Understanding
VACCINES
What They Are How They Work

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health
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Introduction

Vaccines are crucial to maintaining public health: They are a safe, cost-effective, and efficient way to prevent sickness and death from infectious diseases. Vaccines have led to some of the greatest public health triumphs ever, including the eradication of naturally occurring smallpox from the globe and the near eradication of polio.

This booklet contains general information about vaccines

- What they are
- How they prevent disease
- How they are made and tested
- What vaccine research might achieve in the future
What Is a Vaccine?

Chances are you never had diphtheria. You probably don’t know anyone who has suffered from this disease, either. In fact, you may not know what diphtheria is, exactly. (To find out, see “Diphtheria: Remembering an Old Disease” on page 3.) Similarly, diseases like whooping cough (pertussis), measles, mumps, and German measles (rubella) may be unfamiliar to you. In the 19th and early 20th centuries, these illnesses struck hundreds of thousands of people in the United States each year, mostly children, and tens of thousands of people died. The names of these diseases were frightening household words. Today, they are all but forgotten. That change happened largely because of vaccines.

Chances are you’ve been vaccinated against diphtheria. You even may have been exposed to the bacterium that causes it, but the vaccine prepared your body to fight off the disease so quickly that you were unaware of the infection.

Vaccines take advantage of your body’s natural ability to learn how to eliminate almost any disease-causing germ, or microbe, that attacks it. What’s more, your body “remembers” how to protect itself from the microbes it has encountered before. Collectively, the parts of your body that recall and repel microbes are called the immune system. (We’ll take a closer look at the immune system in the section “How Vaccines Work” on page 11.) Without the immune system, the simplest illness—even the common cold—could quickly turn deadly. On average,

Note: Words in bold are defined in the glossary at the end of this booklet.
your immune system takes more than a week to learn how to fight off an unfamiliar microbe. Sometimes that isn’t soon enough. Stronger microbes can spread through your body faster than the immune system can fend them off. Your body often gains the upper hand after a few weeks, but in the meantime you are sick. Certain microbes are so powerful, or virulent, that they can overwhelm or escape your body’s natural defenses. In those situations, vaccines can make all the difference.

Traditional vaccines contain either parts of microbes or whole microbes that have been killed or weakened so that they don’t cause disease. When your immune system confronts these harmless versions of the germs, it quickly clears them from your body. In other words, vaccines trick your immune system but at the same time teach your body important lessons about how to defeat its opponents.

In 1900, diphtheria killed more people in the United States than cancer did. Caused by the toxic bacterium Corynebacterium diphtheriae, this upper airway infection often results in a grayish, thick membrane that grows in the throat and obstructs breathing. Other symptoms include fever, hoarseness, and coughing. Most diphtheria deaths resulted not from blocked airways but from the paralyzing toxin the bacterium secretes, which can cause the heart or other organs to fail. During the 1990s, on average, only three diphtheria cases among U.S. residents were reported each year.
Vaccine Benefits

You and Your Community

Once your immune system is trained to resist a disease, you are said to be immune to it. Before vaccines, the only way to become immune to a disease was to actually get it and, with luck, survive it. This is called naturally acquired immunity. With naturally acquired immunity, you suffer the symptoms of the disease and also risk the complications, which can be quite serious or even deadly. In addition, during certain stages of the illness, you may be contagious and pass the disease to family members, friends, or others who come into contact with you.

Vaccines, which provide artificially acquired immunity, are an easier and less risky way to become immune. Vaccines can prevent a disease from occurring in the first place, rather than attempt a cure after the fact. It is much cheaper to prevent a disease than to treat it. According to one U.S. analysis, for every dollar spent on the measles/mumps/rubella vaccine, 21 dollars are saved.

Vaccines protect not only yourself but also others around you. If your vaccine-primed immune system stops an illness before it starts, you will be contagious for a much shorter period of time, or perhaps not at all. Similarly, when other people are vaccinated, they are less likely to give the disease to you. So vaccines protect not only individuals, but entire communities. That is why vaccines are vital to the public health goal of preventing diseases.
If a critical number of people within a community are vaccinated against a particular illness, the entire group becomes less likely to get the disease. This protection is called community immunity, or herd immunity.

On the other hand, if too many people in a community do not get vaccinations, diseases can reappear. In 1974, the Japanese government stopped vaccinating against pertussis because of public concern about the vaccine’s safety and because no one had died from the disease the previous year. Five years later, a pertussis epidemic in Japan sickened 13,000 people and killed 41.

In 1989, low vaccination rates allowed a measles outbreak to occur in the United States. The outbreak resulted in more than 55,000 cases of measles and 136 measles-associated deaths.

**Passive Immunity** is another way to gain some protection against disease. It is immunity transferred from one person to another. Babies, for example, gain passive immunity to some diseases from the antibodies that are passed to them from their mothers before birth or through breastfeeding. This kind of immunity lasts only a few weeks or months. Another form of passive immunity is generated by giving a person purified blood serum, which contains the antibodies produced after someone successfully fights off an illness. In 2003, researchers began a clinical trial in the United States to test whether antibodies against West Nile virus can be used to treat people who suffer from the most severe form of this mosquito-borne illness. (In that trial, passive immunity is used to treat infection, rather than prevent it.)
Harmful Microbes

Vaccines protect against infectious diseases caused by microbes—organisms too small to see without a microscope. Many microbes, such as bacteria, are made up of only one cell. Viruses, mere snippets of genetic material packed inside a membrane or a protein shell, are even smaller.

Humans evolved an immune system because the world is teeming with these organisms. Many of them don’t bother us; the bacteria that normally live in your digestive tract are, in fact, beneficial. But other microbes break into and take up residence in your body, using your warmth, nutrients, and tissues to survive and reproduce—and doing you great harm in the process.

A few examples of the most serious disease-causing microbes for which vaccines have proved highly effective include the following.

- Variola virus, which causes smallpox, was once the scourge of the world. This virus passes from person to person through the air. A smallpox infection results in fever, severe aches and pains, scarring sores that cover the body, blindness in many cases, and, often, death. In the 18th century, variola virus killed every 7th child born in Russia and every 10th child born in Sweden and France.
Although vaccination and outbreak control had eliminated smallpox in the United States by 1949, the disease still struck an estimated 50 million people worldwide each year during the 1950s. In 1967, that figure fell to 10 to 15 million because of vaccination. That same year, the World Health Organization (WHO) launched a massive vaccination campaign to rid the world of smallpox—and succeeded. The last case of naturally occurring smallpox was in Somalia in 1977.

- The highly infectious poliovirus, the cause of polio, once crippled 13,000 to 20,000 people every year in the United States. In 1954, the year before the first polio vaccine was introduced, doctors reported more than 18,000 cases of paralyzing polio in the United States. Just 3 years later, vaccination brought that figure down to about 2,500. Today, the disease has been eliminated from the Western Hemisphere, and public health officials hope to soon eradicate it from the globe. In 2006, 2,000 cases of polio were reported worldwide, according to WHO.
• The toxic bacterium *Bordetella pertussis* likes to set up home in the human respiratory tract, where it causes whooping cough, also known as pertussis. The wracking coughs characteristic of this disease are sometimes so intense, the victims, usually infants, vomit or turn blue from lack of air. Before scientists created a vaccine against the bacterium, 115,000 to 270,000 people suffered from whooping cough each year in the United States; 5,000 to 10,000 of those died from it. After the vaccine was introduced in the United States in the 1940s, the number of pertussis cases declined dramatically, hitting a low of about 1,000 in 1976. More recently, the annual number of reported cases of pertussis in the United States has been rising from 9,771 in 2002 to 25,616 in 2005. The reasons for the increase are complex. The disease strikes in cycles, and the immunity provided by the vaccine wanes over time, leaving some people susceptible in their teen years and as adults.

Other familiar diseases that vaccines protect against include chickenpox, hepatitis A, hepatitis B, and *Haemophilus influenzae type b* (*Hib*). Hib causes meningitis, an inflammation of the fluid-filled membranes that surround the brain and spinal cord. Meningitis can be fatal, or it can cause severe disabilities such as deafness or mental retardation. This disease has nearly disappeared among babies and children in the United States since the Hib vaccine became widely used in 1989.
Newer vaccines include one to prevent the painful condition called shingles, which can strike anyone who has ever had chickenpox; a vaccine against human papillomavirus, which can cause cervical cancer; and a vaccine against rotavirus, which causes severe diarrheal disease and some 600,000 deaths in children worldwide every year.
What Do Cows Have to Do with Vaccines?

The word “vaccine” comes from the Latin word *vaccinus*, which means “pertaining to cows.” What do cows have to do with vaccines? The first vaccine was based on the relatively mild cowpox virus, which infected cows as well as people. This vaccine protected people against the related, but much more dangerous, smallpox virus.

More than 200 years ago, Edward Jenner, a country physician practicing in England, noticed that milkmaids rarely suffered from smallpox. The milkmaids often did get cowpox, a related but far less serious disease, and those who did never became ill with smallpox. In an experiment that laid the foundation for modern vaccines, Jenner took a few drops of fluid from a skin sore of a woman who had cowpox and injected the fluid into the arm of a healthy young boy who had never had cowpox or smallpox. Six weeks later, Jenner injected the boy with fluid from a smallpox sore, but the boy remained free of smallpox.

Dr. Jenner had discovered one of the fundamental principles of immunization. He had used a relatively harmless foreign substance to evoke an immune response that protected someone from an infectious disease. His discovery would ease the suffering of people around the world and eventually lead to the elimination of smallpox, a disease that killed a million people, mostly children, each year in Europe. By the beginning of the 20th century, vaccines were in use for diseases that had nothing to do with cows—rabies, diphtheria, typhoid fever, and plague—but the name stuck.
How Vaccines Work

The Immune System

To understand how vaccines teach your body to fight infection, let’s first look at how the immune system fends off and learns from a naturally occurring infection. Then we’ll examine how vaccines mimic this process.

Imagine you are a dock worker on the piers of Philadelphia. The year is 1793. As you are unloading crates of tea and spices from an oceangoing ship, a mosquito bites you on the arm. This mosquito carries the virus that causes yellow fever, which the mosquito picked up when it bit a sailor who recently returned from Africa. So now you have thousands of yellow fever viruses swarming into your body. In fact, you have become part of an infamous epidemic that will claim the lives of 10 percent of the people in Philadelphia, and all that stands between you and a fatal case of yellow fever is your immune system.

Your immune system is a complex network of cells and organs that evolved to fight off infectious microbes. Much of the immune system’s work is carried out by an army of various specialized cells, each type designed to fight disease in a particular way. The invading viruses first run into the vanguard of this army, which includes big and tough patrolling white blood cells called macrophages (literally, “big eaters”). The macrophages grab onto and gobble up as many of the viruses as they can, engulfing them into their blob-like bodies.
A mosquito bite transmits the yellow fever virus to an unsuspecting dock worker. In 1793, a yellow fever epidemic claimed the lives of 10 percent of Philadelphians.

How do the macrophages recognize the yellow fever virus? All cells and microbes wear a “uniform” made up of molecules that cover their surfaces. Each of your cells displays marker molecules unique to you. The yellow fever viruses display different marker molecules unique to them. The macrophages and other cells of your immune system use these markers to distinguish among the cells that are part of your body, harmless bacteria that reside in your body, and harmful invading microbes that need to be destroyed.
The molecules on a microbe that identify it as foreign and stimulate the immune system to attack it are called **antigens**. Every microbe carries its own unique set of antigens, and, as we will see, they are central to creating vaccines.

**Antigens Sound the Alarm**

The macrophages digest most parts of the yellow fever viruses but save the antigens and carry them back to the immune system’s base camps, also known as **lymph nodes**. Lymph nodes, bean-sized organs scattered throughout your body, are where immune system cells congregate. In these nodes, macrophages sound the alarm by “regurgitating” the antigens, displaying them on their surfaces so other cells can recognize them. In this particular case, the macrophages will show the yellow fever antigens to specialized defensive white blood cells called **lymphocytes**, spurring them to swing into action.

By this time, about 3 days after the mosquito bite, you are feeling feverish and have a headache. You decide to stay home from work.

**Lymphocytes: T Cells and B Cells**

There are two major kinds of lymphocytes, **T cells** and **B cells**, and they do their own jobs in fighting off your yellow fever. T cells and B cells head up the two main divisions of the immune system army.
T Cells
T cells function either offensively or defensively. The offensive T cells don’t attack the virus directly, but they use chemical weapons to eliminate the cells of your body already infected with the yellow fever virus. (See “How Viruses Work,” page 20.) Because they have been “programmed” by their exposure to the virus antigen, these cytotoxic T cells, also called killer T cells, can “sense” diseased cells that are harboring the yellow fever virus. The killer T cells latch onto these cells and release chemicals that destroy the infected cells and the viruses inside. The defensive T cells, also called helper T cells, defend the body by secreting chemical signals that direct the activity of other immune system cells. Helper T cells assist in activating killer T cells, and helper T cells also stimulate and work closely with B cells.

The work done by T cells is called your cellular or cell-mediated immune response.

B Cells
B cells are like weapons factories. They make and secrete extremely important molecular weapons called antibodies. Antibodies usually work by first grabbing onto the microbe’s antigen, and then sticking to and coating the microbe. Antibodies and antigens fit together like pieces of a jigsaw puzzle—if their shapes are compatible, they bind to each other.
Each antibody can usually fit with only one antigen. So your immune system keeps a supply of millions and possibly billions of different antibodies on hand to be prepared for any foreign invader. Your immune system does this by constantly creating millions of new B cells. About 50 million B cells circulate in each teaspoonful of your blood, and almost every B cell—through random genetic shuffling—produces a unique antibody that it displays on its surface.

Before you contracted yellow fever, somewhere in your body B cells were probably circulating with antibodies that, purely by chance, matched antigens from the yellow fever virus. When these B cells came into contact with their matching yellow fever antigen, they were stimulated to divide into many larger cells called plasma cells that secreted mass quantities of antibodies to yellow fever virus.

**Antibodies in Action**

The antibodies secreted by B cells circulate throughout your body until they run into the yellow fever virus. Antibodies attack the viruses that have not yet infected any cells but are lurking in the blood or the spaces between cells. When antibodies gather on the surface of a microbe, it is bad news for the microbe. The microbe becomes generally bogged down, gummed up, and unable to function. Antibodies also signal macrophages and other defensive cells to come eat the microbe. Antibodies are like big, bright signs stuck to a microbe saying, “Hey, get rid of this!” Antibodies also work with other defensive molecules that circulate in the blood, called complement proteins, to destroy microbes.
Your immune system is a complex network of cells and organs. Cells called macrophages gobble up the invading virus and sound the alarm by showing pieces of the invader to T cells and B cells. B cells produce defensive molecules called antibodies that “stick” to the virus.

The work of B cells is called the **humoral immune response**, or simply the antibody response. The goal of most vaccines is to stimulate this response. In fact, many infectious microbes can be defeated by antibodies alone, without any help from killer T cells.

**Clearing the Infection: Memory Cells and Natural Immunity**

While your immune system works to rid your body of yellow fever, you feel awful. You lie in bed, too dizzy and weak even to sit up. During the next several days, your skin becomes yellow (or jaundiced) and covered with purple spots. You vomit blood. Your doctor looks grim and tired: He knows that as many as 20 percent of people who contract yellow fever die, and the epidemic is spreading fast through the city.
You are one of the lucky ones, though. After about a week, your immune system gains the upper hand. Your T cells and antibodies begin to eliminate the virus faster than it can reproduce. Gradually, the virus disappears from your body, and you feel better. You get out of bed. Eventually, you go back to working the docks.

If you are ever bitten by another mosquito carrying the yellow fever virus, you won’t get the disease again. You won’t even feel slightly sick. You have become immune to yellow fever because of another kind of immune system cell: memory cells. After your body eliminated the disease, some of your yellow-fever-fighting B cells and T cells converted into memory cells. These cells will circulate through your body for the rest of your life, ever watchful for a return of their enemy. Memory B cells can quickly divide into plasma cells and make more yellow
fever antibody if needed. Memory T cells can divide and grow into a yellow-fever-fighting army. If that virus shows up in your body again, your immune system will act swiftly to stop the infection.

**How Vaccines Mimic Infection**

Vaccines teach your immune system by mimicking a natural infection. To show how, let’s jump ahead to the 21st century. Yellow fever is no longer a problem in the United States, but you are a relief worker stationed in a part of the world where the disease still occurs, and the Centers for Disease Control and Prevention (CDC) recommends vaccination prior to your departure.

The yellow fever vaccine, first widely used in 1938, contains a weakened form of the virus that doesn’t cause disease or reproduce very well. (More on how vaccine makers create vaccines a little later.) This vaccine is injected into your arm. Your macrophages can’t tell that the vaccine viruses are duds, so they gobble up the viruses as if they were dangerous, and in the lymph nodes, the macrophages present yellow fever antigen to T cells and B cells. The alarm is sounded, and your immune system swings into action. Yellow-fever-specific T cells rush out to meet the foe. B cells secrete yellow fever antibodies. But the battle is over quickly. The weakened
viruses in the vaccine can’t put up much of a fight. The mock infection is cleared, and you are left with a supply of memory T and B cells to protect you against yellow fever, should a mosquito carrying the virus ever bite you.

Next, we’ll take a closer look at different types of vaccines—not all of them employ killed or weakened microbes—and learn how each type works.
Viruses such as the yellow fever virus are tiny microbes made up of a small number of genes encased in a membrane or protein shell. If you were the size of a cell, a virus would look like a burr (a small, round object covered with tiny bristles) attached to your pants leg.

Like burrs, viruses stick to cells. Then they inject their genetic material inside the cells. Once inside, the virus genes take over the cells' resources and molecular machinery, forcing the cells to make more viruses. The newly formed viruses “bud”—or are released from the surface of the cells and drift off to infect new cells. Cells infected with viruses can't function properly and usually die. Many are eliminated by killer T cells.
Different Types of Vaccines

Imagine that a new infectious disease emerges somewhere in the world and begins to spread around the globe. The infectious agent jumps easily from person to person through the air, and it attacks the lungs, causing terrible coughing, fever, pneumonia, and sometimes paralysis of the respiratory system. Scientists quickly determine that disease X is caused by a new species of toxic bacterium. They call it “bacterium X.” Unfortunately, bacterium X is difficult to fight because it resists most antibiotics, the kind of drug used to treat bacterial infections.

Everyone agrees a vaccine against bacterium X is needed, but how would scientists go about creating one? First, researchers would carefully study bacterium X. They would figure out what nutrients it requires. They would examine how it damages lung tissue. Geneticists would analyze bacterium X’s genes. Immunologists would explore how the immune system responds to bacterium X and why the body sometimes fails to fight off this microbe. They would identify antigens from X that best stimulate the immune system. Other scientists would discover and study the toxin secreted by bacterium X.

Once scientists had some basic information about bacterium X, they could begin designing vaccines that might work against it. Following are some of the options that researchers might pursue. They will give you an idea of the main types of vaccine strategies. (This imaginary new disease is caused by a bacterium, but scientists would use approaches similar to those outlined below to develop a vaccine against a new virus.)
Live, Attenuated Vaccines

Some scientists might explore the possibility of developing a live, attenuated vaccine against X. These vaccines contain a version of the living microbe that has been weakened in the lab so it can’t cause disease. This weakening of the organism is called attenuation. Because a live, attenuated vaccine is the closest thing to a natural infection, these vaccines are good “teachers” of the immune system: They elicit strong cellular and antibody responses, and often confer lifelong immunity with only one or two doses.

Despite the advantages of live, attenuated vaccines, there are some downsides. It is the nature of living things to change, or mutate, and the organisms used in live, attenuated vaccines are no different. The remote possibility exists that the attenuated bacteria X in the vaccine could revert to a virulent form and cause disease. Also, not everyone can safely receive live, attenuated vaccines. For their own protection, people who have damaged or weakened immune systems—because they’ve undergone chemotherapy or have HIV, for example—cannot be given live vaccines.

Another limitation is that live, attenuated vaccines usually need to be refrigerated to stay potent. If the X vaccine needs to be shipped overseas and stored by health care workers in developing countries that lack widespread refrigeration, a live vaccine may not be the best choice.

Live, attenuated vaccines are relatively easy to create for certain viruses. Vaccines against measles, mumps, and chickenpox, for example, are made by this method.
Live, attenuated vaccines use a weakened version of the microbe that has been changed to reduce or eliminate its potential to cause disease. This image shows the live microbe’s antigens, membrane, and genetic material.

Viruses are simple microbes containing a small number of genes, and scientists can therefore more readily control their characteristics. Viruses often are attenuated through a method of growing generations of them in cells in which they do not reproduce very well. This hostile environment takes the fight out of viruses: As they evolve to adapt to the new environment, they become weaker with respect to their natural host, human beings.

Live, attenuated vaccines are more difficult to create for bacteria. Bacteria have thousands of genes and thus are much harder to control. Scientists working on a live vaccine for bacterium X, however, might be able to use recombinant DNA technology to remove several key genes from X. This approach has been used to create a vaccine against the bacterium that causes cholera, *Vibrio cholerae*, although the live cholera vaccine has not been licensed in the United States.
Inactivated Vaccines

An inactivated vaccine, or killed vaccine, might be better for bacterium X. Scientists produce inactivated vaccines by killing the disease-causing microbe with chemicals, heat, or radiation. Such vaccines are more stable and safer than live vaccines: The dead microbes can’t mutate back to their disease-causing state. Inactivated vaccines usually don’t require refrigeration, and they can be easily stored and transported in a freeze-dried form, which makes them accessible to people in developing countries.

Most inactivated vaccines, however, stimulate a weaker immune system response than do live vaccines. So it would likely take several additional doses, or booster shots, to maintain a person’s immunity to bacterium X. This quality could be a drawback in areas where people don’t have regular access to health care and can’t get booster shots on time.

Inactivated or killed vaccines contain microbes that have been inactivated with chemicals, heat, or radiation. The microbe’s antigens, membrane, and genetic material are still present.
Subunit Vaccines

Scientists would certainly look into the possibility of a subunit vaccine for X. Instead of the entire microbe, subunit vaccines include only the antigens that best stimulate the immune system. In some cases, these vaccines use epitopes—the very specific parts of the antigen that antibodies or T cells recognize and bind to. Because subunit vaccines contain only the essential antigens and not all the other molecules that make up the microbe, the chances of adverse reactions to the vaccine are lower.

Subunit vaccines can contain anywhere from 1 to 20 or more antigens. Of course, identifying which antigens from bacterium X best stimulate the immune system would be a tricky, time-consuming process. Once scientists did that, however, they could make subunit vaccines against X in one of two ways. They could grow bacterium X in the laboratory, and then use chemicals to break the bacteria apart and gather the important antigens.

Subunit vaccines contain just the antigens of the microbe that best stimulate the immune system. This image depicts antigens that have been separated from the rest of the microbe for use in a subunit vaccine.
They also could manufacture the antigen molecules from X using recombinant DNA technology. Vaccines produced this way are called **recombinant subunit vaccines**. Such a vaccine has been made for the hepatitis B virus. Scientists inserted hepatitis B genes that code for important antigens into common baker’s yeast. The yeast then produced the antigens, which the scientists collected and purified for use in the vaccine. Research is also continuing on a recombinant subunit vaccine against hepatitis C virus.

**Toxoid Vaccines**

Because our imaginary bacterium X secretes a toxin, or harmful chemical, a **toxoid vaccine** might work against it. These vaccines are used when a bacterial toxin is the main cause of illness. Scientists have found they can inactivate toxins by treating them with **formalin**, a solution of formaldehyde and sterilized water. Such “detoxified” toxins, called **toxoids**, are safe for use in vaccines.
When the immune system receives a vaccine containing a harmless toxoid, it learns how to fight off the natural toxin. The immune system produces antibodies that lock onto and block the toxin. Vaccines against diphtheria and tetanus are examples of toxoid vaccines.

**Conjugate Vaccines**

If bacterium X possessed an outer coating of sugar molecules called polysaccharides, as many harmful bacteria do, researchers would try making a conjugate vaccine for X. Polysaccharide coatings disguise a bacterium’s antigens so that the immature immune systems of infants and younger children can’t recognize or respond to them. Conjugate vaccines, a special type of subunit vaccine, get around this problem.
When making a conjugate vaccine, scientists link antigens or toxoids from a microbe that an infant’s immune system can recognize to the polysaccharides. The linkage helps the immature immune system react to polysaccharide coatings and defend against the disease-causing bacterium.

The vaccine that protects against Hib is a conjugate vaccine.

**DNA Vaccines**

Once the genes from bacterium X had been analyzed, scientists could attempt to create a **DNA vaccine** against it.

Still in the experimental stages, these vaccines show great promise, and several types are being tested in humans. DNA vaccines take immunization to a new technological level. These vaccines dispense with both the whole organism and its parts and get right down to the essentials: the microbe’s genetic material. In particular, DNA vaccines use the genes that code for those all-important antigens.
Researchers have found that when the genes for a microbe’s antigens are introduced into the body, some cells will take up that DNA. The DNA then instructs those cells to make the antigen molecules. The cells secrete the antigens and display them on their surfaces. In other words, the body’s own cells become vaccine-making factories, creating the antigens necessary to stimulate the immune system. A DNA vaccine against X would evoke a strong antibody response to the free-floating X antigen secreted by cells, and the vaccine also would stimulate a strong cellular response against the X antigens displayed on cell surfaces. The DNA vaccine couldn’t cause the disease because it wouldn’t contain bacterium X, just copies of a few of its genes. In addition, DNA vaccines are relatively easy and inexpensive to design and produce.

*DNA vaccines use a microbe’s genetic material, in particular, the genes that code for important antigens. The DNA in these vaccines is a circular form known as a plasmid.*
So-called naked DNA vaccines consist of DNA that is administered directly into the body. These vaccines can be administered with a needle and syringe or with a needle-less device that uses high-pressure gas to shoot microscopic gold particles coated with DNA directly into cells. Sometimes, the DNA is mixed with molecules that facilitate its uptake by the body’s cells. Naked DNA vaccines being tested in humans include those against the viruses that cause influenza and herpes as well as HIV.

Recombinant Vector Vaccines

Recombinant vector vaccines could be another possible strategy against bacterium X. These experimental vaccines are similar to DNA vaccines, but they use an attenuated virus or bacterium to introduce microbial DNA to cells of the body. Vector refers to the virus or bacterium used as the carrier.
In nature, viruses latch on to cells and inject their genetic material into them. (See “How Viruses Work” on page 20.) In the lab, scientists have taken advantage of this process. They have figured out how to take the roomy genomes of certain harmless or attenuated viruses and insert portions of the genetic material from other microbes into them. The carrier viruses then ferry that microbial DNA to cells. Recombinant vector vaccines closely mimic a natural infection and therefore do a good job of stimulating the immune system.

Attenuated bacteria also can be used as vectors. In this case, the inserted genetic material causes the bacteria to display the antigens of other microbes on its surface. In effect, the harmless bacterium mimics a harmful microbe, provoking an immune response.

Researchers are working on both bacterial and viral-based recombinant vector vaccines for HIV, rabies, and measles.

**Many Vaccines Against Bacterium X?**

The search for a vaccine against bacterium X would likely result in several promising candidate vaccines. (Researchers working on an HIV vaccine, for example, have developed dozens of experimental vaccines at various stages of testing, including subunit vaccines, DNA vaccines, and recombinant vector vaccines.) But because of the rigorous research and testing each vaccine must go through, it would take years, possibly decades, before an X vaccine was approved for use in the United States. In “Making Safe Vaccines” on page 38, we’ll take a closer look at how vaccines are tested and regulated.
Vaccine Strategies

One promising, but still experimental, approach to vaccination is the prime-boost strategy. This strategy involves two vaccines. The first (frequently a DNA vaccine) is given to prepare (“prime”) the immune system. Next, this response is boosted through the administration of a second vaccine (such as a viral-based vector vaccine). Several prime-boost HIV vaccine candidates are being tested in humans.

Some vaccines come in combinations. You might be familiar with the DTP (diphtheria, tetanus, pertussis) and the MMR (measles, mumps, rubella) vaccines that children in the United States receive.

Combination vaccines reduce visits to the doctor, saving time and money and sparing children extra needlesticks. Without combination vaccines, parents would have to bring their children in for each vaccination and all its boosters, and the chances would be greater that kids would miss their shots. Missed shots put children, as well as their communities, at risk.

Some people have wondered whether combination vaccines might overwhelm or weaken a child’s immune system, but the immune system contains billions of circulating B and T cells capable of responding to millions of different antigens at once. Because the body constantly replenishes these cells, a healthy immune system cannot be “used up” or weakened by a vaccine. According to one published estimate, infants could easily handle 10,000 vaccines at once.

For more sources of information on this topic, see “Vaccine Concerns, Myths, and Safety Issues on the Web” on page 42.
An adjuvant is an ingredient added to a vaccine to improve the immune response it produces. Currently, the only adjuvant licensed for human use in the United States is an “alum” adjuvant, which is composed of aluminum salts. Adjuvants do a variety of things; they can bind to the antigens in the vaccine, help keep antigens at the site of injection, and help deliver antigens to the lymph nodes, where immune responses to the antigens are initiated. The slowed release of antigens to tissue around the injection site and the improved delivery of antigens to the lymph nodes can produce a stronger antibody response than can the antigen alone. Alum adjuvants are also taken up by cells such as macrophages and help these cells better present antigens to lymphocytes.

Scientists are trying to develop new and better adjuvants. One oil-based adjuvant, MF59, has been used in seasonal influenza vaccines already available in Europe. Other adjuvants under study include tiny spheres made of fatty molecules that carry the vaccine’s antigen, and inert nanobeads that can be coated with antigen.

In addition to adjuvants, vaccines may contain antibiotics to prevent bacterial contamination during manufacturing, preservatives to keep multidose vials of vaccine sterile after they are opened, or stabilizers to maintain a vaccine’s potency at less-than-optimal temperatures.
### Some Vaccine Types and Diseases They Protect Against

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<th>Vaccine Type</th>
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<td>Live, attenuated vaccines</td>
<td>Measles, mumps, rubella, polio (Sabin vaccine), yellow fever</td>
</tr>
<tr>
<td>Inactivated or “killed” vaccines</td>
<td>Cholera, flu, hepatitis A, Japanese encephalitis, plague, polio (Salk vaccine), rabies</td>
</tr>
<tr>
<td>Toxoid vaccine</td>
<td>Diphtheria, tetanus</td>
</tr>
<tr>
<td>Subunit vaccines</td>
<td>Hepatitis B, pertussis, pneumonia caused by <em>Streptococcus pneumoniae</em></td>
</tr>
<tr>
<td>Conjugate vaccines</td>
<td><em>Haemophilus influenzae</em> type b, pneumonia caused by <em>Streptococcus pneumoniae</em></td>
</tr>
<tr>
<td>DNA vaccines</td>
<td>In clinical testing</td>
</tr>
<tr>
<td>Recombinant vector vaccines</td>
<td>In clinical testing</td>
</tr>
<tr>
<td>Advantages</td>
<td>Disadvantages</td>
</tr>
<tr>
<td>----------------------------------------------------------------------------</td>
<td>-------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Produce a strong immune response</td>
<td>Remote possibility that the live microbe could mutate back to a virulent form</td>
</tr>
<tr>
<td>Often give lifelong immunity with one or two doses</td>
<td>Must be refrigerated to stay potent</td>
</tr>
<tr>
<td>Safer and more stable than live vaccines</td>
<td>Produce a weaker immune response than live vaccines</td>
</tr>
<tr>
<td>Don’t require refrigeration: more easily stored and transported</td>
<td>Usually require additional doses, or booster shots</td>
</tr>
<tr>
<td>Teaches the immune system to fight off bacterial toxins</td>
<td></td>
</tr>
<tr>
<td>Targeted to very specific parts of the microbe</td>
<td>When developing a new vaccine, identifying the best antigens can be difficult and time consuming</td>
</tr>
<tr>
<td>Fewer antigens, so lower chance of adverse reactions</td>
<td></td>
</tr>
<tr>
<td>Allow infant immune systems to recognize certain bacteria</td>
<td></td>
</tr>
<tr>
<td>Produce a strong antibody and cellular immune response</td>
<td>Still in experimental stages</td>
</tr>
<tr>
<td>Relatively easy and inexpensive to produce</td>
<td></td>
</tr>
<tr>
<td>Closely mimic a natural infection, stimulating a strong immune response</td>
<td>Still in experimental stages</td>
</tr>
</tbody>
</table>
Vaccines of the Future

Aside from the “ouch factor,” vaccines delivered through a needle in the arm—or elsewhere—have some shortcomings. The needles used to inject vaccines must be kept sterile, for example, which is difficult in some settings. Also, injections usually must be administered by trained personnel, and injecting many people quickly—as would be necessary in case of a widespread outbreak—is not easy. For these reasons, scientists are investigating new ways to deliver vaccines.

Although still a long way off, edible vaccines would make it cheaper and easier to immunize people against diseases, especially in developing countries where storing and administering vaccines is often difficult. Scientists have shown that potatoes genetically engineered to produce an Escherichia coli antigen safely triggered an immune response to this bacterium in people who ate small pieces of the potatoes. Similarly, a potato-based vaccine against hepatitis B virus yielded promising results in an early stage of human testing. Researchers have also modified bananas to protect against norovirus, a common cause of diarrhea, and have created a food-based vaccine containing a protein from respiratory syncytial virus, which can cause serious respiratory illness, especially in young children. Recently, research into plant-based vaccines has focused less on food crops and more on genetically modifying plants that are not normally eaten. Vaccine components are produced in the leaves, which are then freeze-dried, ground up, and placed in gelatin capsules.

Another novel way being investigated to deliver vaccines simply is through a thin skin patch. Skin is one of our best defenses against infection. But it also includes large numbers of certain immune system cells, called dendritic cells, which can react to a vaccine placed on the skin. Skin patch vaccines are being tested for a range of diseases, including travelers’ diarrhea, tetanus, anthrax, and seasonal flu.
In 2003, the Food and Drug Administration (FDA) licensed a new vaccine for seasonal influenza that’s delivered as spray into the nose. The vaccine, created with National Institute of Allergy and Infectious Diseases (NIAID) support, is made from a live, attenuated flu virus. FDA has approved it for healthy people 2 to 49 years old. The vaccine is being tested to see if it can eventually be approved for use in older people and in children under 2 as well. Delivering this vaccine as a nasal mist not only eliminates the needle—making it easier to give to children—but it also closely mimics how the flu virus actually enters your body, which may produce a better immune response. (For more on the vaccine approval process, see “Making Safe Vaccines,” page 38.)

Nasal flu vaccine eliminates the dreaded needle, but people must still get the vaccine every year because the circulating influenza virus strains change. The annual flu shot may become a thing of the past, however, if researchers working on a so-called universal flu vaccine succeed. To make a universal flu vaccine that would work for more than 1 year, scientists incorporate parts of the flu virus that do not change very much.

Typically, vaccines prevent infection or disease. More recently, researchers also have been creating therapeutic vaccines intended for an existing infection or illness. Several are in various stages of development, including ones against some cancers, HIV, certain allergies, and multiple sclerosis.
Making Safe Vaccines

No vaccine is perfectly safe or effective. Each person’s immune system works differently, so occasionally a person will not respond to a vaccine. Very rarely, a person may have a serious adverse reaction to a vaccine, such as an allergic reaction that causes hives or difficulty breathing. But serious reactions are reported so infrequently—on the order of 1 in 100,000 vaccinations—that they can be difficult to detect and confirm. More commonly, people will experience temporary side effects, such as fever, soreness, or redness at the injection site. These side effects are, of course, preferable to getting the illness.

Most vaccines are designed to prevent illness and are given to people who are not sick. That is one reason that the bar of vaccine safety is set so high. To make vaccines as safe as possible, FDA requires extensive research and testing before allowing a vaccine to be licensed for general use. The time between discovery of a disease agent and production of a widely available vaccine has been as long as 50 years. Today, with improved technology and research methods, the length of time from basic research to availability of a licensed vaccine can sometimes be reduced. If a vaccine is approved, FDA and other government agencies continue to monitor it for safety. Following are some of the key measures taken to ensure vaccines are safe.

Lab and Animal Testing

Also known as preclinical testing, this testing is required before the vaccine can be given to people. Researchers test candidate vaccines in cell cultures and in animals such as mice, rabbits, guinea pigs, or monkeys. If the vaccine appears promising in these preclinical experiments, it may go on to be carefully tested in people.
This vaccine researcher uses a multi-channel pipetter to quickly prepare many biological samples for analysis.

**Investigational New Drug Application**

Before any vaccine candidate can be tested in people, its sponsors must submit an Investigational New Drug (IND) application to FDA. This application must explain how the vaccine works, describe how it is manufactured, present all preclinical safety data, and propose a plan for human testing. The IND must also demonstrate the vaccine has passed a series of tests for purity and safety.

**Studies in Humans**

Once researchers have FDA approval to test their candidate vaccine in human volunteers, they begin trials cautiously, starting with a very small **clinical trial**. If all goes well, successively larger phases of testing will be conducted. (See “Volunteering for a Clinical Study,” page 41.) Phase I studies enroll 20 or fewer people and primarily test for safety. Phase II studies involve 50 to several hundred people. Phase II studies continue to test for safety as well as to determine the best dosage and to gather preliminary data on a vaccine’s effectiveness. A Phase III or **efficacy** study, designed to thoroughly test the candidate vaccine’s power to protect against illness, involves many thousands of volunteers.
Because Phase III trials are complex and costly, researchers have introduced the intermediary Phase IIb trial. A Phase IIb trial provides preliminary information about how well the vaccine will work and helps researchers decide whether to move it into a Phase III trial. Phase IIb trials enroll more volunteers than a Phase II trial but fewer than a Phase III trial. A candidate vaccine that tests well in a Phase IIb trial would still need to be tested in a Phase III trial.

Scientists cannot, of course, deliberately expose human volunteers to certain microbes, such as Ebola or anthrax, to determine how well a vaccine works. So, FDA has a rule that in developing vaccines against certain microbes, scientists can gather efficacy information through animal rather than human tests.

**FDA License**

The application to FDA for a license to market a vaccine is called a Biologics License Application (BLA). This application must provide the results of all relevant human studies, describe all manufacturing and testing methods, and show the results of safety and purity tests on batches of the vaccine intended for public use. A BLA must also demonstrate that the vaccine manufacturers comply with all government standards, including those for production facilities, personnel, equipment, packaging, and record-keeping. At this stage, FDA also inspects the manufacturing facility.

The BLA is reviewed first by a team of FDA experts, then by an advisory committee made up of scientists, physicians, statisticians, and consumer representatives. The committee votes on whether or not to recommend that FDA approve the vaccine.
Follow-Up Surveillance

Once a vaccine is on the market, FDA continues to monitor its safety. FDA periodically inspects the manufacturing facility, and it tests samples of the vaccine for potency, safety, and purity for as long as the vaccine is made. The manufacturer must also safety test each batch, or lot, of the vaccine.

In addition, most licensed vaccines continue to be evaluated with very large studies that look at tens of thousands of people who have received the vaccine. These Phase IV studies try to pick up rare or delayed adverse reactions that might not have been apparent in the smaller studies that led to licensure.

Finally, FDA and CDC gather information on licensed vaccines through the Vaccine Adverse Events Reporting System (VAERS). Anyone—health care providers, patients, parents—can report adverse vaccine reactions to VAERS. FDA reviews weekly VAERS reports for each lot of vaccine in use, searching for anything unusual.

Volunteering for a Clinical Study

Clinical trials rely entirely on volunteers—people who contribute their time and energy for the advancement of science and improved health care for all. Tens of thousands of volunteers of all ages and walks of life have participated in these trials.

Typically, a volunteer in a vaccine study agrees to be given the vaccine (or a look-alike placebo), visits a clinic frequently for evaluation, undergoes medical tests, and provides blood samples that researchers will use to assess the vaccine. Because no one knows yet how well the vaccine works, participants should not expect the experimental vaccine to protect them against disease.

Volunteers are fully informed about how the study will be conducted, its potential risks and benefits, and measures taken to ensure their safety and privacy. To find out more about government clinical studies, visit www.clinicaltrials.gov.
Vaccine Concerns, Myths, and Safety Issues on the Web

Now that vaccines have virtually eliminated many once-feared diseases, the possibility of vaccine side effects or adverse reactions loom larger in some people’s minds than the diseases that vaccines prevent. Most parents today have never seen a case of diphtheria or measles, and some wonder why their children must receive so many shots. Rumors and misinformation about vaccine safety abound. For example, many parents are concerned that multiple vaccines may weaken or overwhelm an infant’s immune system or that certain vaccines may cause autism, multiple sclerosis, or diabetes.

For information about vaccine concerns, myths, and safety issues, try the following sources.

**AIDSinfo**  
A service of the U.S. Department of Health and Human Services  
aidsinfo.nih.gov  
800–448–0440

**Centers for Disease Control and Prevention**  
National Immunization Program  
www.cdc.gov/nip  
800–232–2522

**Immunization Safety Review Committee of the Institute of Medicine**  
www.iom.edu/imsafety  
202–334–1342

**Institute for Vaccine Safety**  
Johns Hopkins Bloomberg School of Public Health  
www.vaccinesafety.edu

**National Network for Immunization Information**  
www.immunizationinfo.org  
409–772–0199

**National Partnership for Immunization**  
www.partnersforimmunization.org  
703–836–6110

**Vaccine Education Center at The Children’s Hospital of Philadelphia**  
www.vaccine.chop.edu  
215–590–9990
Despite many accomplishments in vaccine research over the years, much remains to be done. NIAID-supported investigators in the United States and other countries and in NIAID laboratories in Bethesda, Maryland, and Hamilton, Montana, are working to reduce the burden of illness through vaccines against diseases old and new.

Millions around the globe suffer illness and death from the relatively new disease HIV/AIDS and from the ancient scourges of malaria and tuberculosis. For this reason, NIAID has made developing new or improved vaccines for those illnesses a top priority. Other priorities include devising vaccines against disease-causing agents that either arise naturally or that might be deliberately released in an act of bioterrorism. Finding ways to quickly produce vaccines against strains of influenza that experts fear may spark a pandemic is another area in which NIAID-supported researchers are making progress.

Established Record, Continuing Efforts

Some NIAID programs in vaccine development are quite recent, while others have a distinguished record of achievement and continue to advance the field of vaccines to this day.

In 1962, NIAID revolutionized the cumbersome, piecemeal approach to vaccine studies by establishing a network of Vaccine and Treatment Evaluation Units (VTEUs). These
testing sites are based at university medical research centers, public health departments, and community clinics across the country. The network can rapidly recruit volunteers for clinical studies, and it played a major role in the studies that led to the licensing of vaccines for Hib and for a new subunit pertussis vaccine. VTEU investigators have also tested vaccines for pneumonia, influenza, cholera, whooping cough, malaria, and tuberculosis. More recently, they have been called upon to conduct critical studies of smallpox vaccines and pandemic flu.

In 1988, the world’s first HIV vaccine trial began at the National Institutes of Health in Bethesda. That same year, NIAID established the AIDS Vaccine Evaluation Group (AVEG), a network of testing centers at universities in the United States devoted exclusively to HIV vaccines. In 1999, NIAID built upon AVEG by creating the HIV Vaccine Trials Network (HVTN), a collaboration of investigators in the United States and abroad that tests candidate HIV vaccines in clinical trials. The HVTN includes sites in Africa, Asia, South America, and the Caribbean. The international sites enable studies that examine differences in genetic makeup, nutrition, access to health care, and HIV subtypes in various populations, all crucial factors in creating a vaccine that is effective worldwide.

In 2000, NIAID established the Dale and Betty Bumpers Vaccine Research Center (VRC) in Bethesda. At the VRC, vaccines can be developed from initial concept to final product. Scientists at the center conduct basic research on microbes and the immune system’s response to them,
design candidate vaccines, and with their collaborators, test the most promising vaccines in preclinical and clinical trials. VRC scientists work on vaccines against multiple microbes, with an emphasis on developing therapeutic and preventive vaccines against HIV. A new prime-boost vaccine targeted at multiple HIV subtypes, which was developed at the VRC, entered a Phase II clinical trial in 2005, while the first human trial of an Ebola vaccine began in the center’s clinic in 2003. In 2006, the world’s first human trial of a DNA vaccine against the H5N1 avian influenza opened to volunteers.

NIAID is currently supporting the creation of a national network of laboratories that will augment our nation’s capacity to develop vaccines against infectious agents, whether they arise naturally, such as West Nile virus, SARS (severe acquired respiratory syndrome), and tuberculosis, or are deliberately introduced. Vaccines against such emerging microbes must be safe, easy to administer, and fast-acting—even to the point of providing immunity shortly after exposure to the microbe. NIAID-funded scientists are developing improved vaccines against smallpox, anthrax, plague, avian flu, and other emerging disease threats.

Established by NIAID in 2005, the Center for HIV/AIDS Vaccine Immunology (CHAVI) is a consortium of researchers based at institutions across the country who are working together to tackle some of the biggest obstacles in developing an HIV vaccine. Among their efforts, CHAVI scientists are seeking a better understanding of the earliest events in the immune
system’s response to HIV infection; identifying which immune reactions give the best indications that a candidate vaccine is eliciting a protective response; and testing new HIV vaccines in early phase clinical trials.

In recent years, researchers have increased their understanding of the immune system and how it fights off harmful microbes. Scientists working on vaccines also have advanced technology to draw on, including recombinant DNA technology and the ability to “read” and analyze the genomes of disease-causing organisms. This new knowledge and technology promises to usher in a renaissance in the already vital field of vaccinology.
More Information

National Institute of Allergy and Infectious Diseases
National Institutes of Health
6610 Rockledge Drive, MSC 6612
Bethesda, MD 20892-6612
301–496–5717
www.niaid.nih.gov

Dale and Betty Bumpers Vaccine Research Center
National Institutes of Health
40 Convent Drive
Bethesda, MD 20892
www.niaid.nih.gov/vrc

National Library of Medicine
MedlinePlus
8600 Rockville Pike
Bethesda, MD 20894
www.medlineplus.gov

Centers for Disease Control and Prevention
1600 Clifton Road
Atlanta, GA 30333
1–800–311–3435 or 404–639–3534
www.cdc.gov

Food and Drug Administration
5600 Fishers Lane
Rockville MD 20857-0001
1–888–INFO–FDA (1–888–463–6332)
www.fda.gov

World Health Organization
Avenue Appia 20
1211 Geneva 27
Switzerland
41–22–791–21–11
www.who.int
Glossary

**adjuvant**—a substance sometimes included in a vaccine formulation to enhance the immune-stimulating properties of the vaccine.

**antibody**—a molecule produced by a B cell in response to an antigen. When an antibody attaches to an antigen, it helps destroy the microbe bearing the antigen.

**antigen**—a molecule on a microbe that identifies it as foreign to the immune system and stimulates the immune system to attack it.

**artificially acquired immunity**—immunity provided by vaccines, as opposed to naturally acquired immunity, which is acquired from exposure to a disease-causing organism.

**attenuation**—the weakening of a microbe so that it can be used in a live vaccine.

**B cell** or **B lymphocyte**—a white blood cell, crucial to the immune defenses. B cells come from bone marrow and develop into blood cells called plasma cells, which are the source of antibodies.

**bacteria**—microscopic organisms composed of a single cell and lacking a defined nucleus and membrane-enclosed internal compartments.

**booster shot**—supplementary dose of a vaccine, usually smaller than the first dose, that is given to maintain immunity.
**cell-mediated immune response** (also called cellular immune response)—immune protection provided by the direct action of immune cells (as distinct from that provided by molecules such as antibodies).

**clinical trial**—an experiment that tests the safety and effectiveness of a vaccine or drug in humans.

**complement protein**—a molecule that circulates in the blood whose actions “complement” the work of antibodies. Complement proteins destroy antibody-coated microbes.

**conjugate vaccine**—a vaccine in which proteins that are easily recognizable to the immune system are linked to the molecules that form the outer coat of disease-causing bacteria to promote an immune response. Conjugate vaccines are designed primarily for very young children because their immune systems cannot recognize the outer coats of certain bacteria.

**contagious**—able to transmit disease to other people.

**cytotoxic T cells** or **killer T cells**—a subset of T cells that destroy body cells infected by viruses or bacteria.

**dendritic cell**—immune cell with threadlike tentacles called dendrites used to enmesh antigen, which it presents to T cells.
DNA vaccine or naked DNA vaccine—a vaccine that uses a microbe’s genetic material, rather than the whole organism or its parts, to stimulate an immune response.

edible vaccines—foods genetically engineered to produce antigens to specific microbes and safely trigger an immune response to them.

efficacy—in vaccine research, the ability of a vaccine to produce a desired clinical effect, such as protection against a specific infection, at the optimal dosage and schedule in a given population.

formalin—a solution of water and formaldehyde, used in toxoid vaccines to inactivate bacterial toxins.

gene—a unit of genetic material (DNA). Genes carry directions a cell uses to perform a specific function.

genetic material—molecules of DNA (deoxyribonucleic acid) or RNA (ribonucleic acid) that carry the directions that cells or viruses use to perform a specific function, such as making a particular protein molecule.

genomes—all of an organism’s genetic material. A genome is organized into specific functional units called genes.

*Haemophilus influenzae* type b (Hib)—a bacterium found in the respiratory tract that causes acute respiratory infections, including pneumonia, and other diseases such as meningitis.
helper T cells—a subset of T cells that function as messengers. They are essential for turning on antibody production, activating cytotoxic T cells, and initiating many other immune functions.

herd immunity or community immunity—the resistance to a particular disease gained by a community when a critical number of people are vaccinated against that disease.

HIV—human immunodeficiency virus, the virus that causes AIDS.

humoral immune response or antibody response—immune protection provided by B cells, which secrete antibodies in response to antigen (as distinct from that provided by the direct action of immune cells, or the cellular immune response).

immune—have a high degree of resistance to or protection from a disease.

immune system—a collection of specialized cells and organs that protect the body against infectious diseases.

inactivated vaccine or killed vaccine—a vaccine made from a whole virus or bacteria inactivated with chemicals or heat.

live, attenuated vaccine—a vaccine made from microbes that have been weakened in the laboratory so that they can’t cause disease. (See attenuation.)
lymph node—a small bean-shaped organ of the immune system, distributed widely throughout the body and linked by lymphatic vessels. Lymph nodes are gathering sites of B, T, and other immune cells.

lymphocyte—a white blood cell central to the immune system’s response to foreign microbes. B cells and T cells are lymphocytes.

macrophage—a large and versatile immune cell that devours and kills invading microbes and other intruders. Macrophages stimulate other immune cells by presenting them with small pieces of the invaders.

memory cells—a subset of T cells and B cells that have been exposed to antigens and can then respond more readily and rapidly when the immune system encounters the same antigens again.

microbe—a microscopic organism. Microbes include bacteria, viruses, fungi, and single-celled plants and animals.

molecule—a building block of a cell. Some examples are proteins, fats, and carbohydrates.

mutate—to change a gene or unit of hereditary material that results in a new inheritable characteristic.

naturally acquired immunity—immunity produced by antibodies passed from mother to fetus (passive), or by the body’s own antibody and cellular immune response to a disease-causing organism (active).
organism—an individual living thing.

Passive immunity—immunity acquired through transfer of antibody or lymphocytes from an immune donor.

Pertussis or whooping cough—a respiratory infection caused by the toxic bacterium *Bordetella pertussis*. The wracking coughs characteristic of this disease are sometimes so intense that victims, usually infants, vomit or turn blue from lack of air.

Placebo—an inactive substance administered to some clinical trial participants. Other participants receive the agent being evaluated, which provides a basis for comparing the agent’s effects.

Plasma cell—a cell produced by a dividing B cell that is entirely devoted to producing and secreting antibodies.

Polysaccharide—a long, chain-like molecule made up of a linked sugar molecule. The outer coats of some bacteria are made of polysaccharides.

Preclinical testing—required laboratory testing of a vaccine before it can be given to people in clinical trials. Preclinical testing is done in cell cultures and in animals.

Recombinant DNA technology—the technique by which genetic material from one organism is inserted into a foreign cell or another organism in order to mass-produce the protein encoded by the inserted genes.
recombinant subunit vaccine—a vaccine made using recombinant DNA technology to engineer the antigen molecules of the particular microbe. (See subunit vaccine.)

recombinant vector vaccine—a vaccine that uses modified viruses or bacteria to deliver genes that code for microbial antigens to cells of the body.

rubella or German measles—a viral disease often affecting children and spread through the air by coughs or sneezes. Symptoms include a characteristic rash, low-grade fever, aching joints, runny nose, and reddened eyes. If a pregnant woman gets rubella during her first 3 months of pregnancy, her baby is at risk of having serious birth defects or dying.

subunit vaccine—a vaccine that uses one or more components of a disease-causing organism, rather than the whole, to stimulate an immune response.

T cell or T lymphocyte—a white blood cell that directs or participates in immune defenses. (See cytotoxic T cells and helper T cells.)

tissue—a group of similar cells joined to perform the same function.

toxin—agent produced by plants and bacteria, normally very damaging to cells.

toxoid or inactivated toxin—a toxin, such as those produced by certain bacteria, that has been treated by chemical means, heat, or irradiation and is no longer capable of causing disease.
**toxoid vaccine**—a vaccine containing a toxoid, used to protect against toxins produced by certain bacteria.

**vector**—in vaccine technology, a bacterium or virus that cannot cause disease in humans and is used in genetically engineered vaccines to transport genes coding for antigens into the body to induce an immune response.

**virulent**—toxic, causing disease.

**virus**—a very small microbe that does not consist of cells but is made up of a small amount of genetic material surrounded by a membrane or protein shell. Viruses cannot reproduce by themselves. To reproduce, viruses must infect a cell and use the cell’s resources and molecular machinery to make more viruses.