LOOKING AHEAD

June 5, 2011 marked 30 years since the Centers for Disease Control and Prevention (CDC) reported the first cases of AIDS in the United States in its weekly Morbidity and Mortality Weekly Report (MMWR). The chronological milestone provides an opportunity to reflect upon the status of HIV/AIDS in the world today. Since these first five cases were reported, nearly 600,000 people have died in the United States as a result of HIV/AIDS. Worldwide, 30 million people have died of HIV-related causes. There is still no vaccine available to prevent this viral disease. However, there remains hope that this viral disease will be conquered one day. Development of antivirals to treat patients, along with improved HIV diagnosis methods, have increased the life expectancy of U.S. patients after HIV diagnosis from 10.5 to 22.5 years.

This opening chapter introduces acquired immune deficiency syndrome (AIDS) by exploring the development of its epidemic in the United States and the world and by describing the research to uncover its cause. On completing the chapter, you should be able to . . .

- Understand the conditions that led public health officials to realize that an epidemic of AIDS was in progress.
- Recognize some broad features of AIDS and characterize the individuals at risk for the disease.
- Summarize the research leading to the isolation and identification of the AIDS virus.
- Conceptualize the transmission of the AIDS virus from chimpanzees to humans.
- Discuss some theories for the origin of the AIDS epidemic and its spread in the United States and the world.
- Note the current magnitude of the AIDS epidemic and describe where it is likely to spread in the future.

The end of this chapter contains a Healthline Q & A section that addresses questions you may have as you read and digest the information presented.

INTRODUCTION

Human perception can lead to false understandings; however, when observing new patterns in the world, often all we have are our perceptions. This is the case with our early thoughts about AIDS. Physicians and scientists could not adequately
A fable tells of six blind men (seen here as blindfolded) invited to examine an elephant and report what they believed it to be. Each touched the elephant at a different part and reported something completely unlike the others. In the early years of the AIDS epidemic, physicians, researchers, and members of the general public saw disease in different ways, much as different blind men perceived the elephant.

Define and describe AIDS because they did not know at what they were looking. This inability to see the “big picture” is best illustrated by the old South Asian fable about six blind men invited to examine an elephant. The first man, falling against the elephant’s side, claimed it was a wall. The second, seizing a leg, declared the elephant a tree. Another, grasping a tusk, thought the elephant was a spear. The fourth man, grabbing the trunk, decided he was holding a snake. The fifth, touching the ear, believed it to be a fan. The last blind man, holding the tail, proclaimed the elephant a rope (Figure 1.1).

So it was in the early 1980s with AIDS: The elephant was the disease, and the blind men were the scientists and doctors grappling with its emergence in an epidemic. Without a clear vision of AIDS, they were forced to treat the epidemic piecemeal—to try and explain each bit of knowledge as it came forth. Physicians were seeing patients whose immune systems were profoundly suppressed, but they had no idea what was causing this problem. Public health officers were charting the course of the AIDS epidemic without knowing its cause. Manufacturers were searching out new drug therapies, but they were unsure about what they were trying to eliminate. Physicians and scientists did not really know what they were seeing and could not adequately describe what was going on.

Even though physicians and scientists could not identify the causes of what was happening or completely describe all of the features of the disease, it was clear from very early on that a large problem had been presented to public health in the United States. Physicians saw it as a medical problem, economists as a potential disaster to the healthcare system, employers as a threat to the smooth operation of their businesses, healthcare workers as a problem requiring personal protection, and politicians as yet another drain on public funds. Until 1984, there was no clear definition of AIDS. No test was available to confirm a diagnosis and no cure was in sight. Most scientists agreed that a cure would follow only after they found a cause and understood the natural history of the disease.

Focus on HIV

There were approximately 34.2 million people living with HIV in 2011.
Despite the early pessimism, however, scientists found the cause of AIDS in a shorter span of time than had been required for any previous infectious disease. So quickly was the cause of AIDS found by scientists that it highlighted the astounding advances made during the 1970s when the ongoing revolution in modern molecular biology began. These advances and rapid identification of the cause of AIDS, however, did not prepare physicians, scientists, patients, and our society for the slow and ongoing progress made in combating AIDS. Indeed, in the early 1980s, when the cause of AIDS was identified, there was a sense that it would soon be a historical side note in the annals of infectious disease. No one was prepared for what has followed.

The Early Years

By 1981, most observers believed that infectious diseases were largely under control in the Western world. There had been no smallpox anywhere since October 1977, and diseases such as typhoid fever, polio, and whooping cough were rarely encountered. Even childhood diseases such as measles, mumps, and rubella appeared to be relics of the past. Indeed, the speed with which an effective therapy for Legionnaires’ disease was discovered in 1976 and the success in interrupting the outbreak of toxic shock syndrome in 1978 had strengthened public confidence that scientists could defeat any epidemic.

Moreover, in the early 1980s, American researchers had largely turned away from the negative aspects of microorganisms and were pursuing their practical uses. For instance, bacteria had become mainstays of genetic engineering, which was fast developing as the technology of the future. (A 1981 Time magazine article described genetic engineering as “the most powerful and awesome skill acquired by man since the splitting of the atom.”) Genetically engineered insulin was already in production. Synthetic vaccines were in the planning stage, and breathtaking developments in DNA technology were in the headlines daily. The mood of the day was optimism.

The First Observations

On June 5, 1981, the CDC published a brief but significant article in Morbidity and Mortality Weekly Report (MMWR). This article, appearing between discussions of dengue fever and measles, described the case reports of five young men treated at three different hospitals in Los Angeles, California. All five men were sexually active and gay, and all five were suffering from Pneumocystis pneumonia. By the time of the article’s publication, two of the five patients had died from what was reported to be a yeast-like fungal lung infection with Pneumocystis jiroveci. The terms Pneumocystis pneumonia or pneumocystosis, as they first appeared in these reports, remain an accurate way to discuss this infection.

In the CDC article, the writer observed that three of the patients had “profoundly depressed numbers of thymus-dependent lymphocyte cells and profoundly depressed . . . responses to mitogens and antigens.” Because lymphocyte cells are components of the immune system and because responses to mitogens and antigens are among the important functions of the immune system, it was apparent that the patients’ immune systems were under stress. Then, in perhaps the understatement of 1981, the writer noted this: “The occurrence of pneumocystosis in these five previously healthy individuals with underlying immunodeficiency is unusual.”

The CDC article of June 5, 1981 is considered a benchmark: the unofficial beginning of the AIDS epidemic in the United States. Statistics were compiled from that
The CDC

The CDC, one of six major agencies of the U.S. Public Health Service, has its headquarters in Atlanta, Georgia. Originally established as the Communicable Disease Center in 1946, the CDC was the first government health organization ever set up to coordinate a national control program against infectious diseases. At first, it was concerned with diseases spread from person to person, from animals to people, or from the environment to humans. Eventually, however, all communicable diseases came under its aegis. Atlanta was selected as the site for the CDC because it was a convenient central point for the study of malaria, which was then common in the South.

In April 1955, two weeks after release of the Salk vaccine for polio, the CDC received reports of six cases of polio in vaccinated children. Two days later, it established the Polio Surveillance Unit and began collecting data on the occurrence of polio and summarizing it for health professionals. More than 80% of vaccine-associated polio cases were related to a single manufacturer, whose vaccine was withdrawn at once. This incident established the role of the CDC in health emergencies, and soon it became a national resource for the development and dissemination of information on communicable diseases. In 1960, the CDC moved its headquarters to a new complex adjoining Emory University. The unassuming appearance of the facility belies its importance.

Reorganized under its current name in 1980 (the words “and Prevention” were added in 1992, but the CDC acronym was retained), the CDC is charged with protecting the public health of the U.S. population by providing leadership and direction in the prevention and control of infectious disease and other preventable conditions, such as cancer. It is concerned with urban rat control, quarantine measures, health education, and the upgrading and licensing of clinical laboratories. The CDC also provides international consultation on disease and participates with other nations in the control and eradication of communicable infections.

Today the CDC employs 10,500 employees and 5,000 contractors, of which 72% of the staff is located at the Headquarters office in Atlanta, Georgia while only 2% are assigned overseas, with the remaining employees located at 11 other locations. Nearly 50% of the workforce holds Master or Doctoral degrees. In 2009, its fiscal budget was $10.1 billion, of which 11% is used for HIV/AIDS, STD, and TB prevention.

Its publication MMWR is distributed each week to thousands of health professionals. In 2011, the CDC celebrated its 65th anniversary of its founding on July 1, 1946.

Such reports arrived quickly. On July 3, 1981, another article appeared in the CDC’s MMWR, this time describing Kaposi’s sarcoma as well as pneumocystis in 26 young homosexual men. Twenty patients were from New York City, and six lived in California. All had been diagnosed during the previous 30 months. Kaposi’s sarcoma is normally a relatively mild skin cancer affecting mainly older men of Mediterranean descent, but in these 26 patients, it was aggressive and deadly, with skin and mucous membrane lesions of blue to violet color (Figure 1.2). In 10 of the patients, the Kaposi’s sarcoma was accompanied by Pneumocystis pneumonia. In several others, doctors reported diseases not normally observed in persons with functional immune systems. This article did not comment on the patients’ immune systems. It did, however, encourage physicians to continue reporting similar cases.
Because the new disease appeared to be affecting primarily homosexual men, scientists asked what practices might be unique in the homosexual community. They postulated that amyl nitrate, a drug used by some homosexual men to increase sexual pleasure, might be at fault, or perhaps certain disease organisms prevalent in homosexual men might be to blame. One such organism, the cytomegalovirus, was a prime candidate. Another theory was that the immune systems of the homosexual patients were suppressed by a constant barrage of sexually transmitted diseases (STDs). In some publications, the disease was given the pejorative name gay-related immune deficiency (GRID). The idea of a transmissible infectious disease had not yet taken hold.

Then data about further victims began to filter in. Late in 1981, the CDC received reports of heroin addicts and other injection drug users in New York City who were suffering from Pneumocystis pneumonia and immune deficiency (Figure 1.3). By early 1982, it appeared that heterosexuals could transmit the disease to one another, and within months, the disease surfaced among blood transfusion recipients and hemophiliacs. By June 11, 1982, the CDC had details on 355 cases from five different states (California, Florida, New Jersey, New York, and Texas). The clustering of cases within several groups and the pattern of spread made it apparent that a transmissible agent, probably a virus, was involved.
On September 3, 1982, the disease was given a new name. In the MMWR of that date, the CDC, acting on a recommendation from biologist Bruce Voeller, noted that “the group of clinical entities, along with its specific immune deficiency, is now called acquired immune deficiency syndrome (AIDS).” The thrust of the article, however, was a warning that a hepatitis B vaccine in use at the time might be a possible agent of transmission and should be used with caution. It was a type of warning that was becoming commonplace whenever blood or blood products were involved.

By early 1983, 16 countries were reporting AIDS cases, and more than 1,000 Americans from 34 states had been diagnosed with the disease (more than half of these patients had died by that time). Also in 1983, physicians in Newark, New Jersey, and New York City reported the first cases of what appeared to be mother-to-child transmission of AIDS. Concern also mounted that the nation’s supply of blood in blood banks was contaminated. One public health administrator wrote of a “nightmare time bomb ticking away in the blood supply.” Privately, the CDC (Box 1.1) began pressuring blood suppliers to consider ways to protect the public, but without knowing what the agent was and how it was transmitted, blood banks were unable to take meaningful action.

Alarm climbed a notch higher when a woman in California contracted AIDS through sexual intercourse with her husband, who suffered from hemophilia. The woman then passed the disease to her newborn child. It was becoming apparent to the general public that anyone could be at risk. Whatever fantasies Americans had that AIDS was exclusively a disease of homosexual men and injection drug users were clearly over.

The Breakthrough

During the first three years of the AIDS epidemic, the number of diagnosed cases doubled about every six months. To many observers, every six months also brought a new theory of the epidemic’s cause. As noted previously here, some scientists initially related the disease to use of amyl nitrate or to immune system depression by a variety...
of diseases, but these ideas were soon discarded. Certain scientists held to the belief that the agent was the virus that causes African swine fever, as this virus can induce immune suppression in pigs (a temporary alert on undercooked pork was issued); others believed that the agent was a “slow virus”—one that apparently multiplies at an extremely low rate in the body and manifests itself after years or more.

At the fringe were a number of other beliefs. One group maintained that the agent was a viral escapee from a genetics engineering laboratory; another attributed it to a failed biological war against Cuba, and still another suggested that AIDS was due to mutations arising from “secret Soviet Union electromagnetic warfare against the United States.” Eventually, however, most scientists focused on a virus as the most likely cause of AIDS. Some opponents were quick to point out, however, that such an assumption had been erroneous before. In the previous decade, they noted, scientists had assumed that viruses were responsible for Legionnaires’ disease, Lyme disease, and toxic shock syndrome. In each case, the agent was eventually shown to be a bacterium.

By 1982, two cancer research laboratories were involved in the hunt for an AIDS agent. At the Pasteur Institute in Paris, a group led by Luc Montagnier was intrigued by the possibility that the mysterious AIDS agent could also be the cause of Kaposi’s sarcoma. In the United States, at the National Cancer Institute, a team headed by Robert C. Gallo was attempting to prove that AIDS was due to a retrovirus similar to certain other viruses related to cancer. In May 1983, both the Gallo and Montagnier groups published reports hinting that they had found the virus responsible for AIDS. There was a sense of excitement in the medical community.

Then, on April 23, 1984, at a press conference in Washington, D.C., Gallo announced that his group had identified a virus in the blood of 48 persons with AIDS. In addition, he and his colleagues found antibodies to the virus in blood samples from 88% of all those diagnosed as having AIDS. Gallo recommended that the virus be named human T-cell lymphotropic virus type III (HTLV-III). Four articles in the May 4, 1983 issue of the highly respected magazine Science carried the details of the research performed by Gallo’s group.

Before the articles in Science appeared, however, the Montagnier group rushed to call attention to their work on an AIDS virus. In interviews with the international press, Montagnier described a virus that his team had located in the blood of patients with the early manifestations of AIDS. Like the Americans, the French researchers reported evidence of the virus in more than 80% of blood samples from AIDS patients. Montagnier’s group suggested that the virus be called lymphadenopathy-associated virus (LAV). The virus appeared to be identical to that isolated by the Americans.

In the months that followed, a rivalry developed between the American and French groups, each claiming to have isolated the virus first. At issue were international awards, research grants, and millions—perhaps billions—of dollars in patent rights for products that might be derived using the AIDS virus, such as an AIDS test. Time did little to sort out the differences between the groups, and the scientific community began referring to the virus as HTLV-III/LAV (in France, it was called LAV/HTLV-III). By February 1985, the American and French teams reported that their viruses were virtually identical. Montagnier and Gallo received much international acclaim (Figure 1.4).

Because of legal pressure and the scientific review process, in 1991, Gallo conceded that the virus he identified had originated in tissue samples sent to him by Montagnier. Gallo explained that inadvertent contamination had probably allowed the French virus to enter the tissue samples with which his team was working and
from which the American virus was eventually isolated. However, Gallo insisted that Montagnier’s work had relied on techniques developed in Gallo’s laboratory in which T-cell cultures were supplemented with interleukin-2, a technique that led directly to the development of blood tests for HIV and the ability to screen donated blood for this virus. Indeed, it was in April 1985 that Gallo’s group announced this development of a blood test for AIDS, and by May 1985, the test was perfected and in use. The test was so effective that over the next five years, only four cases of AIDS were linked to transfused blood. The two scientists continued to be in a bitter dispute between the United States and France over royalties from the blood test patent until 1987, when they agreed to share credit for the discovery of HIV. In light of these developments, in 1994, the U.S. government conceded that France’s Pasteur Institute deserved a higher percentage of patent royalties from AIDS tests that use the virus, as the Pasteur Institute had gained greater recognition for its role in discovering the virus. Under this arrangement, the French government receives 50% of the royalty monies, the U.S. government 25%, and the World AIDS Foundation 25%. (The World AIDS Foundation funds AIDS research in the developing world.) Consequently, today it is generally agreed that Montagnier’s group first identified HIV, although Gallo’s group is credited with much of the science that made the discovery by Montagnier possible and, although Montagnier found the virus first, Gallo is credited for showing that it was the cause of AIDS and being the first to grow the virus in culture. The Gallo–Montagnier dispute came to a close in the November 29, 2002 issue of *Science*, in which Gallo and Montagnier coauthored an article in which they both acknowledged the pivotal roles that each had played in the discovery of HIV.

The year 1986 brought a name change for the AIDS virus. That summer, an international commission of prominent virologists and molecular biologists recommended that the name of the virus be changed from HTLV-III/LAV to the human immunodeficiency virus, or HIV. The commission noted that the new name conforms to common nomenclature for related viruses, that it does not incorporate the term
AIDS (because HIV could cause other diseases), that it was chosen without regard to priority of discovery, and that it allows for further names as strains are isolated. Acceptance of the commission’s recommendation and confirmation by the scientific community brought one phase of the AIDS saga to an end (Figure 1.5).

Another AIDS Virus
No sooner had HIV been identified than another human immunodeficiency virus emerged. Identified in 1985 by Pasteur Institute scientists led by Luc Montagnier, this virus was designated HIV-2, and the original strain began to be referred to as HIV-1. HIV-2 appears to be less pathogenic and progress more slowly, taking longer to damage the immune system after infection; however, although they are different strains, HIV-1 and HIV-2 are the same virus and share many similarities. For example, the modes of HIV-1 and HIV-2 transmission are the same—sexual contact, sharing needles, and so forth. Furthermore, people infected with HIV-2 are subject to the same opportunistic infections as those infected with HIV-1, and although they progress to AIDS more slowly, people infected with HIV-2 do get AIDS. Furthermore, HIV-1 and HIV-2 are treated with the same medications and can be detected with the same antibody blood test for CD4 monitoring; however, the efficacy of the medications against HIV-2 is less than that for HIV-1, and some HIV-2 infections do not show cross-reactivity with the HIV-1 anti-CD4 antibody. A specific antibody test for HIV-2 has been developed. The differences between HIV-1 and HIV-2 are as noted before; HIV-2 weakens the immune system more slowly than HIV-1. When compared with HIV-1–infected individuals, patients with HIV-2 are less infectious early in the course of the disease yet more infectious later in the course of disease. These differences are likely due to the entry of HIV-2 into the human population through a different and less common route, thus its discovery in human blood after HIV-1.

Blood tests have shown that HIV-2 is rare in the United States but relatively common in parts of Africa, especially West Africa and countries such as Senegal, Nigeria, Ghana, and the Ivory Coast. Researchers at Harvard University studied 574 women from Dakar, Senegal, and found that five years after infection, one-third of the women infected with HIV-1 had progressed to AIDS, whereas none of those infected with HIV-2 had any sign of AIDS. Moreover, the destruction of immune system cells was substantially more extensive in those with HIV-1 than in those with HIV-2. Clearly, HIV-2 takes longer to
develop in humans than HIV-1. This is due to the ability of humans to mount a more effective immune response to HIV-2 compared with HIV-1. This possibility has spurred researchers to study closely the interaction between humans and HIV-2.

A Pandemic

In 1985, reports from health officers in Africa indicated that the AIDS epidemic was widespread on that continent. Fearing stigmatization, some African government officials at first sought to distance themselves and deny that AIDS was occurring in their countries; however, the signs of AIDS were unmistakable. Thousands of men and women were affected with severe weight loss, emaciation, and disrupted immune systems, and the epidemic was spreading; indeed, it had become worldwide—a pandemic.

Within three years, international health officials recognized that Africa was the continent hit hardest by AIDS. The disease was present not only in homosexual men (more specifically, men who have sex with men) and injection drug users but also in heterosexual men and women, where it appeared to spread by sexual contact.

AIDS was not confined to Africa, however. By 1988, almost 5,000 cases were reported in Europe, and scientists estimated that between 500,000 and one million individuals from European countries were infected with HIV. In Asia, the situation was becoming increasingly severe, and in Australia, AIDS was spreading as fast as in the United States and Europe.

Two years previously, in 1986, the World Health Organization (WHO) had established its Global Program on AIDS. Under the direction of Jonathan Mann, the program began carefully to overcome national sensitivities and gain the confidence of the world's health leaders. Soon it was receiving reports from regional offices and the ministries of health of 175 countries. By 1988, 138 of those countries had reported at least one case of AIDS, and many had more than 1,000 total cases. In 2003, worldwide AIDS cases increased by approximately 4.8 million, and by the year 2004, the total global number of people with AIDS or living with HIV infection rose to 39.4 million, with the highest infection rates seen in sub-Saharan Africa and in South and Southeast Asia. As the leader of the world's health community, the WHO continues to chart the development of the AIDS epidemic all over the globe. The WHO also supports the development of national AIDS prevention and control programs in 120 countries throughout the world. In addition, it collects information about cases and maintains a virus bank because HIV strains from different parts of the world can vary somewhat in their biochemistry. Finally, it makes recommendations on international travel and related issues and serves as a forum for discussing the scientific and practical implications of the AIDS pandemic.

Supplementing the WHO's work is the United Nations Programme on HIV/AIDS (UNAIDS), a joint effort of various subdivisions of the United Nations, including the United Nations Children's Fund. Established in 1995 and currently under the direction of Michel Sidibé, UNAIDS coordinates the UN's efforts in dealing with the AIDS pandemic. Among other activities, the program works with governments of the world to channel resources, identify directions for global research, and implement educational initiatives. Most recently, UNAIDS has become the chief advocate for worldwide action against AIDS. It has brought together 10 organizations of the United Nations system, including the WHO, around a common agenda on AIDS. UNAIDS has established a global database on the rates of HIV infection based on regions and countries. From their database, some good news is emerging. Since 2004 (39.4 million worldwide infections), the global rate of HIV infection appears to be leveling off with 34 million living with HIV worldwide at the end of 2011 (Figure 1.6).
Origin of the AIDS Epidemic

Throughout recorded history, epidemics have sprung up to ravage human populations. In the influenza epidemic of 1918–1919, for example, an estimated 20 to 40 million people died worldwide, a number comparable to mortality rates during the infamous Black Death in Europe in the 1300s. Although the source of the influenza epidemic was never found, other outbreaks of disease have defined origins. For instance, when the Spanish arrived in the Americas in 1520, they brought smallpox with them. The Aztec population of Mexico was without any immunity to this disease, and the raging smallpox epidemic that followed reduced that population by half. The sources of some other epidemics are also clear. When the first European navigators reached South Pacific islands in the 1700s, they found the people robust, happy, and well adapted to their environment. The explorers introduced syphilis, tuberculosis, and whooping cough (pertussis), however, and these diseases swept through the population virtually unchecked. Hawaii was struck especially hard. When Captain Cook landed there in 1778, the island's population was about 300,000; by 1860, it had been reduced to fewer than 37,000.

These examples are somewhat reminiscent of the course of AIDS during the twentieth and twenty-first centuries. The disease seemed to burst on the scene during the early 1980s and spread out from central foci in major cities of the United States and Africa and other parts of the world. Setting aside claims that HIV is an entirely new virus or the product of a genetic engineering laboratory, the prevailing hypothesis among scientists is that the virus existed somewhere in nature and emerged at this particular period in history to infect human populations. In this section, we explore where it may have originated and why it came forth at that particular time.
The Origin of HIV

If we assume that HIV existed somewhere in the world prior to its appearance in humans, then the next logical question is, “Where?” During the mid 1980s, Max Essex of Harvard’s School of Public Health was among the first to provide evidence that HIV originated in African primates such as monkeys, baboons, and chimpanzees. Essex’s research resulted in recovery of a virus called the simian immunodeficiency virus (SIV) from African green monkeys (Figure 1.7a). This virus had enough biochemical similarities to HIV to support the notion that the two viruses are related. Essex and his group theorized that SIV crossed the species barrier to humans through a primate bite or scratch.

Further evidence for a primate–human transmission was offered by evidence that HIV-2 crossed the species barrier to humans from the sooty mangabey, a type of monkey belonging to the species Cercocebus atys (Figure 1.7b). Vanessa Hirsh, a primate researcher at the National Institute of Allergy and Infectious Diseases, established this link in the early 1990s. Hirsh demonstrated that the SIVsm, the SIV strain from the sooty mangabey, has genes nearly identical to those of HIV-2. Research performed by British scientists indicated that SIVsm from the sooty mangabey monkey might have caused six HIV-2 epidemics, which blended together to give the impression of a single West African epidemic.

The research of Essex and Hirsh was expanded and further developed by a host of other scientists, notably the group led by Beatrice Hahn of the University of Alabama at Birmingham. In 1999, Hahn and her coworkers pieced together what was hailed as the best case yet for connecting human HIV to chimpanzees (Figure 1.7c). Their research indicates that different subspecies of chimpanzees harbor different strains of HIV-like viruses and that one particular subspecies is the probable source of the HIV-1 (the “original” HIV) that is causing the current pandemic.

**FIGURE 1.7**

(a) The African green monkey. The simian immunodeficiency virus (SIV), a virus similar to the human immunodeficiency virus, was recovered from such an animal in the mid 1980s. © François Etienne du Plessis/Shutterstock, Inc. (b) The sooty mangabey monkey, believed to be the source of HIV-2 in humans. © Jan van der Hoeven/Shutterstock, Inc. (c) The chimpanzee Pan troglodytes troglodytes, which is believed to be the source of HIV-1 in humans. © Timothy E. Goodwin/Shutterstock, Inc.
Before Hahn’s work, scientists had identified only three chimpanzees infected with SIVs. The strains of SIV in these animals were designated SIV_{cpz}. Then Hahn’s group identified a fourth chimpanzee infected with a strain of SIV_{cpz}. The researchers began an exhaustive and systematic study to examine these SIV strains carefully and the four animals from which they came. The study focused on the nucleic acid of the virus, one of its major chemical components and the substance of which its genes are made. Using sophisticated genetic analyses, Hahn’s group compared the nucleic acid content (the genes) of the four SIV_{cpz} strains with that of various samples of HIV obtained from humans.

The results of the research were the key to the origin of HIV: Three of the four SIV_{cpz} strains were found to be closely related (i.e., 70% to 90% genetically identical) to HIV particles isolated from humans. All three strains came from the chimpanzee subspecies *Pan troglodytes troglodytes*. Significantly, the natural range of the chimpanzee *Pan troglodytes troglodytes* coincides precisely with regions of West Africa where the AIDS epidemic has existed for the longest period of time. The fourth SIV_{cpz} strain had a nucleic acid content (genes) much less similar to that of HIV; importantly, it came from the chimpanzee subspecies *Pan troglodytes schweinfurthii* normally found in far-distant East Africa. Hahn’s group concluded that chimpanzees living in Gabon, Cameroon, and nearby regions of West Africa were the source of HIV-1 in humans. They surmised that once the virus made its way into humans, it mutated into the existing strains scientists now recognize, while adapting normally to its new host. We discuss when this crossover presumably happened in the next section.

Hahn’s research has several key implications, not the least of which is that it apparently resolves the question of HIV’s origin. Moreover, the three SIV strains found in *Pan troglodytes troglodytes* are the presumed forerunners of the three groups of HIV-1 now known to exist. This finding indicates that chimpanzees have been the starting point for at least three independent crossings to humans. It is reasonable to believe that these cross-species transmissions occurred when humans who hunted and butchered chimpanzees for meat were exposed to their blood via a wound or scratch. Moreover, additional transmissions may have occurred and may still be occurring because the hunting and killing of chimpanzees continues in western equatorial Africa.

The significance of the research is further underscored by the observation that chimpanzees in the wild apparently do not develop AIDS, even though the genetic material of humans and chimpanzees is 98.5% identical. Thus, investigators hope to locate a resistance mechanism in the animals that can be applied to humans; however, strengthening the human–chimpanzee link will require finding SIV_{cpz} in wild chimpanzee populations. To do that, a concerted effort will be launched to save these endangered animals for study.

To study the human–primate link further, researchers began to try to determine whether SIV exists in wild baboons and monkeys of varying species. Results reported in 2001 strengthened that link. Investigators led by Beatrice Hahn and Eric Delaporte collected blood samples from 384 wild primates representing 17 species. They found that 18% of the primates harbor SIV antibodies that bind strongly to HIV proteins. The finding indicates that other variants of SIV occur in wild primates and are capable of making the crossover to humans. A collaborative 2010 study led by Preston Marx reported that than more than 40 species of African nonhuman primates were infected by SIV for more than 32,000 years. Thus, for millennia, many subtypes of SIV could continue to pose risks for humans during sporadic encounters as these animals are hunted for meat or kept as pets.

**Origin of the AIDS Epidemic**

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The Jump to Humans

Scientists now generally agree that a strain of SIV made the crossing from chimpanzees to humans and later evolved to the current strains of HIV. Exactly when the crossing occurred is uncertain, but an estimate appears to be provided by analysis of the HIV obtained from the oldest documented case of infection. The analysis shows that the passage to humans probably occurred during the late 1940s or early 1950s.

The research leading to this conclusion was performed by Toufo Zhu of the University of Washington and David Ho of New York’s Aaron Diamond AIDS Research Center. The scientists began with the insight that about 1% of HIV’s genetic material mutates each year. Then they analyzed HIV fragments obtained from the blood of a Bantu man who lived in what is now Kinshasa in the Democratic Republic of the Congo. The blood had been drawn in 1959, shortly before the man died.

Although evidence of HIV had been observed in the man’s blood in 1986 by Max Essex, the methods for studying HIV’s genetic material were not then sophisticated enough to gain much information; but in 1998, Zhu and Ho used state-of-the-art technology to multiply the genetic material of HIV available in the blood many millions of times, thus yielding a sufficient supply to work with. Then, using extensive databases and advanced computers, they compared the genetic material from the 1959 HIV to genetic material from current strains of HIV as well as strains of HIV isolated during many intervening years. The comparisons yielded a “family tree” of HIV, showing the progression of changes occurring in its genetic material over a 39-year period. The data indicated that HIV probably entered the human population after World War II had ended, as noted previously here. This estimate is important because it renders unlikely a hypothesis that the AIDS epidemic originated in the 1950s from contaminated lots of polio vaccine (Box 1.2).

Moreover, the finding is more than a historical footnote. Comparing the 1959 virus with modern forms yields information on how extensively HIV has evolved over the decades and how much it can be expected to evolve in future years. These data helped in linking HIV to SIV in chimpanzees because Hahn’s group could compare the genes of the 1959 virus with those of SIV and search for common features. In addition, identifying when HIV entered the human population puts a time frame on the start of the AIDS epidemic, and by examining social trends of the period, public health officials can understand why the epidemic exploded as rapidly as it did (which we discuss later here).

Finally, knowing about the early form of the virus could conceivably help scientists pinpoint the parts of HIV’s genetic material that have changed the least, a finding that would assist vaccine researchers. One problem in HIV vaccine research is how to produce a vaccine that can be effective against the multiple strains of HIV known to exist. A vaccine based on features common between ancestral and modern forms might prove more universal in fighting a global epidemic than a vaccine based on a combination of modern types.

Genetic analyses like this one are used to calculate the dates when strains of an organism mutate and split off from the ancestral strain. At best, this analysis gives an estimate of when the HIV lineage began to diversify, not necessarily when the virus was transmitted to humans. An example of the uncertainty of the data is illustrated by research reported in 2000. A genetic analysis performed by scientists indicates that the M group of HIV (the group that causes the vast majority of AIDS cases) came into existence in 1931, with a 95% confidence interval of 1915 to 1941. Although this
Controversy Over the Origin of HIV

The controversy apparently began with a 1992 article in *Rolling Stone* magazine by journalist Tom Curtis and gathered momentum with a 1999 book by science writer Edward Hooper entitled, *The River: A Journey to the Source of HIV and AIDS*. Both Curtis and Hooper theorized that the AIDS epidemic was ignited when an oral polio vaccine was tested in the late 1950s on hundreds of volunteers in what is now the Democratic Republic of the Congo. Hooper contended that the vaccine was contaminated with simian immunodeficiency virus (SIV), which infects monkeys, chimpanzees, and other primates. The contamination occurred, according to Hooper’s research, when kidney cells from infected chimpanzees were used to cultivate the poliovirus. In the book, he posits that the earliest cases of AIDS occurred where and when the vaccine was tested.

One of the leaders of the 1950s campaign against polio was Hilary Koprowski from the Wistar Institute in Philadelphia. Answering the hypotheses of Curtis and Hooper, Koprowski maintained that to make the polio vaccine his group had used cells from Asian macaque monkeys rather than chimpanzees. He pointed out that samples of the vaccine were preserved in freezers at the Institute and suggested that they be analyzed.

Three independent laboratories were hired to make the analyses. One laboratory analyzed the DNA in a vaccine sample to determine whether the DNA was from a macaque monkey or a chimpanzee—the results indicated that it was from a macaque monkey. A second laboratory tested the vaccine sample for genes associated with either HIV or SIV—genes for neither virus were found. A third laboratory ran tests duplicating those performed by the other two labs—its results confirmed theirs. Augmenting these results were testimonials from 16 of Koprowski’s collaborators who stated that they never worked with chimpanzee cells. Moreover, evidence from genetic analyses indicates an origin of HIV in humans that predates the 1950s. These analyses also show that chimpanzees from the region where Koprowski worked do not harbor the SIV that was the ancestor of HIV.

In his book, Hooper made the point of calling for analysis of the archived vaccine samples, as Koprowski offered; however, when the results were reported, and even though they countered his hypothesis, Hooper refused to retract his theory. In contrast, *Rolling Stone* printed a “clarification” in 1993, and Koprowski won a lawsuit against the magazine claiming defamation of character.

Out of Africa

Working on the assumption that HIV made the jump from chimpanzees to Africans somewhere between the 1930s and early 1950s, the next question is this: Why did AIDS become such an explosive pandemic in the following years?

No one knows for sure, but historians point out that the 1960s and 1970s were decades of great turmoil in Africa when the epidemic could have easily gathered momentum. Civil wars were commonplace. National boundaries were redrawn, and population shifts were unprecedented. Demographers note that millions of people in Africa changed from an agrarian lifestyle to an urban lifestyle. It is conceivable that infected people moved from remote areas to the cities and brought the virus to these population centers. Sexual intercourse could then have spread the virus rapidly,

Origin of the AIDS Epidemic
especially because those decades saw the emergence of a sexual revolution. Given the roughly 10-year incubation period for the disease, an outbreak in the 1980s appears reasonable. Moreover, a 1988 study indicated that the number of blood samples testing positive for HIV in a city in Zaire increased tenfold in a 10-year span.

Another possibility is that soldiers from Caribbean countries serving as mercenaries in the civil wars could have acquired the virus from remote African populations. The virus may then have made its way to the United States via a Caribbean city. Many people from Haiti, for example, were known to suffer from AIDS early in the epidemic. There is also the possibility that contaminated blood used for transfusions could have been the source of HIV, either by administration to travelers passing through the region or by exportation to other countries.

Most discussions of Africa as the origin of the AIDS virus are bitterly resented by Africans, who do not wish their continent to be thought responsible for the AIDS epidemic. Such discussions have made many African government officials suspicious of foreign scientists and relief organizations and, in some cases, have impeded the flow of information from that continent. To ease tensions, the World Health Assembly passed a 1987 resolution stating that HIV is a “naturally occurring [virus] of undetermined geographic origin.” Writing in 1989, Robert Gallo attempted to diffuse the sensitivity further by suggesting that “tracing the origins of the virus to a particular location doesn’t imply blame—we don’t blame Lyme, Connecticut for Lyme disease.”

Entry into the United States

The AIDS virus was in the United States well before the first cases of AIDS were identified in 1981. The case of a Missouri boy points up this fact (Box 1.3), as does evidence from blood samples frozen and stored in the late 1970s. During that period, more than 7,000 homosexual men came to public health clinics in San Francisco and New York to participate in a government-sponsored study of hepatitis B. They donated blood samples, and researchers preserved many of the vials for study at a later date. A decade passed before the vials of blood were thawed and tested for evidence of HIV.

The results reported in 1987 revealed some interesting patterns: Of 6,700 participants in the San Francisco area, at least 70% had blood samples positive for exposure to HIV; more than 600 of the participants had AIDS, and about 400 of the 600 had already died.

The results provided substantial evidence that HIV was in the United States well before the first cases of AIDS showed up in 1981. Moreover, the results revealed how rapidly the disease was spreading among men who have sex with men: Of blood samples donated in 1978, 3% had evidence of exposure to HIV; of those donated in 1979, 12% showed HIV exposure, and by 1981, 45% were HIV positive. It was clear that the epidemic was gathering steam even before public health agencies recognized its existence.

How the AIDS virus entered the United States is still unknown. One possible source is contaminated blood imported from another country (Figure 1.8). Another possibility is sexual contact by Americans with foreigners harboring HIV. Sharing contaminated syringes and needles with infected injection drug users is a third possibility.

Another possible mode of entry into the United States may involve Haiti. Scientists have theorized that cultural exchanges between Zaire and Haiti, both French-speaking countries, offered possibilities for transporting the virus from Africa. American homosexual men vacationing in Haiti could then have acquired the virus and brought it to the United States. This view is supported by the observation that
Although the “official” beginning of the AIDS epidemic in the United States is considered to be June 1981, there is evidence that AIDS may have made its appearance as early as 1969. The basis for this belief is a report published in October 1987. In the report, researchers related the case of Robert R., a 16-year-old boy from Missouri, who may have died of AIDS-related causes in 1969.

The researchers told of the teenager who came to St. Louis City Hospital in 1968 with substantial swelling of the legs and genital organs and an impaired immune system. A bacterial disease named Chlamydia was diagnosed, and Robert was put on a regimen of antibiotics; however, the drugs did not work. In the ensuing weeks, his muscles wasted away. His lungs filled with fluid (an unmistakable sign of pneumonia), and he died in May 1969. During the subsequent autopsy, pathologists found in his organs the purplish lesions of Kaposi’s sarcoma, a type of cancer now known to be related to AIDS.

Unable to locate a microbial cause for Robert’s death, doctors froze samples of his blood and tissues, hoping that someday the mystery could be solved. In June 1986, the samples were sent to Tulane University for analysis for HIV. Virologists at the university found that Robert R.’s blood reacted with all nine chemical markers for HIV. There was little question that the virus had been present in the boy’s blood.

Is it possible that the AIDS virus may have been in the United States in a less lethal form in the 1960s? Perhaps so, believe some researchers, but they also question where that virus is today. Did all of that less lethal virus simultaneously mutate to a more lethal form? Not likely is the opinion of most. What, then, would explain the more than 10-year lapse before the epidemic’s breakout? Thus far there is no answer.
AIDS was present in Haitians as well as in American homosexual men in the 1980s; however, AIDS may have been introduced to Haiti by North Americans. The evidence that American men were exposed to AIDS before Haitians bolsters this view. Rather than a source, Haiti may have been a recipient of the virus. This question was finally answered in 2010 by Michael Woroby's collaborative research.

By 2010, technology was available to create viral gene trees to further investigate the hypotheses as to how HIV/AIDS began its world travels into the Americas. Teams led by Woroby conducted a molecular analysis on archived blood samples (collected in 1982–1983) from five Haitian AIDS patients. All of the patients recently immigrated to the United States and were among the first recognized as AIDS victims. Their genetic data suggests that HIV came out of Africa, then to Haiti in 1966, and subsequently to the United States. Most of the circulating viruses can be traced to a viral relative that came from Haiti around 1969. This explains why there were early observations of a high prevalence of AIDS in Haiti. Haiti became the popular sex tourism destination for gay men in the mid-1970s as well as the stepping-stone that allowed HIV-1 to flourish and spread to the United States and other countries. The current HIV status in the United States is in the Mapping HIV box.

### Mapping HIV

**United States**
The annual number of new HIV infections has stabilized.

| 1.2 million people are living with HIV | 1.4% of the prison population lives with HIV or AIDS (21,987 in 2008) |
| 1 in 5 (20%) are unaware of their infection | HIV/AIDS diagnosis in seniors (persons over 50 years of age) is increasing |
| ~50,000 new infections/year | Florida has the highest number of people living with HIV: 90,909 in 2009 |
| ~13 children under the age of 13 were diagnosed in 2009 | States with the highest total number of people diagnosed with HIV (2009) are: New York, California, Florida |
| ~60% of new infections occur in gay and bisexual men | States with the least total number of people diagnosed with HIV (2009) are: North Dakota, Wyoming, Montana |
| 20–24 years of age group has the highest number of new diagnoses (6,237 in 2009) | By race, blacks/African Americans face the most severe burden of HIV (10,800 MSM* new infections in 2009) |

*MSM: gay, bisexual, and other men who have sex with men*


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### The First Decades and Beyond

In late 2000, health officials from the UNAIDS made a startling prediction: They announced that if current trends continued, deaths associated with AIDS could exceed those of the Great Plague of the 1300s (the Black Death) and the catastrophic worldwide influenza epidemic of 1918–1919. AIDS would then become the deadliest contagion in world history. As of 2006, estimates are that nearly 25 million people...
have died from AIDS since 1985. In 2007, nearly 2.5 million died from AIDS and that annual number seems to have stabilized, suggesting that in the next 5 to 10 years, HIV may very well have claimed more lives than any other single infectious agent.

**Thirty-Plus Years of AIDS**

In the more than 30 years since MMWR carried the first report of pneumocystosis in immune-deficient individuals, the statistics attending the AIDS epidemic have reflected the emergence of a major health crisis. One of the first notable benchmarks was reached in the August 18, 1989 issue of MMWR, when the CDC reported that more than 100,000 cases of AIDS had been diagnosed in the United States through July 1989. AIDS-related deaths had reached about 60,000. The CDC also pointed out that the first 50,000 cases of AIDS were reported from 1981 to late 1987 (six years) and the second 50,000 cases between December 1987 and July 1989 (1.5 years). AIDS had become a major cause of illness and death among children and young adults in the United States; in 1988, it ranked 15th among the leading causes of death for Americans.

By 1989, homosexual and bisexual men were still accounting for most reported AIDS cases, but injection drug users, their sexual contacts, and their children represented an increasing proportion of all cases. For example, 63% of AIDS cases occurred in homosexual men before 1985, but only 56% of new cases did in 1989. In contrast, injection drug users accounted for 18% of cases in 1985, but this percentage rose to 23% by 1989. The number of women involved was also rising: Before 1985, only 7% of AIDS cases were in women, but in 1989, the number rose to 11%.

In the January 23, 1991 issue of MMWR, the CDC updated its statistics. By that time, more than 100,000 persons had died of AIDS (compared with 100,000 cases in 1989). Among American men aged 25 to 44 years, AIDS had become the second leading cause of death, surpassing heart disease, cancer, and suicide. For women aged 25 to 44, AIDS was projected to be among the top five causes of death. By 1995, the prediction had become reality, and AIDS was the leading cause of death in women in 15 U.S. cities.

Things began to change in 1996, however. That year, new optimism surfaced with the news that protease inhibitors, a class of drugs that complement azidothymidine (AZT), could be used to reduce blood concentrations of HIV to undetectable levels. Also that year, investigators uncovered striking new clues about how HIV binds to host cells—clues that kindled hopes for new therapies, especially because a genetic defect that prohibits binding apparently makes some individuals immune to AIDS. These advances in therapeutic and basic research were augmented by development of a new test—the viral load test—which uses state-of-the-art biotechnology to measure precisely the number of HIV particles in a sample of blood. This direct measurement of infection is far superior to measurements of host cell destruction for gauging a patient’s response to drugs or predicting long-term survival. The optimistic mood of 1996 marked a turning point in the battle against AIDS and persuaded the editors of *Science* magazine to name the collection of advances as the Breakthrough of the Year. 1997 was the last year-to-date that HIV/AIDS appeared in the top 15 causes of deaths in Americans.

By December 1999, the AIDS epidemic had been affecting the United States for over two decades. As the world celebrated the closing of the twentieth century, the CDC reported that there had been a total of 733,374 AIDS cases in the United States since the first case were recorded in 1981. Of this total, 81% of cases had occurred in men, 18% in women, and 1% in children. Statisticians noted that the epidemic was
shifting toward a growing percentage of cases in women, African Americans, and Hispanic Americans, and that a decreasing percentage was occurring in homosexual men. Despite this statistic, homosexual men continue to remain the largest single exposure group. In addition to the confirmed cases, almost a million individuals were living with HIV in 1999 but remained undiagnosed. Over 425,000 had died of AIDS-associated illnesses.

In the United States, the good news at the end of the century was the steep decline in AIDS in newborns. AIDS cases in newborns reached a peak in 1992, leveled off during 1993, and then began a dramatic drop-off in 1994 that continues today, as Figure 1.9 shows. The most apparent reason was improved diagnosis of HIV infection in pregnant women combined with rapid implementation of therapy with AZT to prevent transmission from mother to child. AZT interferes with the replication of HIV in infected cells. Improved treatment of HIV-infected newborns is another notable reason for the decrease because the treatment delays the progression from HIV infection to AIDS.

In the rest of the world at the end of the century, however, the news was much grimmer. Worldwide, the UNAIDS reported in 2007 that over 36 million people were living with HIV or experiencing AIDS and that an astounding 4.1 million had become infected that year. Already, over 25 million individuals have died from AIDS-related causes since the beginning of the pandemic, with roughly 2.4 million deaths in 2007 alone. Roughly 67% of all individuals who are infected with HIV are from sub-Saharan Africa.

As the new century opened, the AIDS crisis in the United States had lessened. To some observers, the disease had practically dropped off the proverbial radar screen. Many people infected with HIV were living almost normal lives thanks to a sophisticated combination of anti-HIV drugs. Moreover, the infection rate had leveled off and even declined for some groups (although it was rising for others), and the public was becoming somewhat complacent about the epidemic. Public health officials warned that, despite the level rate of approximately 35,000 new infections per year in 2006, in the foreseeable future, AIDS will continue to affect homosexual men while becoming more prevalent among poor African-American and Hispanic-American heterosexuals.
living in the inner cities. Contributing to this prediction is the observation that the rate at which homosexual men contract AIDS has reached a plateau, whereas the rate has risen dramatically among injection drug users, particularly those of minority groups. In New York City, for instance, in a recent year, four of five AIDS cases attributed to sharing needles occurred among African-American and Hispanic-American individuals. Public health officials stress that fighting the spread of AIDS among drug addicts and their sex partners will require significant increases in drug treatment programs as well as education programs that target poor urban areas.

As we have noted, the situation was much different in Africa: AIDS was threatening to be more devastating than civil wars and famines put together. Each day at the turn of the century, between 6,000 and 7,000 people in sub-Saharan Africa were dying of the effects of AIDS, and public health scientists estimated that HIV had infected over 35 million adults. Those numbers remain high, with roughly 5,500 deaths daily in 2007 in sub-Saharan Africa. This death rate is drastically affecting life expectancy in sub-Saharan Africa, and Figure 1.10 shows some of the alarming projections related to the AIDS epidemic in 2009.

![Figure 1.10](image_url)

The devastating long-term effects of HIV/AIDS. (a) The number of people living with HIV in Eastern Europe and Central Asia is increasing. (b) Trends in women living with HIV. (c) The number of children living with HIV in Eastern Europe and Central Asia is increasing. Data from 2010 Global Report: UNAIDS Report on the Global AIDS Epidemic (UNAIDS).
In the early 1980s, AIDS was an unknown entity, shrouded in uncertainty and conjecture, but the disease began to reveal itself through the mid and late 1980s when the scientific base of information expanded (Table 1.1). We do not understand major aspects of the interaction of HIV with the infected individual, nor do we fully comprehend the nature of the host response.

**Table 1.1 A Brief Chronology of the AIDS Epidemic**

<table>
<thead>
<tr>
<th>Date</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>June 5, 1981</td>
<td>Five cases of <em>Pneumocystis</em> pneumonia reported in the CDC's MMWR</td>
</tr>
<tr>
<td>December 1981</td>
<td><em>Pneumocystis</em> pneumonia reported in New York City drug addicts</td>
</tr>
<tr>
<td>June 11, 1982</td>
<td>365 cases of immune deficiency reported from five states in United States</td>
</tr>
<tr>
<td>September 3, 1982</td>
<td>The name acquired immune deficiency syndrome (AIDS) coined</td>
</tr>
<tr>
<td>Early 1983</td>
<td>16 countries reporting AIDS; 34 states in United States with AIDS cases</td>
</tr>
<tr>
<td>April 1983</td>
<td>Research groups led by Gallo and Montagnier independently report discovery of AIDS virus</td>
</tr>
<tr>
<td>May 1985</td>
<td>Blood test for AIDS antibody made available</td>
</tr>
<tr>
<td>August 1986</td>
<td>AIDS virus named human immunodeficiency virus (HIV)</td>
</tr>
<tr>
<td>1987</td>
<td>Azidothymidine (AZT) licensed for use in AIDS patients; AIDS vaccine research ongoing</td>
</tr>
<tr>
<td>July 1989</td>
<td>100,000 cases of AIDS in United States; 60,000 deaths in United States from AIDS and complications</td>
</tr>
<tr>
<td>January 1991</td>
<td>501,310 cumulative cases of AIDS in United States; 311,381 deaths</td>
</tr>
<tr>
<td>October 31, 1995</td>
<td>100,000 cumulative deaths associated with AIDS in United States</td>
</tr>
<tr>
<td>1996</td>
<td>Protease inhibitors licensed for use in United States; new discoveries on HIV binding to host cells; new HIV detection tests approved; declining number of cases in newborns</td>
</tr>
<tr>
<td>2003</td>
<td>AIDSvax, the first AIDS vaccine tested in a large number of people, fails to show protection</td>
</tr>
<tr>
<td>2004</td>
<td>Over 500,000 cumulative deaths due to AIDS in the United States; 4.9 million new HIV infections worldwide; 3.1 million deaths due to AIDS worldwide; approximately 40 million people living with HIV/AIDS worldwide</td>
</tr>
<tr>
<td>2006</td>
<td>Over 1.0 million cumulative cases of HIV/AIDS in the United States, and over 5 million total deaths due to AIDS in the United States</td>
</tr>
<tr>
<td>2007</td>
<td>MRK-Ad5, an HIV/AIDS vaccine, fails in phase III trials</td>
</tr>
<tr>
<td>2009</td>
<td>Gero Hütter and colleagues published the results of a rare bone-marrow transplantation that has apparently cured an HIV-positive man of AIDS</td>
</tr>
<tr>
<td>2009</td>
<td>In 33 countries, HIV incidence fell by more than 25% between 2001 and 2009</td>
</tr>
<tr>
<td>2010</td>
<td>Approximately 6.6 million people have access to AIDS medications</td>
</tr>
<tr>
<td>2012</td>
<td>FDA approves Truvada to use as a preventative measure for people who are at high risk of acquiring HIV through sexual activity</td>
</tr>
<tr>
<td>2012</td>
<td>FDA panel backs first rapid, over-the-counter home HIV test</td>
</tr>
</tbody>
</table>
Now, in the first decades of the twenty-first century, our vision of AIDS is clearer, although far from perfectly in focus. The first three decades of research brought hopes of great advances but no effective vaccine. But our society’s ability to alter risk-taking behaviors is still limited. In 2012, the U.S. Food and Drug Administration (FDA) approved the antiviral Truvada to use as a preventative measure for people who are at high risk of acquiring HIV through sexual activity. HIV testing is one of the most important means to slow new infections. In 2012, a 17-member FDA board unanimously recommended approval of the first, rapid, over-the-counter OraQuick in-home HIV test for sale in pharmacy stores and online to anyone age 17 and older. A single use test costs $39.99. It uses a sample of fluid from the mouth for testing. Results are obtained within 20–40 minutes but additional testing should be done in a medical setting to confirm a positive result.

In 2009, the first HIV positive patient was cured of AIDS by a rare bone-marrow transplantation. Two more similar cases of “cured” patients were presented at the International AIDS conference held in Washington D.C. in 2012. Also, in 2012, the cancer drug vorinostat was reported to target dormant HIV to come out of hiding or dormancy, potentially allowing antivirals to combat the viral infection.

According to the 2011 UNAIDS World AIDS Day Report, we are on the verge of a significant breakthrough in the AIDS response. New HIV infections are falling and more people are starting treatment. The number of people dying of AIDS-related illnesses fell to 1.8 million in 2010 (down from 2.2 million in 2005). Only a few countries do not fit this overall trend. Five of these countries are in Eastern Europe and Central Asia. AIDS incidence has increased by more than 25% between 2001 and 2009 in these countries. This incidence is correlated with intravenous drug use, especially use of homemade heroin.

Wealthier nations must continue to make important scientific and medical strides toward understanding the biology of HIV and preventing AIDS and, second, then deliver this information, medicine, and biotechnology to the regions of the world most affected by HIV. Finally, those populations at particular risk for increasing rates of HIV infection—intravenous drug injectors, the economically underprivileged, and women—must be the focus of education, liberation, medical care, and preventative medicine. Public health officials wonder what hope the poorer nations have and what the economic impact of the pandemic will be. Can the rise of the relative infection rate in women be brought to a plateau or reduced? Can the United States keep HIV from broadening its net? As you read the pages ahead, try to bear in mind that the history of AIDS is being written minute by minute. Answers to some of these questions are probably emerging as you read.

Looking Back

In the early 1980s, AIDS was compared with an elephant being examined by blind men because scientists and public health officials were ignorant of the disease’s cause, transmission, symptoms, and other characteristics. Reports beginning in June 1981 made it clear that suppression of the immune system was occurring in homosexual men and that diseases not ordinarily considered dangerous had led to death in many of these men. Similar symptoms were later observed in injection drug users, blood transfusion recipients, hemophiliacs, heterosexual individuals, and newborns.

Many theories purporting to explain the cause of AIDS existed in the early 1980s, but in April 1984, a virus was identified as the agent. The discoverers were members of a group headed by Luc Montagnier of France. Though initially called HTLV-III/LAV, the virus was renamed human immunodeficiency virus (HIV) in 1986 on the
recommendation of an international commission. Another AIDS virus called HIV-2 has been identified in people from West Africa. The disease it causes seems to be milder than that caused by the original HIV, now known as HIV-1.

AIDS was recognized as a global problem as early as 1985. The African continent has been particularly hard-hit, with high infection rates in sub-Saharan Africa. Researchers believe that HIV-1 originated in chimpanzees of the subspecies *Pan troglodytes troglodytes* and was probably passed to humans via a scratch or bite from one of these animals. The crossover to humans occurred at least three times, probably in the late 1940s or early 1950s, although some dispute remains about the exact timing. The possibility that HIV was introduced to human populations through tests of polio vaccines has been discounted. Decades of turmoil in Africa encouraged the virus to spread to the remaining world.

By the beginning of the twenty-first century, more than 700,000 cases of AIDS had been reported in the United States, but there was hope of forestalling the epidemic because a cocktail of drugs used since 1996 was shown to decrease the number of deaths associated with AIDS. Moreover, studies indicate that when azidothymidine (AZT) is used in HIV-infected pregnant women, the transmission of HIV to their newborns can be interrupted. Furthermore, the percentage of AIDS cases in sexually active homosexual men was dropping, but the percentage in injection drug users and women was rising. The AIDS elephant is becoming visible after two decades of discoveries, but some of its features, such as its susceptibility to a preventative vaccine, remain obscure.

For the first time in 22 years, the world’s largest international AIDS conference convened in Washington D.C. in July 2012. This was possible because the travel ban against HIV-positive people from entering the United States had been lifted by President Barack Obama in 2010. The main worrisome issues confronting the AIDS epidemic included: a global economic recession that which threatened the dollars needed to invest in science, medicine, and education to fight AIDS; getting medication to the poor (including in the United States); treating more pregnant women so they won’t spread HIV to their babies; and ways to urge the public and policy makers to pay attention to the disease. The theme of the conference, *Turning the Tide Together*, captured the idea that we now have the potential to change the course of HIV and AIDS if we can scale up intervention and continue the scientific momentum for a cure and vaccine.

### Healthline Q & A

**Q1** Exactly what is AIDS?

* A defining AIDS can be difficult because AIDS is a complex disease. Basically, AIDS is an infectious disease in which a virus attacks cells of the immune system and thereby renders the body susceptible to microorganisms that otherwise would be held in check. Symptoms of AIDS can be very general (fever, weight loss, night sweats, and diarrhea), or they can be more specific (pneumonia and skin cancer). Multiple stages of AIDS are recognized, beginning with infection by the virus, progressing to “early AIDS,” and culminating with full-blown AIDS.

**Q2** I’ve heard that AIDS is caused by a virus. What is that?

* A virus is one of the smallest microorganisms known. It consists of a segment of nucleic acid (such as DNA or RNA) surrounded by a coat of protein and, in some cases, an enclosing membrane. Viruses do not grow, use food, or perform any metabolic processes associated with living things. Inside cells, however, they multiply very efficiently.
Q3 **Exactly what is the immune system?**

A. The immune system is a network of cells and a group of chemical compounds largely responsible for the body’s defense against infectious disease, cancer, and other maladies. The system is distributed throughout the body, primarily in the spleen and the lymph nodes of the neck, armpits, and groin. Certain cells of the immune system produce highly specific proteins known as antibodies, which interact with and neutralize microorganisms. Other immune system cells attack microorganisms directly.

**REVIEW**

This chapter explored the development of the AIDS epidemic during two decades, touching on its origin, method of spread, and magnitude. To test your knowledge of these concepts, consider the following statements. Write T for “true” if a statement is correct as it stands. If the statement is false, change the underlined word or phrase to correct the statement. The correct answers are listed elsewhere in the text.

1. Although the agent responsible for AIDS was probably in the United States during the 1970s, the “official” beginning of the AIDS epidemic in the United States occurred in 1991.
   - **T**

2. Two diseases that physicians commonly observe in AIDS patients are *Pneumocystis* pneumonia and a form of skin cancer known as *adenocarcinoma*.
   - **T**

3. It is now generally recognized that AIDS is caused by a *virus*.
   - **T**

4. One of the important modes of transmission for the human immunodeficiency virus (HIV) is contaminated food.
   - **F**

5. AIDS is a disease that occurs in homosexual men as well as in injection drug users.
   - **T**

6. In France, the research team that confirmed the identity of the AIDS virus was led by Bernard Schwartlander.
   - **T**

7. The AIDS virus, originally designated HTLV-III/LAV, is now known by the acronym HIV.
   - **T**

8. Since the introduction of blood tests for AIDS, the number of transfusion-linked cases of AIDS has increased sharply.
   - **T**

9. Because of its global involvement, the AIDS epidemic is more properly termed an AIDS endemic.
   - **T**

10. By 1989, the number of cases of AIDS diagnosed in the United States had passed 1 million.
    - **T**

11. A global program to combat the spread of AIDS has been established by the World Health Organization.
    - **T**

12. One theory relating to the origin of the AIDS virus suggests that it may have existed in African *birds* before being transmitted to humans.
    - **T**
13. The form of AIDS caused by HIV-2 appears to be deadlier than the form caused by HIV-1.

14. The current research thinking is that epidemics of AIDS due to HIV-2 originated from SIV in the sooty mangabey monkey.

15. At the beginning of the twenty-first century, the AIDS pandemic was particularly severe on the continent of Africa.

FOR ADDITIONAL READING


