	Human Immunodeficiency Virus
VIG	Vaccinia immune globulin
WHO	World Health Organization

## WEB RESOURCES

### Advisory Committee on Immunization Practices (ACIP)

<http://www.cdc.gov/nip/acip/default.htm>

### Center for Civilian Biodefense Strategies

<http://www.hopkins-biodefense.org/pages/agents/agentsmallpox.html>

### Centers for Disease Control and Prevention

<http://www.bt.cdc.gov/agent/smallpox/smallpoxgen.asp>

### University of Alabama at Birmingham's Bioterrorism Web site

[www.bioterrorism.uab.edu](http://www.bioterrorism.uab.edu)

### VACCINE MANUFACTURER:

#### Acambis

<http://www.acambis.com>

virus from such facilities was destroyed or submitted to the WHO reference laboratories. However, according to recent smallpox vaccination recommendations made by the Advisory Committee on Immunization Practices, the threat of an attack on the US using a smallpox virus has been assessed as low.<sup>9</sup>

### Risk-Benefit Analysis of Vaccination

The only weapons against smallpox are vaccination and patient isolation.<sup>1</sup> Smallpox vaccine contains vaccinia virus, which is in the same family as variola virus (the virus that causes smallpox disease). However, vaccinia virus is genetically distinct from variola virus and its use in vaccines precludes vaccinees from developing or transmitting smallpox, while developing immunity to that disease.<sup>2</sup>

More than 95% of first-time vaccinees will develop detectable antibodies against smallpox disease. Smallpox vaccine efficacy has never been measured precisely in controlled trials but studies have shown a 91% to 97% reduction of disease among vaccinees who were later exposed to a smallpox patient in their household.<sup>2</sup>

Three to five days following vaccination with vaccinia, a lesion develops at the site of inoculation. Once healed, this lesion leaves a permanent scar at the immunization site. The lesion/scar is an indication that viral replication has taken place and that the vaccination was successful. In addition, vaccination can produce minor reactions in vaccinees, including vaccination site swelling and tenderness up to two to four weeks after the lesion has healed. Approximately 70% of children will experience at least one day of fever of 100 degrees Fahrenheit or more for 4 to 14 days following vaccination.<sup>2</sup>

The most frequent complication of smallpox vaccination is the transfer of vaccinia from the vaccination site to another part of the body, most commonly the face, eyelid, nose, mouth genitalia and rectum. Most of these lesions heal without specific treatment. Moderate and severe complications of smallpox vaccination also can occur. A localized or systemic dissemination of vaccinia may occur in persons with a history of eczema. One out of every 4,000 primary vaccinations will result in rash. Progressive vaccinia in immunocompromised individuals, that frequently results in death, occurs in one out of every 600,000 primary vaccinations. Post-vaccination encephalitis, occurring in one vaccinee per 80,000 primary vaccinations, will lead to death in 15% to 25% of affected vaccinees and permanent neurologic disease in 25% of affected vaccinees. Although fewer than 50 cases have been reported, fetal vaccinia infection can result in a stillbirth or death of the infant following delivery. Death among vaccinees occurs in one out of 1,000,000 primary vaccinations and one out of 4,000,000 revaccinations.<sup>2</sup>

Despite these complications, vaccination has successfully and safely been administered to persons of all ages. Before 1972, smallpox vaccination was recommended for all US children at one year of age. Routine vaccination in the US stopped in 1972. It is likely that the immune status of those who were vaccinated more than 29 years ago has waned; however, previously vaccinated persons would be expected to exhibit an accelerated immune response if re-vaccinated or exposed to the smallpox virus.<sup>5</sup>

Immunization post-exposure to smallpox has been shown to offer some protection against the disease. Studies in Pakistan and India have shown that cases of smallpox among household contacts

of smallpox patients who were vaccinated post-exposure were reduced by 91%. The lowest disease rates among these household contacts was found in those vaccinated less than seven days following exposure. Post-exposure vaccinees who did contract smallpox disease generally experienced a less severe form of disease.<sup>2</sup>

When this vaccine was routinely used in the US, complications associated with it were high. Potential adverse reactions included severe skin reactions, spread of the vaccine virus to other parts of the body and spread of the vaccine virus to other people. Rarely (about one case per 300,000 vaccinations), a vaccine-related brain infection occurred. During the US smallpox vaccination program, approximately seven to nine deaths per year were attributed to vaccination, with the highest risk for death in infants. Most of these infant deaths were attributed to postvaccination encephalitis.<sup>14</sup> Most primary vaccinations in the US were administered to children, so less is known about adverse events in adults.<sup>15</sup>

Vaccinia immune globulin (VIG) was once given following vaccination to protect those who needed vaccination but were at risk of experiencing vaccine-related complications. The Advisory Committee on Immunization Practices (ACIP) now recommends that VIG be reserved for treatment of vaccine complications with serious clinical manifestations. It has been estimated that if one million persons were vaccinated, as many as 250 would experience adverse reactions of the type that would require administration of VIG. Presently available supplies of VIG, also maintained by the CDC, are very limited in quantity. However, VIG can be obtained from the blood serum of persons one week following smallpox vaccinations. Therefore, VIG supply could be replenished with the reintroduction of smallpox vaccination.<sup>5</sup>

Transmission of vaccinia may occur when a recently vaccinated person has contact with a susceptible person. Among the participants of the CDC 10-state survey of complications of smallpox vaccination, the risk of transmission to contacts was 27 infections per one million total vaccinations; 44% of these contact cases occurred among children five years of age and younger.<sup>14</sup>

Such transmission is very dangerous when it involves individuals at high risk for developing severe reactions from the vaccine. These individuals include persons with eczema, the immunocompromised (including organ transplant recipients, HIV or AIDS patients and cancer patients) and pregnant women. A recent study has estimated that 15% of the US population would fall into one of these categories and therefore should not receive the smallpox vaccine. In addition, close contacts of these persons (another 10% of the US population) should also not receive the smallpox vaccine in order to avoid accidental transmission and subsequent severe reactions in the high risk persons.<sup>16</sup>

In the absence of a confirmed smallpox case and given the low risk of attack, smallpox vaccine has only been recommended for persons predesignated by the appropriate bioterrorism and public health authorities to conduct investigation and follow-up of initial smallpox cases as well as for healthcare personnel at risk of exposure to initial cases of smallpox in facilities that are predesignated to receive these patients.<sup>10</sup>

In the event that a smallpox outbreak would occur, smallpox vaccine is currently available and more vaccine doses are on their way. Approximately 15 million doses of vaccine were produced

by Wyeth Laboratories, Lancaster, PA in the 1970s and are currently stockpiled in the US.<sup>11</sup> A study evaluating the effectiveness of diluted smallpox vaccine found that these doses could be diluted significantly and still provide protection.<sup>12</sup> In addition, Aventis Pasteur has provided the government with 80 million doses of potent vaccine from their storage facilities. According to the CDC, enough smallpox vaccine will be available for everyone in the US by the end of 2002.<sup>13</sup>

### Safety Studies

- A recent study estimated that vaccinating all persons aged 1 to 65 years of age in the US would result in approximately 4,600 serious adverse events and 285 deaths. This estimation excluded all high-risk individuals and their contacts.<sup>16</sup>
- No randomized controlled clinical trials have been performed to evaluate how effective the smallpox vaccine was in preventing disease in patients who suffered smallpox vaccine complications. Smallpox vaccination protocols were developed based on data consisting of case series and anecdotal reports, as well

as controlled data suggesting that VIG may modify smallpox vaccine virus infection if administered at the same time as the vaccine.<sup>15</sup>

- Limited data support the efficacy of VIG in helping to prevent the development of smallpox following exposure to the disease. In a trial conducted in Madras, India, 705 family contacts of 208 smallpox patients were randomized to receive smallpox vaccine or smallpox vaccine plus VIG as soon as possible after the patient was admitted to the hospital. Smallpox developed in 5 of 326 contacts who received VIG compared with 21 of 379 controls, for a relative efficacy of 70% in preventing natural smallpox.<sup>15</sup>
- The potential for VIG to prevent post-vaccine encephalitis when administered with vaccine was studied among Dutch military recruits. More than 106,000 recruits received either VIG plus smallpox vaccine or placebo plus smallpox vaccine. Three cases of smallpox vaccine-associated encephalitis occurred in the VIG group compared with 13 cases of encephalitis in the placebo group.<sup>17</sup>

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## TYPHOID FEVER

### General Disease Information

Typhoid fever is an acute generalized infection that is caused by the bacterium *Salmonella typhi*. Severe forms of the disease are characterized by persistent high fever, abdominal discomfort, malaise and headache. Worldwide, an estimated 16 million cases of typhoid fever and 600,000 related deaths are reported.<sup>1</sup> Transmission of typhoid fever occurs in areas where sanitation is primitive and where water supplies are not treated. In such situations, human fecal material can contaminate water supplies.<sup>2</sup>

Prior to the introduction of antibiotics, this much-feared disease ran its course over several weeks and caused death in 10% to 20% of cases. But with the introduction of water treatment in the 20<sup>th</sup> century, the incidence of typhoid fever significantly decreased in large US cities. Typhoid fever remains endemic in most of the less-developed areas of the world, including parts of Africa, Asia and Latin America, where fecal contamination of water sources still occurs. This disease remains the main intestinal disease threat faced by children in developing countries after they have survived a plethora of diarrheal and dysenteric infections (all of which are not currently preventable by vaccines) during their first five years of life.<sup>2</sup>

### Risk-Benefit Analysis of Vaccination

The three populations that are at particularly high risk of developing typhoid fever are children in endemic areas, travelers and military personnel from industrialized countries who visit endemic areas in developing countries and clinical microbiology technicians.<sup>2</sup> Between 1992 and 1994, an estimated 2.6 cases of typhoid fever per one million US international travelers were reported. However, since 1990, *Salmonella typhi* in Asia and northeast Africa have increasingly been resistant to many clinically relevant antibiotics.<sup>2</sup> The two typhoid fever vaccines licensed for use in the US (Vi polysaccharide and Ty21a typhoid fever vaccines) provide protection against disease in 50% to 80% of vaccinees.<sup>1</sup>

Local reactions are the most frequently reported adverse reactions for the Vi polysaccharide typhoid fever vaccine. Fever has been reported in up to 1% and headache in up to 3% of vaccinees. The side effects of the Ty21a typhoid fever vaccine are rare and consist mainly of abdominal discomfort, nausea, vomiting and rash. Up to 5% of vaccinees have reported fever and headache.<sup>1</sup>

### Safety Studies

- Controlled Phase II trials in US adults reported local reactions, including pain and tenderness at the injection site as the most common adverse events of the Vi polysaccharide vaccine.<sup>3-4</sup>
- Rates of adverse reactions in the vaccine recipients of three studies assessing the safety of the Ty21a typhoid fever vaccine were not significantly higher than those for the placebo group for any sign or symptom.<sup>5-7</sup>
- Large-scale field trials of 550,000 school children in Chile and 32,000 in Egypt as well as 32,000 persons ages three years to adulthood in Indonesia using Ty21a typhoid vaccine have not identified any vaccine-related adverse reactions.<sup>7-12</sup>

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## GLOSSARY TERMS

Acute	Placebo
Adverse events	Polysaccharide
Antibiotic	Polysaccharide vaccine
Cases	Risk
Disease	<i>Salmonella typhi</i>
Dysenteric infections	Typhoid fever
Endemic	Vaccine
Malaise	Vaccinees

## WEB RESOURCES

**Division of Bacterial and Mycotic Diseases**  
[http://www.cdc.gov/ncidod/dbmd/diseaseinfo/typhoidfever\\_g.htm](http://www.cdc.gov/ncidod/dbmd/diseaseinfo/typhoidfever_g.htm)

**National Center for Infectious Diseases**  
<http://www.cdc.gov/travel/diseases/typhoid.htm>

### VACCINE MANUFACTURERS:

**Aventis Pasteur**  
<http://www.aventispasteur.com>

**Berna Products**  
<http://www.bernaproducts.com>

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## YELLOW FEVER

### General Disease Information

Yellow fever is a disease caused by a RNA virus transmitted to humans by mosquitoes or ticks.<sup>1</sup> The severity of this disease ranges from flu-like symptoms to severe hepatitis and hemorrhagic fever.<sup>2</sup> This disease kills an estimated 30,000 people per year and occurs only in sub-Saharan Africa, where the majority of cases are reported, and in tropical South America.<sup>2,3</sup> In Africa, 23% of yellow fever cases in infants and children will result in death. But in South America, cases occur primarily in young men and approximately 65% of cases die.<sup>1</sup>

Although yellow fever has rarely occurred in travelers, the disease has caused serious, life-threatening infections in unvaccinated international travelers.<sup>4</sup> In March 2002, a previously healthy, unvaccinated Texan died from yellow fever disease he contracted during a fishing trip in Brazil. During his trip, this 47 year-old man slept aboard an air-conditioned fishing boat and wore DEET insecticide-impregnated clothing while fishing.<sup>5</sup>

### Risk-Benefit Analysis of Vaccination

Vaccination is the most efficient preventive measure against this disease, and the yellow fever vaccine is highly effective.<sup>1,4</sup> Some researchers believe that the risk of unvaccinated travelers developing yellow fever is probably increasing because potential yellow fever transmission zones are expanding to include urban areas with large populations of susceptible humans and abundant mosquitoes that can transmit the disease.<sup>6</sup>

No placebo-controlled trial has ever been performed to assess adverse reactions associated with this vaccine.<sup>1</sup> However, reported reactions to the yellow fever vaccine have been generally mild. Up to 5% of persons vaccinated against yellow fever have mild headaches, muscle pain, low-grade fevers or other minor symptoms for five to 10 days.<sup>7</sup> A review of reports submitted to the Vaccine Adverse Events Reporting System (VAERS) in the US from 1990 to 1997 found that anaphylaxis characterized by rash, hives and/or asthma, is uncommon after yellow fever vaccination, and occurs at a rate of one per 131,000 vaccine doses (this adverse event occurred principally among persons with histories of egg allergy<sup>6</sup>).<sup>8</sup> Of an estimated 54 million doses of vaccine that were administered in Brazil from 1996 through 2001, only two cases of serious adverse events were reported.<sup>3</sup> However, at the June 2001 meeting of the Advisory Committee on Immunization Practices (ACIP), seven cases of multiple organ system failure in recipients of the yellow fever vaccine between 1996-2001 were discussed. All seven persons became ill within two to five days of vaccination and required intensive care; six died.<sup>6</sup>

### Safety Studies

- A study utilizing VAERS data found that the rate of reported adverse events following yellow fever vaccination among elderly persons was higher than among persons 25 to 44 years of age. The rate of systemic illness requiring hospitalization or leading to death after yellow fever vaccination was 3.5 per 100,000 among people 65 to 75 years of age and 9.1 per 100,000 for people 75 years of age and older.<sup>4</sup>
- Reactogenicity to yellow fever vaccine was monitored in 10 clinical trials conducted between 1953 and 1994. Self-limited and mild local reactions and systemic reactions (headache, headache and fever, and fever without symptoms) occurred in a minority of subjects five to seven days after immunization.<sup>1</sup>

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## GLOSSARY TERMS

Adverse events	Immunization
Advisory Committee on Immunization Practices	Placebo
Allergy	Reactogenicity
Anaphylaxis	Ribonucleic acid
Asthma	Risk
Cases	Systemic
Clinical trials	Vaccine
DEET	Vaccine Adverse Events Reporting System
Disease	Virus
Hemorrhagic fever	Yellow fever
Hepatitis	

## ACRONYMS

ACIP	Advisory Committee on Immunization Practices
DEET	N,N-diethyl-m-toluamide
RNA	Ribonucleic acid
VAERS	Vaccine Adverse Events Reporting System

## WEB RESOURCES

### Advisory Committee on Immunization Practices Recommendations

<http://www.cdc.gov/epo/mmwr/preview/mmwrhtml/00001620.htm>

### Division of Vector-Borne Infectious Diseases

<http://www.cdc.gov/ncidod/dvbid/yellowfever/index.htm>

### National Center for Infectious Diseases

<http://www.cdc.gov/travel/yelfever.htm>

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#### Aventis Pasteur

<http://www.aventispasteur.com>

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