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

National Institute of Allergy and Infectious Diseases

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NIAID SCIENCE EDUCATION

Understanding VACCINES

What They Are How They Work

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Contents

Introduction

This booklet contains information about vaccines: what they are, how they prevent disease, how they are made and tested, and what vaccine research might achieve in the future. For more in-depth information about vaccines, consult resources at your local library or ask your health care provider.

The Internet can be a valuable source as well. Start with the National Institutes of Health (NIH) Web site at *www.nih.gov* for information on the broad range of research supported by NIH. For information on vaccine research, a good place to start is *www.niaid.nih.gov*, the Web site for the National Institute of Allergy and Infectious Diseases (NIAID). Another good source is MEDLINE*plus*, an information service of the National Library of Medicine *www.nlm.nih.gov/medlineplus/*. There is also information on vaccines on the Web site of NIAID's Dale and Betty Bumpers Vaccine Research Center, *www.vrc.nih.gov*. Finally, a list of Web sources about vaccine concerns, myths, and safety issues appears on page 41 of this booklet.

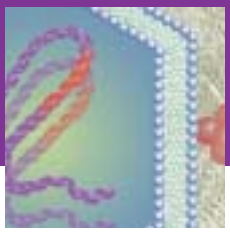
Note: Words in bold are defined in the glossary at the end of this booklet.

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.") Similarly, diseases like whooping cough (**pertussis**), measles, mumps, and 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. 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 diseases are called the **immune system**. (We'll take a closer look at the immune system in the section "How Vaccines Work.") Without the immune system, the simplest illness—even the common cold—could quickly turn deadly.



On average, 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 fix the fight but at the same time teach your body important lessons about how to defeat its opponents.

Diphtheria: Remembering an Old Disease

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, an average of 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 are one of the few medicines that prevent a disease from occurring in the first place, rather than attempting a cure after the fact. It is much cheaper to prevent a disease than to treat it. According to one analysis, every dollar spent on vaccinating children against **rubella**, or German measles, in the United States saves nearly $8 in costs associated with treating the disease.

Vaccines protect not only you but everyone around you. If your vaccine-primed immune system nips an illness in the bud, 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

Community immunity: If a critical number of people in a community are vaccinated against a particular illness, the entire group becomes less likely to get the disease, even those who are not vaccinated.

protect not only individuals, but entire communities. That is why vaccines are key 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 **herd immunity**, or community immunity.

On the other hand, if enough people in a community forgo 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 in the United States. The epidemic resulted in more than 55,000 cases of measles and 136 measles-associated deaths.

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.

Here are a few examples of some of the most serious disease-causing microbes for which vaccines exist.

- 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. There is no effective treatment. In the 18th century, variola virus killed every seventh child born in Russia and every tenth child born in Sweden and France. Although vaccination and outbreak control 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 natural case of smallpox occurred 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 1 out of 200 cases, this virus attacks the spinal cord, paralyzing limbs or leaving victims unable to breathe on their own. 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 2001, only 537 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

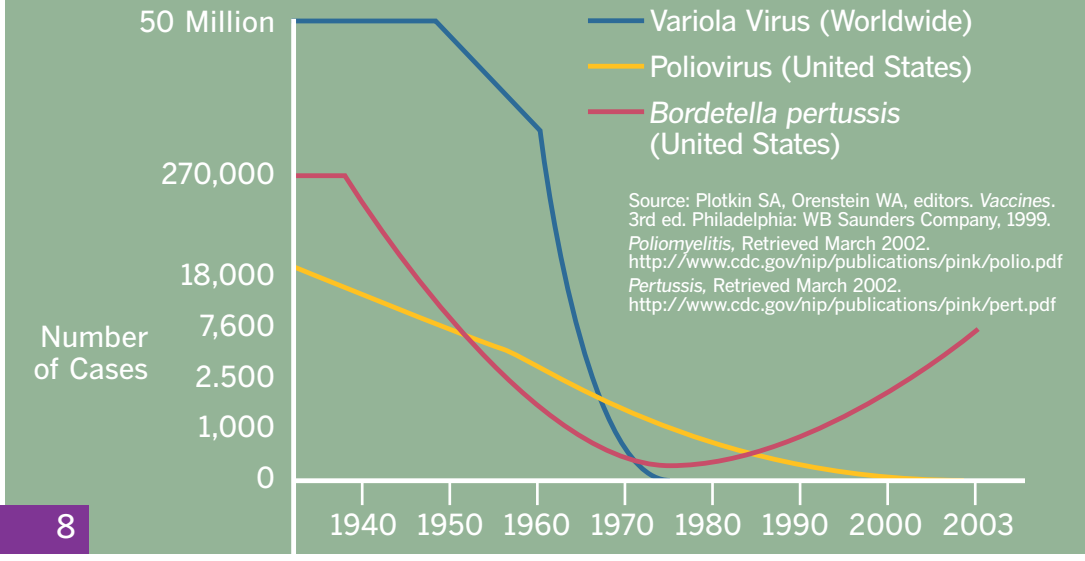
Vaccine-Preventable Infectious Diseases

Anthrax
Bacterial meningitis
Chickenpox
Cholera
Diphtheria
Haemophilus influenzae type b
Hepatitis A
Hepatitis B
Influenza
Measles
Mumps
Pertussis
Pneumococcal pneumonia
Polio
Rabies
Rubella
Tetanus
Yellow fever

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, pertussis has been on the upswing in the United States, reaching 4,600 cases in 1994 and 7,600 in 2001. 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 and 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.

Vaccines at Work



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.

Dr. Edward Jenner

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.

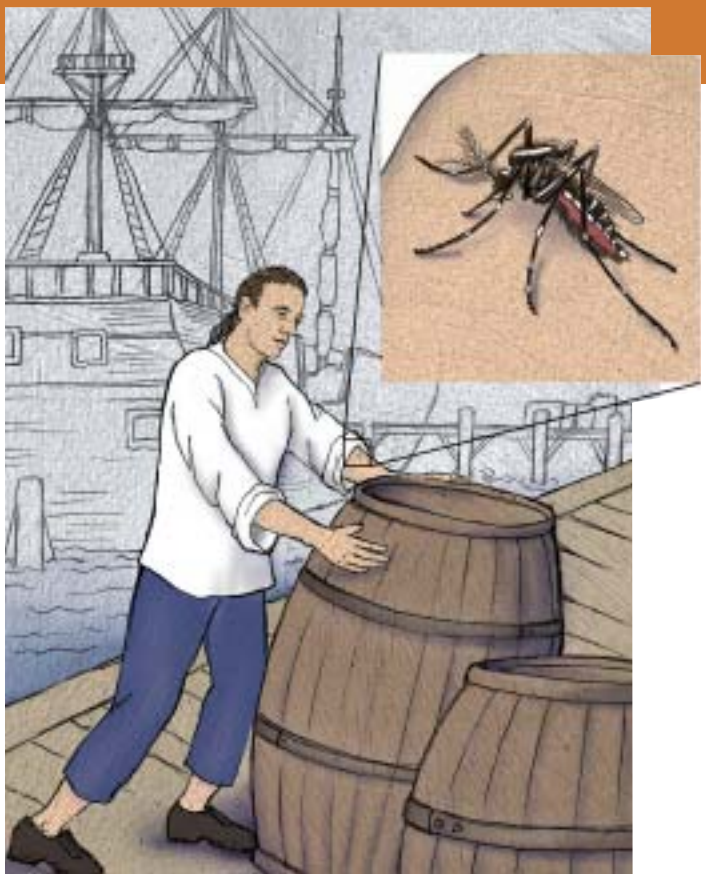
How Vaccines Work

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. Unfortunately, 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, 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. By "feeling" for these markers, the macrophages and other cells of your immune system can 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. As we will see, these molecules 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 particular, the macrophages 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 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," p. 18) 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

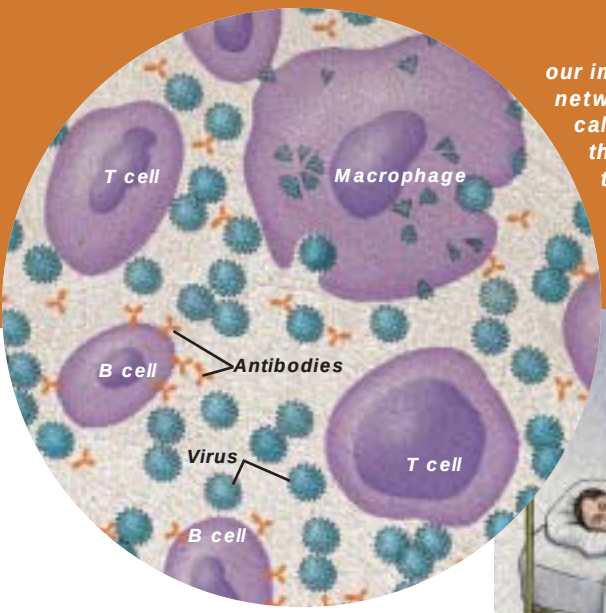
B cells are like weapons factories. They secrete extremely important molecular weapons called **antibodies**. Antibodies usually work by sticking to and coating microbes, and antibodies use the microbe's antigens to grip them. Antibody molecules fit with antigen molecules like pieces of a jigsaw puzzle fit together—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 a cell 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.



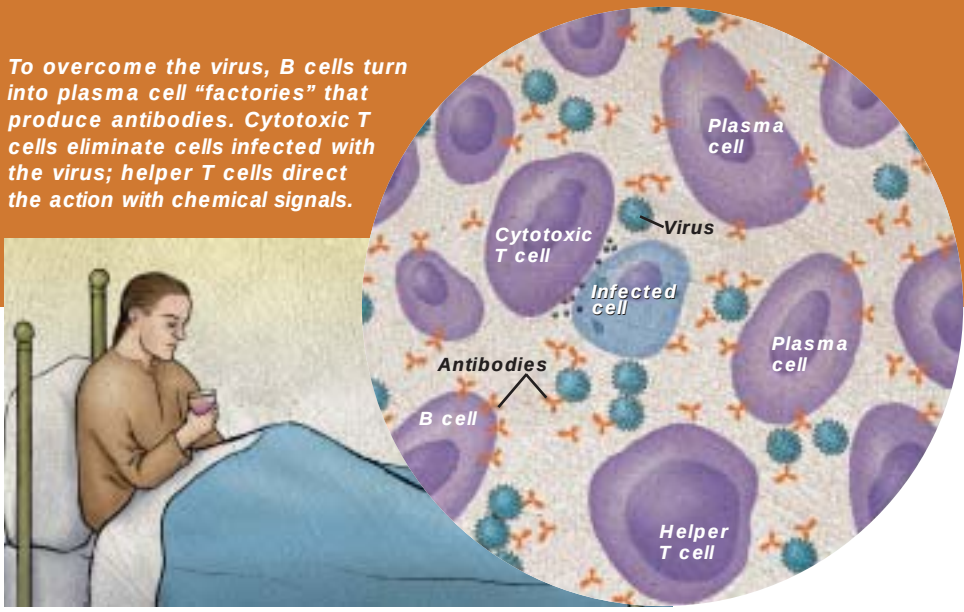
our immune system is a complex network of cells and organs. Cells called macrophages gobble up the invading virus and sound the alarm by showing pieces of the invader to T cells and B cells. B cells produce defensive molecules called antibodies that "stick" to the virus.

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 are feeling 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.

To overcome the virus, B cells turn into plasma cell "factories" that produce antibodies. Cytotoxic T cells eliminate cells infected with the virus; helper T cells direct the action with chemical signals.



After about a week, however, 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 bitten by another yellow-fever-infested mosquito, 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 do that a little later.) This vaccine is injected into your arm. Your macrophages can't tell the vaccine viruses are duds. The macrophages gobble up the viruses as if they were dangerous and, in the lymph nodes, present yellow fever antigen to T 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.

How Viruses Work

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 attached to your pants leg—a small, round object covered with tiny bristles.

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.