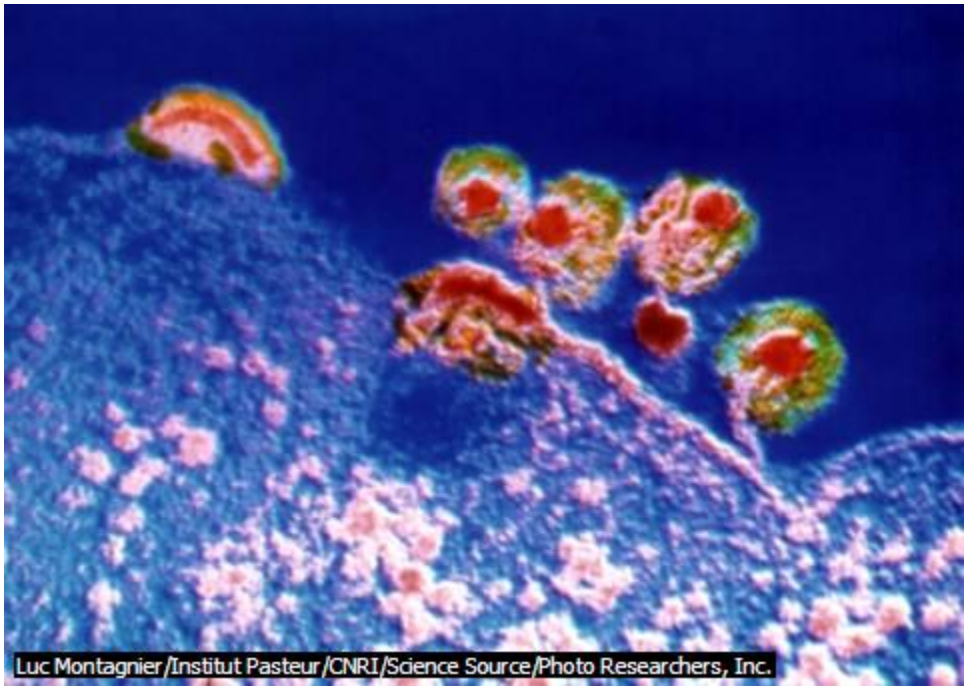
HIV EXAMINER

A Monthly Newsletter of Writers Against Aids and Tobacco Smoking

February Edition

ACQUIRED IMMUNODEFICIENCY SYNDROME

I Introduction



Human Immunodeficiency Virus

The human immunodeficiency virus (HIV), which causes acquired immunodeficiency syndrome (AIDS), principally attacks CD4 T-cells, a vital part of the human immune system. As a result, the body's ability to resist opportunistic viral, bacterial, fungal, protozoal, and other infection is greatly weakened. Pneumocystis carinii pneumonia is the leading cause of death among people with HIV infection, but the incidence of certain types of cancers such as B-cell lymphomas and Kaposi's sarcoma is also increased. Neurological complications and dramatic weight loss, or "wasting," are characteristic of endstage HIV disease (AIDS). HIV can be transmitted sexually; through contact with contaminated blood, tissue, or needles; and from mother to child during birth or

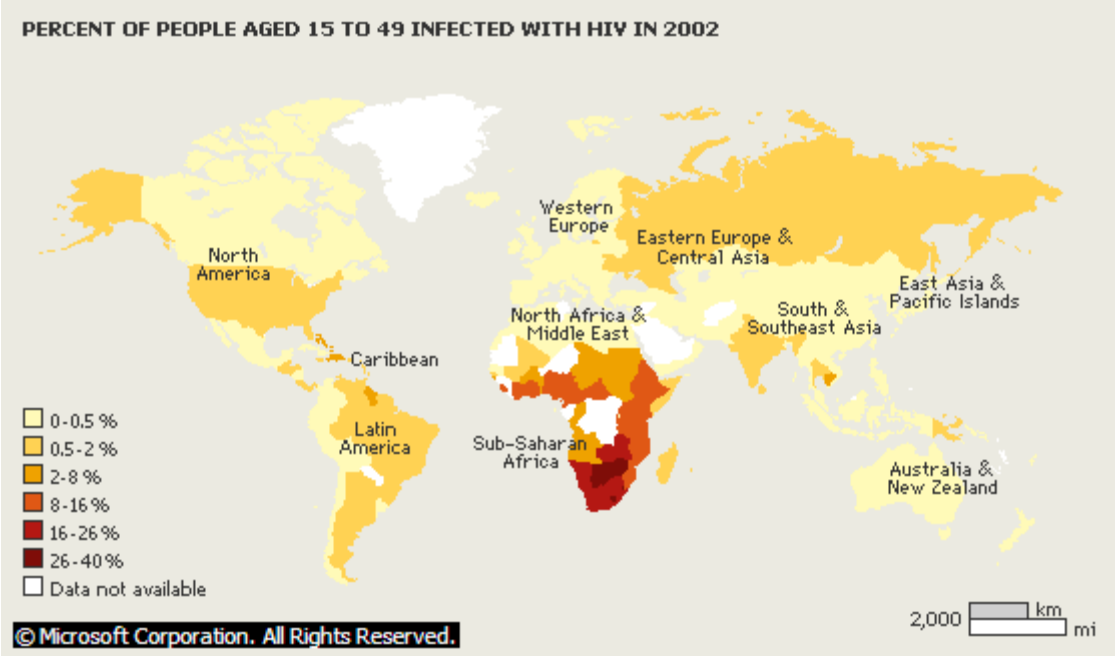
breastfeeding. Full-blown symptoms of AIDS may not develop for more than 10 years after infection.

Luc Montagnier/Institut Pasteur/CNRI/Science Source/Photo Researchers, Inc.

Acquired Immunodeficiency Syndrome (AIDS), human viral disease that ravages the immune system, undermining the body's ability to defend itself from infection and disease. Caused by the human immunodeficiency virus (HIV), AIDS leaves an infected person vulnerable to opportunistic infections—infection by microbes that take advantage of a weakened immune system. Such infections are usually harmless in healthy people but can prove life-threatening to people with AIDS. Although there is no cure for AIDS, new drugs are available that can prolong the life spans and improve the quality of life of infected people.

Transmission of HIV—the AIDS-causing virus—occurs most commonly as a result of sexual intercourse. HIV also can be transmitted through transfusions of HIV-contaminated blood or by using a contaminated needle or syringe to inject drugs into the bloodstream. Infection with HIV does not necessarily mean that a person has AIDS. Some people who have HIV infection may not develop any of the clinical illnesses that define the full-blown disease of AIDS for ten years or more. Physicians prefer to use the term *AIDS* for cases where a person has reached the final, life-threatening stage of HIV infection.

II PREVALENCE OF AIDS



A Global Epidemic

More than 42 million people around the world are currently infected with human immunodeficiency virus (HIV), the virus that causes acquired immunodeficiency syndrome (AIDS). New HIV infections have leveled off or even declined in most developed countries, but the virus is spreading rapidly through much of the developing world. In some areas of sub-Saharan Africa, one in four adults is carrying the virus.

AIDS is one of the deadliest epidemics in human history. It was first identified in 1981 among homosexual men and intravenous drug users in New York and California. Shortly after its detection in the United States, evidence of AIDS epidemics grew among heterosexual men, women, and children in sub-Saharan Africa. AIDS quickly developed into a worldwide epidemic, affecting virtually every nation. The United Nations Program on HIV/AIDS (UNAIDS) estimates that the worldwide number of new cases of HIV infection peaked in the late 1990s with more than 3 million people newly infected each year. However, some regions of the world, especially Vietnam, Indonesia, and other countries in southeast Asia, continued to see an increase in the early 2000s. In addition,

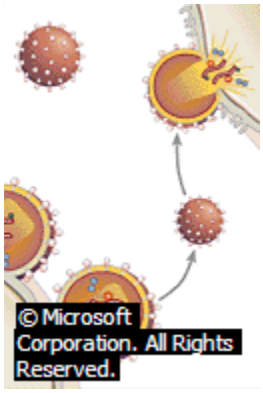
the number of people living with HIV or AIDS has continued to rise as the result of new drug treatments that lengthen life.

While cases of AIDS have been reported in every nation of the world, the disease affects some countries more than others. About 90 percent of all HIV-infected people live in the developing world. AIDS has struck sub-Saharan Africa particularly hard. Two-thirds of all people living with HIV infection reside in African countries south of the Sahara, where AIDS is the leading cause of death.

In countries hardest hit, AIDS has sapped the population of young men and women who form the foundation of the labor force. Most die while in the peak of their reproductive years. Moreover, the epidemic has overwhelmed health-care systems, increased the number of orphans, and caused life expectancy rates to plummet. These problems have reached crisis proportions in parts of the world already burdened by war, political upheaval, or unrelenting poverty.

For statistics on AIDS and HIV cases in the United States and other countries, see the tables in this article.

III CAUSE OF AIDS



Life Cycle of Human Immunodeficiency Virus

The human immunodeficiency virus (HIV), the cause of acquired immunodeficiency syndrome (AIDS), is genetically programmed to do one thing: highjack the reproductive

machinery of a human cell, then trick it into churning out as many copies of the virus as it can before the cell dies. The current best hope for the treatment of AIDS requires that patients take a number of different drugs, each of which interferes with certain steps of the HIV infection process.

AIDS is the final stage of a chronic infection with the human immunodeficiency virus. There are two types of this virus: HIV-1, which is the primary cause of AIDS worldwide, and HIV-2, found mostly in West Africa. Inside the body HIV enters cells of the immune system, especially white blood cells known as T cells. These cells orchestrate a wide variety of disease-fighting mechanisms. Particularly vulnerable to HIV attack are specialized "helper" T cells known as CD4 cells. When HIV infects a CD4 cell, it commandeers the genetic tools within the cell to manufacture new HIV virus. The newly formed HIV virus then leaves the cell, destroying the CD4 cell in the process. No existing medical treatment can completely eradicate HIV from the body once it has infected human cells.

The loss of CD4 cells endangers health because these cells help other types of immune cells respond to invading organisms. The average healthy person has over 1,000 CD4 cells per microliter of blood. In a person infected with HIV, the virus steadily destroys CD4 cells over a period of years, diminishing the cells' protective ability and weakening the immune system. When the density of CD4 cells drops to 200 cells per microliter of blood, the infected person becomes vulnerable to AIDS-related opportunistic infections and rare cancers, which take advantage of the weakened immune defenses to cause disease.

IV HOW HIV INFECTION SPREADS

Scientists have identified three ways that HIV infections spread: sexual intercourse with an infected person, contact with contaminated blood, and transmission from an infected mother to her child before or during birth or through breast-feeding.

A Sex with an Infected Person

HIV transmission occurs most commonly during intimate sexual contact with an infected person, including genital, anal, and oral sex. The virus is present in the infected person's semen or vaginal fluids. During sexual intercourse, the virus gains access to the bloodstream of the uninfected person by passing through openings in the mucous membrane—the protective tissue layer that lines the mouth, vagina, and rectum—and through breaks in the skin of the penis. In the United States and Canada, HIV is most commonly transmitted during sex between men, but the incidence of HIV transmission between men and women has rapidly increased. In most other parts of the world, HIV is most commonly transmitted through heterosexual sex.

B Contact with Infected Blood

Direct contact with HIV-infected blood occurs when people who use heroin or other injected drugs share hypodermic needles or syringes contaminated with infected blood. Sharing of contaminated needles among intravenous drug users has been a primary cause of HIV infection in parts of eastern Europe and central Asia.

Less frequently, HIV infection results when health professionals accidentally stick themselves with needles containing HIV-infected blood or expose an open cut to contaminated blood. Some cases of HIV transmission from transfusions of infected blood, blood components, and organ donations were reported in the 1980s. Since 1985 government regulations in the United States and Canada have required that all donated blood and body tissues be screened for the presence of HIV before being used in medical procedures. As a result of these regulations, HIV transmission caused by contaminated

blood transfusion or organ donations is rare in North America. However, the problem continues to concern health officials in sub-Saharan Africa.

C Mother-to-Child Transmission

HIV can be transmitted from an infected mother to her baby while the baby is still in the woman's uterus or, more commonly, during childbirth. The virus can also be transmitted through the mother's breast milk during breast-feeding. Mother-to-child transmission accounts for 90 percent of all cases of AIDS in children. Mother-to-child transmission is particularly prevalent in Africa.

D Misperceptions About HIV Transmission

The routes of HIV transmission are well documented by scientists, but health officials continually grapple with people's unfounded fears concerning the potential for HIV transmission by other means. HIV differs from other infectious viruses in that it dies quickly if exposed to the environment. No evidence has linked HIV transmission to casual contact with an infected person, such as a handshake, hugging, or kissing, or even sharing dishes or bathroom facilities. Studies have been unable to identify HIV transmission from modes common to other infectious diseases, such as an insect bite or inhaling virus-infected droplets from an infected person's sneeze or cough.

V SYMPTOMS OF AIDS

Without medical intervention, AIDS progresses along a typical course. Within one to three weeks after infection with HIV, most people experience flu-like symptoms, such as fever, sore throat, headache, skin rash, tender lymph nodes, and a vague feeling of discomfort. These symptoms last one to four weeks. During this phase, known as acute retroviral syndrome, HIV reproduces rapidly in the blood. The virus circulates in the blood throughout the body, particularly concentrating in organs of the lymphatic system.

The normal immune defenses against viral infections eventually activate to battle HIV in the body, reducing but not eliminating HIV in the blood. Infected individuals typically enter a prolonged asymptomatic phase, a symptom-free period that can last ten years or more. While persons who have HIV may remain in good health during this period, HIV continues to replicate, progressively destroying the immune system. Often an infected person remains unaware that he or she carries HIV and unknowingly transmits the virus to others during this phase of the infection.

When HIV infection reduces the number of CD4 cells from around 500 to 200 per microliter of blood, the infected individual enters an early symptomatic phase that may last a few months to several years. HIV-infected persons in this stage may experience a variety of symptoms that are not life-threatening but may be debilitating. These symptoms include extensive weight loss and fatigue (wasting syndrome), periodic fever, recurring diarrhea, and thrush, a fungal mouth infection. An early symptom of HIV infection in women is a recurring vaginal yeast infection. Unlike earlier stages of the disease, in this early symptomatic phase the symptoms that develop are severe enough to cause people to seek medical treatment. Many may first learn of their infection in this phase.

A Opportunistic Infections

If CD4 cell levels drop below 200 cells per microliter of blood, the late symptomatic phase develops. This phase is characterized by the appearance of any of the opportunistic infections and rare cancers known as AIDS-defining conditions. The onset of these illnesses is a sign that an HIV-infected person has developed full-blown AIDS. Without medical treatment, this stage may last from several months to years. The cumulative effects of these illnesses usually cause death.

Often the first opportunistic infection to develop is pneumocystis pneumonia, a lung infection caused by the fungus *Pneumocystis carinii*. This fungus infects most people in

childhood, settling harmlessly in the lungs where it is prevented from causing disease by the immune system. But once the immune system becomes weakened, the fungus can block the lungs from delivering sufficient oxygen to the blood. The lack of oxygen leads to severe shortness of breath accompanied by fever and a dry cough.

In addition to pneumocystis pneumonia, people with AIDS often develop other fungal infections. Up to 23 percent of people with AIDS become infected with fungi from the genus *Cryptococcus*, which cause meningitis, inflammation of the membranes that surround the brain. Infection by the fungus *Histoplasma capsulatum* affects up to 10 percent of people with AIDS, causing general weight loss, fever, and respiratory complications.

Tuberculosis, a severe lung infection caused by the bacterium *Mycobacterium tuberculosis*, typically becomes more severe in AIDS patients than in those with a healthy immune system. Between the 1950s and the late 1980s, tuberculosis was practically eradicated in North America. In the early 1990s, doctors became alarmed when incidence of the disease dramatically escalated. This resurgence was attributed to the increased susceptibility to tuberculosis of people infected with HIV. Infection by the bacterium *Mycobacterium avium* can cause fever, anemia, and diarrhea. Bacterial infections of the gastrointestinal tract contribute to wasting syndrome.

Opportunistic infections caused by viruses, especially members of the herpesvirus family, are common in people with AIDS. One of the herpesviruses, cytomegalovirus (CMV), infects the retina of the eye and can result in blindness. Another herpesvirus, Epstein-Barr virus (EBV), may cause certain types of blood cancers. Infections with herpes simplex virus (HSV) types 1 or 2 may result in sores around the mouth, genital area, or anus.

Many people with AIDS develop cancers. The destruction of CD4 cells impairs the immune functions that halt the development of cancer. Kaposi's sarcoma is a cancer of blood vessels caused by a herpesvirus. This cancer produces purple lesions on the skin,

which can spread to internal organs and cause death. B cell lymphoma affects certain cells of the lymphatic system that fight infection and perform other vital functions. Cervical cancer is more common in HIV-infected women than in women free from infection.

A variety of neurological disorders are common in the later stage of AIDS. Collectively called HIV-associated dementia, they develop when HIV or another microbial organism infects the brain. The infection produces degeneration of intellectual processes such as memory and, sometimes, problems with movement and coordination.

B Symptoms in Children

HIV infection in children progresses more rapidly than in adults, most likely because a child's immune system has not yet built up immunity to many infectious agents. The disease is particularly aggressive in infants—more than half of infants born with an HIV infection die before age two. Once a child is infected, the child's undeveloped immune system cannot prevent the virus from multiplying quickly in the blood, and the disease progresses rapidly. In contrast, when an adult becomes infected with HIV, the adult's immune system generally fights the infection. Therefore, HIV levels in adults remain lower for an extended period, delaying the progression of the disease.

Children develop many of the opportunistic infections that befall adults but also exhibit symptoms not observed in older patients. Among infants and children, HIV infection produces wasting syndrome and slows growth (generally referred to as failure to thrive). HIV typically infects a child's brain early in the course of the disease, impairing intellectual development and coordination skills. While HIV can infect the brains of adults, it usually does so toward the later stages of the disease and produces different symptoms.

Children show a susceptibility to more bacterial and viral infections than adults. More than 20 percent of HIV-infected children develop serious, recurring bacterial infections, including meningitis and pneumonia. Some HIV-infected children suffer from repeated bouts of viral infections, such as chicken pox. Healthy children generally develop immunity to these viral illnesses after an initial infection.

VI DETECTING AND MONITORING HIV INFECTION

Since HIV was first identified as the cause of AIDS in 1983, a variety of tests have been developed that help diagnose HIV infection as well as determine how far the infection has progressed. Other tests can be used to screen donated blood, blood products, and body organs for the presence of HIV.

Doctors determine if HIV is present in the body by identifying HIV antibodies, specialized proteins created by the immune system to destroy HIV. The presence of these antibodies indicates HIV infection because they form in the body only when HIV is present. HIV antibodies form anywhere from five weeks to three months after HIV infection occurs, depending upon the individual's immune system. The antibodies are produced continually throughout the course of the infection.

The standard test to detect HIV antibodies in the blood is the enzyme-linked immunosorbent assay (ELISA). In this test, a blood sample is mixed with proteins from HIV. If the blood contains HIV antibodies, they attach to the HIV proteins, producing a telltale color change in the mixture. This test is highly reliable when performed two to three months after infection with HIV. The test is less reliable when used in the very early stage of HIV infection, before detectable levels of antibodies have had a chance to form. Doctors routinely confirm a positive result from an ELISA test by using the Western Blot test, which can detect lower levels of HIV antibodies. In this test a blood sample is applied to a paper strip containing HIV proteins. If HIV antibodies are present in the blood, they bind to the HIV proteins, producing a color change on the paper. The

combination of the ELISA and the Western Blot test is more than 99.9 percent accurate in detecting HIV infection within 12 weeks following exposure.

Once tests confirm an HIV infection, doctors monitor the health of the infected person's immune system by periodically measuring CD4 cell counts in the blood. The progressive loss of CD4 cells corresponds to a worsening of the disease as the immune system becomes increasingly impaired. Doctors also measure the viral load—the amount of the virus in the blood—using polymerase chain reaction (PCR) technology. PCR tests measure the level of viral ribonucleic acid (RNA), or HIV particles, in an infected person's blood to determine how actively the virus is replicating and how fast the disease is progressing. Knowing the viral load helps doctors make decisions about the treatment and its effectiveness.

A modified ELISA test that detects p24 antigen, a protein produced by HIV, can determine if specific drug treatments are having a positive effect on a patient. Blood banks, plasma centers, clinical laboratories, private clinics, and public health departments also use this p24 antigen test to screen for the presence of HIV in blood, blood components, and organs before they are used in medical procedures.

VII DIAGNOSING AIDS

Physicians prefer to differentiate between people who have HIV infection and those who have AIDS. The Centers for Disease Control and Prevention (CDC), based in Atlanta, Georgia, recommends that physicians reserve the diagnosis of AIDS for HIV-infected individuals whose CD4 count falls below 200 cells per microliter of blood. A diagnosis of AIDS can also be made without confirmation of CD4 levels if someone who has no other reason for immune system damage develops an opportunistic disease.

VIII TREATMENT

While no medical treatment cures AIDS, in the relatively short time since the disease was first recognized, new methods to treat the disease have developed rapidly. Health-care professionals focus on three areas of therapy for people living with HIV infection or AIDS: antiretroviral therapy using drugs that suppress HIV replication; medications and other treatments that fight the opportunistic infections and cancers that commonly accompany HIV infection; and support mechanisms that help people deal with the emotional repercussions as well as the practical considerations of living with a disabling, potentially fatal disease.

A Antiretroviral Therapies

Understanding the specific steps in the HIV replication cycle is critical in order for scientists to develop drugs that attack vulnerable stages within the cycle. HIV belongs to a unique group of viruses known as retroviruses, so named because these viruses reverse the usual flow of genetic information within an infected cell. Most viruses store their genetic material in deoxyribonucleic acid (DNA), the double-helix structure that makes up genes. When a virus infects a cell, the viral DNA forms the template for the creation of messenger RNA, a type of ribonucleic acid. This messenger RNA directs the formation of specific proteins, and these proteins, in turn, build new virus particles (*see* Genetics). In HIV, however, genetic material is stored in two single-stranded RNA molecules. When HIV infects a cell, an enzyme called reverse transcriptase copies the genetic instructions in the virus's RNA and moves it into the DNA. This movement of genetic information from RNA to DNA is the opposite of that which occurs in most cells during protein synthesis.

Another HIV enzyme, called integrase, helps the newly formed viral DNA to become part of the structure of the infected cell's DNA. The viral DNA then forces the infected cell to manufacture HIV particles. A third HIV enzyme, called protease, packages these HIV particles into a complete and functional HIV virus. Over the last decade researchers have created a variety of drugs that block the action of some of the enzymes used in HIV

replication. The main classes of drugs used against HIV are nucleoside analogues, non-nucleoside reverse transcriptase inhibitors, protease inhibitors, and fusion inhibitors.

Nucleoside analogues (also called nucleoside reverse transcriptase inhibitors (NRTIs)) impede the action of reverse transcriptase, the HIV enzyme that converts the virus's genetic material into DNA. During this conversion process, these drugs incorporate themselves into the structure of the viral DNA, rendering the DNA useless and preventing it from instructing the infected cell to make additional HIV. The nucleoside analogue known as azidothymidine (AZT), which became available in 1987, was the first drug approved by the United States Food and Drug Administration (FDA) to treat AIDS. AZT slows HIV growth in the body, permitting an increase in the number of CD4 cells, which boosts the immune system. AZT also prevents transmission of HIV from an infected mother to her newborn. Since the introduction of AZT, additional nucleoside analogues have been developed, including didanosine (sold under the trade name *Videx*), zalcitabine (*Hivid*), stavudine (*Zerit*), lamivudine (*Epivir*), abacavir (*Ziagen*), and emtricitabine (*Emtriva*). These drugs are not particularly powerful when used alone, and often their benefits last for only 6 to 12 months. But when nucleoside analogues are used in combination with each other, they provide longer-lasting and more effective results.

Non-nucleoside reverse transcriptase inhibitors (NNRTIs), introduced in 1996, use a different mechanism to block reverse transcriptase. These drugs bind directly to reverse transcriptase, preventing the enzyme from converting RNA to DNA. Three NNRTIs are available: nevirapine (*Viramune*), delavirdine (*Rescriptor*), and efavirenz (*Sustiva*). NNRTIs work best when used in combination with nucleoside analogues.

The third group of antiviral drugs, called protease inhibitors, cripples protease, the enzyme vital to the formation of new HIV. When these drugs block protease, the defective HIV that forms is unable to infect new cells. Protease inhibitors are more powerful than nucleosides and NNRTIs, producing dramatic decreases in HIV levels in the blood. This reduced viral load, in turn, enables CD4 cell levels to skyrocket. The first

protease inhibitor, saquinavir (*Invirase*), was approved in 1995. Since then other protease inhibitors have been approved, including ritonavir (*Norvir*), indinavir (*Crixivan*), nelfinavir (*Viracept*), amprenavir (*Agenerase*), tipranavir (*Aptivus*), and darunavir (*Prezista*).

A class of drugs known as fusion inhibitors became available in 2003. That year the FDA approved the use of enfuvirtide, sold under the brand name Fuzeon. Fusion inhibitors prevent the binding or fusion of HIV to CD4 cells. When used with other antiretroviral medicines, fusion inhibitors can reduce the amount of HIV in the blood and increase the number of CD4 cells. A related drug, called an entry inhibitor, was introduced in 2007 as maraviroc (*Selzentry*). It, too, is designed to prevent HIV from infecting CD4 cells.

A1 Drug Resistance

When a single antiretroviral drug is used alone, its benefits last only a short time, as clinical studies of treatments with the drugs soon demonstrated. This short-term effectiveness is due to mutation, or changes in the genetic structure, of HIV that makes the virus resistant to the drug. The genetic material in HIV provides instructions for the manufacture of critical enzymes needed to replicate the virus. Scientists design antiretroviral drugs to impede the activity of these enzymes. If the virus mutates, the structure of the virus's enzymes changes and the drugs no longer work against the enzymes or the virus.

Genes mutate during the course of viral replication, so the best way to prevent mutation is to halt replication. Studies have shown that the most effective treatment for halting HIV replication employs a combination of three drugs taken together—for instance, a combination of two nucleoside analogues with a protease inhibitor. This regimen, called triple therapy, maximizes drug potency while reducing the chance for drug resistance. The combination of three drugs is often referred to as an AIDS cocktail. In HIV-infected patients who have undergone triple therapy, the viral loads reduced significantly,

sometimes to undetectable levels. Their CD4 cell count gradually increased, and they sustained good health with no complications. With this treatment, some patients who were near death were able to return to work and normal physical activity. Triple therapy was introduced in the United States in 1996. That year AIDS deaths in the United States decreased 26 percent, the first decrease since the beginning of the epidemic. In 1997 U.S. AIDS deaths decreased by 56 percent from the year before.

Despite its success, triple therapy has had some drawbacks. This multidrug therapy has been quite complicated, requiring patients to take anywhere from 2 to 20 pills a day on a specific schedule. Some drugs must be taken with food, and some cannot be taken at the same time as other pills. Even the most organized people find it difficult to take the pills correctly. Yet, just one or two lapses in treatment may cause the virus to develop resistance to the drug regimen.

In July 2006 the FDA approved a new three-drug combination that can be taken as a single pill once a day with or without food. Marketed under the name Atripla, the new drug combines the existing drugs Sustiva (the NNRTI efavirenz) and Truvada (the NRTIs emtricitabine and tenofovir) in a special formulation. The product is seen as a breakthrough in AIDS and HIV treatment for its simplicity and convenience. The once-daily pill form should help patients take the drugs on a regular, uninterrupted schedule that will not allow the HIV in their bodies to develop resistance to the drugs. The new pill could prove particularly useful in developing countries, where following complex regimens of different AIDS drugs is often impractical.

Many people find it difficult to deal with the unpleasant side effects produced by antiretroviral drugs. Common side effects include nausea, diarrhea, headache, fatigue, abdominal pain, kidney stones, anemia, and tingling or numbness in the hands and feet. Some patients may develop diabetes mellitus, while other patients develop collections of fat deposits in the abdomen or back, causing a noticeable change in body configuration. Some antiretroviral drugs produce an increase in blood fat levels, placing a patient at risk

for heart attack or stroke. Some patients suffer more misery from the drug treatment than they do from the illnesses produced by HIV infection.

Perhaps the greatest drawback to triple therapy has been its cost, which has ranged from $10,000 to $12,000 a year. This high cost is well beyond the means of people with low incomes or those with limited health-care insurance. As a result, the most effective therapies currently available have remained beyond the reach of the majority of HIV-infected people worldwide.

To decrease the toxic effects of drugs and to defer costly therapy, in 2001 United States federal health officials recommended delaying drug treatment for HIV infection in people showing no symptoms and who have been infected with HIV for more than six months. The new guidelines call for delaying treatment until an infected person's CD4 cells fall below 350 cells per microliter of blood or the HIV viral load exceeds 30,000 per microliter of blood. Evidence suggests that delaying treatment poses no harm to infected people and, in fact, benefits them by deferring the toxic side effects of the drugs.

A2 Postexposure Prevention

Studies show that under certain circumstances, administering antiretroviral drugs within 24 hours (preferably within one to two hours) after exposure to HIV can protect a person from becoming infected with the virus. Although the effectiveness of postexposure antiretroviral therapy following sexual exposure to HIV remains uncertain, the CDC recommends that health-care personnel exposed to HIV infection from a needle stick or other accident take antiretroviral drugs.

A3 **Development of New Drugs**

Scientists continue to develop more powerful HIV treatments that have fewer side effects and fewer resistance problems. Some drugs under investigation block the HIV enzyme

integrase from inserting viral DNA into the infected cell. Other drugs prevent HIV from binding with a CD4 cell in the first place, thereby barring HIV entry into cells.

Some scientists focus on ways to fortify the immune system. A biological molecule called interleukin-2 shows promise in boosting the immune system's arsenal of infection-fighting cells. Interleukin-2 stimulates the production of CD4 cells. If enough CD4 cells can be created, they may trigger other immune cell responses that can overpower HIV infection.

In other research, doctors hope to bolster the immune system with a vaccine (*see* Immunization). Most vaccines available today, including those that prevent measles or poliomyelitis, work by helping the body to create antibodies. Such vaccines mark specific infectious agents, such as the measles and polio viruses, for destruction. But many experts believe that an effective HIV vaccine will need to do more than just stimulate anti-HIV antibodies. Studies are underway to develop vaccines that also elevate the production of T cells in the immune system. Scientists hope that this dual approach will prime the immune system to attack HIV as soon as it appears in the body, perhaps containing the virus before it spreads through the body in a way that natural immune defenses cannot. The genetic variability of HIV frustrates efforts to develop a vaccine: A vaccine effective against one type of HIV may not work on a virus that has undergone genetic mutation.

B Treatment of Opportunistic Infections

In addition to antiretroviral therapy to combat HIV infection, effective drug treatments are available to fight many of the medical complications that result from HIV infection. Doctors try to prevent infections before they begin to avoid taxing a patient's weakened immune system unnecessarily. A doctor instructs an HIV-infected person on ways to avoid exposure to infectious agents that produce opportunistic infections common in people with a weakened immune system. Doctors usually prescribe more than one drug to

forestall infections. For example, for those who have a history of pneumocystic pneumonia and a CD4 cell count of less than 200 cells per microliter, doctors may prescribe the antibiotics sulfamethoxazole and trimethoprim to prevent further bouts of pneumonia. Patients suffering from recurring thrush may be given the antifungal drug fluconazole for prolonged periods. For people with CD4 cell counts of less than 100 cells per microliter, doctors may prescribe clarithromycin or azithromycin to prevent *Mycobacterium avium* infections.

C Support Mechanisms

AIDS Quilt

The AIDS quilt travels on display to promote public awareness of acquired immunodeficiency syndrome (AIDS). The quilt project, initiated in 1986 by the NAMES Project organization, consists of thousands of panels. Each panel is individually designed and is dedicated to the memory of someone who has died of AIDS.

A. Reininger/Woodfin Camp and Associates, Inc.

A person diagnosed with HIV infection faces many challenges, including choosing the best course of treatment, paying for health care, and providing for the needs of children in the family while ill. In addition to these practical considerations, people with HIV infection must cope with the emotional toll associated with the diagnosis of a potentially fatal illness. The social stigma that continues to surround a diagnosis of AIDS because of the disease's prevalence among gay men or drug users causes many people to avoid telling family or friends about their illness. People with AIDS often feel incredibly lonely as they try to cope with a devastating illness on their own. Loneliness, anxiety, fear, anger, and other emotions often require as much attention as the medical illnesses common to HIV infection.

Since the AIDS epidemic began in the United States in 1981, grassroots organizations have been created to meet the medical and emotional needs of people who have AIDS and also to protect their civil rights. The Gay Men's Health Crisis, founded in 1982, was the first nonprofit organization to provide medical, education, and advocacy services for people with AIDS. The Los Angeles Shanti Group was established in 1983 to provide emotional support and medical guidance to people with AIDS and other life-threatening illnesses. Activist organizations such as the AIDS Coalition to Unleash Power (ACT UP), founded in 1986, have been created to initiate faster change in public policies and to speed up the course of AIDS clinical research. American Foundation for AIDS Research (AMFAR), created in 1985, is the nation's leading nonprofit organization dedicated to the support of AIDS research and the advocacy of fair and compassionate AIDS-related public policies. In Canada, the AIDS Committee of Toronto (ACT) was established in 1983 by community activists intent on fighting for the civil rights of people infected with HIV. As the AIDS epidemic grew, ACT expanded its mission to help people disabled by the disease and to spread health information to halt the spread of the disease. AIDS Vancouver (AV), also established in 1983, became the principal education, prevention, and support service organization for that city.

Counseling centers and churches provide individual or group counseling to help people with HIV infection or AIDS share their feelings, problems, and coping mechanisms with others. Family counseling can address the emotions of other family members who are disturbed by the diagnosis of HIV infection in another family member. Grief counseling also helps people who have lost friends or family members to AIDS.

In the United States and Canada, government-funded and privately funded organizations help people cope with disease. For instance, local, city-funded clinics provide AIDS testing as well as counseling to prepare people for a test result that indicates HIV infection. Health experts at clinics explain the medical progression of the illness, arrange medical appointments with health-care specialists, and help people choose appropriate treatment options. State-appointed social workers and community nonprofit organizations help people find federally funded programs that offset the high cost of medical care and child care.

The United States Congress has passed legislation to help HIV-infected individuals. In 1990 the Americans with Disabilities Act (ADA) was enacted, protecting people with disabling diseases, including AIDS, from discrimination in activities such as applying for jobs or buying a house. The Ryan White Comprehensive AIDS Resources Emergency Act was established in 1990 and reauthorized in 1996. This program provides medical and dental care, counseling, transportation, and home and hospice care for low-income or uninsured people living with AIDS. The AIDS Drug Assistance Program (ADAP) is funded in large part by this act and administered by all 50 states. It pays for costly AIDS medications for people who do not have private insurance and who are not poor enough to be eligible for Medicaid.

IX PREVENTION OF AIDS

With a vaccine for AIDS years away and no cure on the horizon, experts believe that the most effective treatment for AIDS is to prevent HIV infection. Health officials focus

public education programs on altering risky behaviors linked to HIV transmission, particularly unsafe sexual practices and needle-sharing by intravenous drug users. Safe-sex campaigns sponsored by health clinics, social centers, schools, and churches encourage sexual abstinence or monogamy (sexual relations with only one partner). Education programs instruct about the proper way to use condoms to provide a protective barrier against transmission of HIV during sexual intercourse. Needle-exchange programs, which provide clean needles to drug users, enable intravenous drug abusers to avoid sharing HIV-contaminated needles. Needle-exchange programs have been widely criticized because they seem to condone illicit drug use. However, numerous U.S. government-funded studies have indicated that such programs reduce HIV transmission without promoting greater drug use. To reduce the accidental transmission of HIV during medical procedures, both the United States and Canada have established strict guidelines for health-care settings, including the use of protective clothing and proper instrument disposal.

In the United States, the effectiveness of public education programs that target people at risk for HIV infection was well demonstrated in the gay community of San Francisco, California, in the 1980s. In 1982 and 1983, 6,000 to 8,000 people in San Francisco became infected with HIV. The gay community rallied to promote condom use and advocate monogamy through extensive education programs and public health advertisements geared for gay men. These public education programs were credited with reducing the number of gay men in San Francisco who became HIV infected. By 1993 the number of new infections declined to 1,000, and by 1999, fewer than 500 people were infected each year.

Public education about AIDS has also proven effective in other countries. Uganda was one of the first African countries to report cases of HIV infection. The first cases of AIDS were reported there in 1982, and by the late 1980s Uganda had one of the highest rates of HIV infection in the world. The Ugandan government was one of the first countries to set

up a partnership with WHO to create a national AIDS control program called the AIDS Information Centre (AIC). The AIC has established extensive education programs promoting condom use and other methods to prevent HIV from spreading further. The program has also worked with community organizations to change social behaviors that increase the risk of HIV infection. The AIC promotes its message using innovative drama, song, and dance programs, a particularly effective communication method for African communities. AIC established confidential HIV testing services that provide same-day results and community counseling programs. As a result of Uganda's quick response to the AIDS epidemic, the number of HIV infected people in that country declined significantly after 1993, during a time when most other African nations faced a frightening increase in the incidence of HIV infection.

Public health officials have learned that education programs that teach and reinforce safe behaviors through a series of meetings are more effective than one-time exposure to public-health information provided in a class lecture, magazine article, advertisement, or pamphlet. Education programs tailored to reflect specific ethnic and cultural preferences prove even more effective. For example, the Canadian Aboriginal AIDS Network creates HIV education programs that fight the common misperception among the indigenous peoples of Canada that AIDS is primarily a disease of white, affluent people. Among indigenous communities, the network promotes programs that use colloquial language to increase awareness about safe sex practices and needle use.

Another recently proposed approach to AIDS prevention is development of simple microbicidal creams or gels that women could use before sex to reduce the risk of HIV infection. Such topical anti-HIV products would be especially useful in developing countries where women may not have access to other forms of protection such as condoms. Currently, a number of different products are undergoing clinical trials in Africa.

Research conducted in Africa demonstrated that male circumcision could reduce by more than half a man's risk of contracting AIDS through heterosexual intercourse. The findings were announced by the U.S. National Institutes of Health in 2006. They were not expected to affect AIDS prevention strategies in the United States, where most men are circumcised. However, adult circumcision could be a prevention strategy in developing countries where circumcision is less common. Male circumcision also lowers the risk of transmitting AIDS to women, but its effect on AIDS risk for men who have sex with men is not yet known.

X HISTORY OF AIDS

In the short time since the first cases of the AIDS epidemic were reported in 1981, scientists have identified the viral cause of the illness, the basic modes of transmission, accurate tests for the presence of infection, and effective drugs that slow or halt the progression of the disease. During that same period, governments and grassroots organizations around the world were spurred into action to meet the growing need for AIDS education, counseling, patients' rights, and clinical research. Despite these advances, critics observe that many governments were slow to respond to the crisis. For example, United States president Ronald Reagan did not discuss AIDS in public until 1987, more than six years after the start of the AIDS epidemic. By that time, 41,000 Americans had already died from the disease. AIDS advocates believe that the lack of federal support for AIDS research in these early years delayed the development of an effective vaccine or a cure for the disease.

A Origin of the AIDS Virus

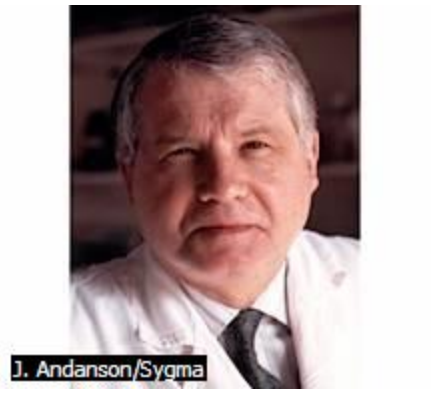
Using computer technology to study the structure of HIV, scientists have determined that HIV originated around 1930 in rural areas of Central Africa, where the virus may have been present for many years in isolated communities. The virus probably did not spread because members of these rural communities had limited contact with people from other

areas. But in the 1960s and 1970s, political upheaval, wars, drought, and famine forced many people from these rural areas to migrate to cities to find jobs. During this time, the incidence of sexually transmitted infections, including HIV infection, accelerated and quickly spread throughout Africa. As world travel became more prevalent, HIV infection developed into a worldwide epidemic. Studies of stored blood from the United States suggest that HIV infection was well established there by 1978.

In 1970, at about the same time that the HIV epidemic was taking hold in Africa, American molecular biologist David Baltimore and American virologist Howard Temin independently discovered the enzyme reverse transcriptase, which could be used to identify retroviruses. Over the next ten years, many retroviruses were identified in animals. But not until 1980, shortly before the first AIDS cases were recognized in the United States, did American virologist Robert Gallo identify the first human retroviruses, HTLV-I and HTLV-II (HTLV stands for human T cell lymphotropic virus).

Other studies demonstrated that these human retroviruses were more closely related to a retrovirus found in African chimpanzees than to each other. This discovery suggests that the human retroviruses may have evolved from retroviruses that originally infected chimpanzees. The chimpanzee retrovirus likely infected people and underwent mutations to form the human retrovirus. In 1999 scientists confirmed that HIV spread from chimpanzees to humans on at least three separate occasions in Central Africa, probably beginning in the 1940s or 1950s.

B AIDS Identified



Luc Montagnier

In 1983 French biologist and cancer specialist Luc Montagnier and his research team isolated the human immunodeficiency virus (HIV), the virus that causes AIDS. Montagnier has since become a champion of AIDS prevention education and has devoted his career to developing an AIDS vaccine.

J. Andanson/Sygma

Beginning in June 1981 the CDC published reports on clusters of gay men in New York and California who had been diagnosed with pneumocystic pneumonia or Kaposi's sarcoma. These two rare illnesses had previously been observed only in people whose immune systems had been damaged by drugs or disease. These reports triggered concern that a disease of the immune system was spreading quickly in the homosexual community. Initially called gay-related immunodeficiency disease (GRID), the new illness soon was identified in population groups outside the gay community, including users of intravenous drugs, recipients of blood transfusions, and heterosexual partners of infected people. In 1982 the name for the new illness was changed to acquired immunodeficiency syndrome, or AIDS.

While the disease was making headlines for the speed with which it was spreading around the world, the cause of AIDS remained unidentified. Fear of AIDS and ignorance of its causes resulted in some outlandish theories. Some thought the disease was God's punishment for behaviors that they considered immoral. These early theories created a social stigma surrounding the disease that still lingers.

Scientists quickly identified the primary modes of transmission—sexual contact with an infected person, contact with infected blood products, and mother-to-child transmission. From these modes of transmission it was clear that the new illness was spread in a specific manner that matched the profile of a viral infection. In 1983 French cancer specialist Luc Montagnier and his colleagues isolated what appeared to be a new human retrovirus from AIDS patients. They named it lymphadenopathy virus (LAV). Eight months later Gallo and his colleagues isolated the same virus in AIDS patients, naming the virus HTLV-III. Eventually, scientists agreed to call the infectious agent human immunodeficiency virus (HIV). In 1985 a new AIDS-causing virus was discovered in West Africa. Named HIV-2, the new virus is closely related to the first HIV, but it appears to be less harmful to cells of the immune system and reproduces more slowly than HIV-1.

Research leading to the development of the ELISA test was conducted simultaneously by teams led by Gallo in the United States and Montagnier in France. In 1985 the ELISA test to identify HIV in blood became available, followed by the development of the Western Blot test. These tests were first employed to screen blood for the presence of HIV before the blood was used in medical procedures. The tests were later used to identify HIV-infected people, many of whom did not know they were infected. These diagnostic tests also helped scientists study the course of HIV infection in populations.

C Defining AIDS

The CDC presented its first definition of AIDS in 1982. The CDC recommended that physicians diagnose AIDS if a person has an illness known to be caused by immune deficiency, as long as there is no known cause for this immune deficiency. (Radiation therapy for cancer and certain drugs also may impair the immune system). As more information became known about the course of HIV infection and the nature of the virus itself, this definition of AIDS was revised repeatedly to expand the list of illnesses considered diagnostic indicators of the disease. Early definitions were based on the

opportunistic infections commonly found in HIV-infected men. As a result, many women who did not have symptoms covered in the official AIDS definition were denied disability benefits and AIDS-related drug therapies.

The current definition of AIDS was created in 1993 and includes 26 opportunistic infections and cancers, known as diagnostic indicators, which affect both men and women. The definition also emphasizes the importance of the level of CD4 cells in the blood. Today doctors make the diagnosis of AIDS in anyone with a CD4 count below 200 cells per microliter of blood, regardless of the associated illnesses they may have.

XI SOCIAL PERSPECTIVES ON AIDS

Although new and effective AIDS drugs have brought hope to many HIV-infected persons, a number of social and ethical dilemmas still confront researchers and public-health officials. The latest combination drug therapies are far too expensive for infected persons in the developing world—particularly in sub-Saharan Africa, where the majority of AIDS deaths have occurred. In these regions, where the incidence of HIV infection has soared, the lack of access to drugs can be catastrophic.

A Testing AIDS Drugs and Vaccines

AIDS research in the developing world has raised ethical questions pertaining to the clinical testing of new therapies and potential vaccines. For example, controversy erupted over 1997 clinical trials that tested a shorter course of AZT therapy in HIV-infected pregnant women in developing countries. Earlier studies had shown that administering AZT to pregnant women for up to six months prior to birth could cut mother-to-child transmission of HIV by up to two-thirds. The treatment's $800 cost, however, made it too expensive for patients in developing nations.

The controversial 1997 clinical trials, which were conducted in Thailand and other regions in Asia and Africa, tested a shorter course of AZT treatment, costing only $50. Some pregnant women received AZT, while others received a placebo—a medically inactive substance often used in drug trials to help scientists determine the effectiveness of the drug under study. Ultimately the shorter course of AZT treatment proved to be successful and is now standard practice in a growing number of developing nations. However, at the time of the trials, critics charged that using a placebo on HIV-infected pregnant women—when AZT had already been shown to prevent mother-to-child transmission—was unethical and needlessly placed babies at fatal risk. Defenders of the studies countered that a placebo was necessary to accurately gauge the effectiveness of the AZT short-course treatment. Some critics speculated whether such a trial, while apparently acceptable in the developing nations of Asia and Africa, would ever have been viewed as ethical, or even permissible, in a developed nation like the United States.

Similar ethical questions surround the testing of AIDS vaccines in developing nations. Vaccines typically use weakened or killed HIV to spark antibody production. In some vaccines, these weakened or killed viruses have the potential to cause infection and disease. Critics have questioned whether it is ethical to place all the risk on test subjects in developing regions such as sub-Saharan Africa, where a person infected by a vaccine would have little or no access to medical care. At the same time, with AIDS causing up to 5,500 deaths a day in Africa, others feel that developing nations must pursue any medical avenue for stemming the epidemic and protecting people from the virus.

B Economic Burden

For the struggling economies of some developing nations, AIDS has brought yet another burden: AIDS tends to kill young adults in the prime of their lives—the primary breadwinners and caregivers in families. According to figures released by the United Nations in 1999, AIDS has shortened the life expectancy in some African nations by an average of seven years. In Zimbabwe, life expectancy for adults declined from 61 years

in 1993 to 38 in 2003, according to the World Health Organization (WHO). The next few decades may see average life expectance fall even lower in sub-Saharan Africa. Millions of children around the world have been orphaned by the AIDS epidemic. Those children who survive face poverty, a high risk of malnutrition and disease, and the absence of a family support structure.

In Africa, the disease has had a heavy impact on urban professionals—educated, skilled workers who play a critical role in the labor force of industries such as agriculture, education, transportation, and government. The decline in the skilled workforce has already damaged economic growth in Africa, and economists warn of disastrous consequences in the future.

C Social Stigma and Discrimination

AIDS Prevention Sign, Botswana

A road sign in Botswana about acquired immunodeficiency syndrome (AIDS) says "AIDS: Your Problem, Control With Condoms." Africa accounts for more than 70 percent of adults infected with human immunodeficiency virus (HIV), the cause of AIDS.

M.P. Kahl/Photo Researchers, Inc.

From the early days of the identification of AIDS, the disease has been powerfully linked to behaviors that are illegal (such as illicit drug use) or are considered immoral by many people (such as promiscuity and homosexuality). Consequently, a diagnosis of AIDS was a mark of disgrace, although medical research revealed that the disease follows well-defined modes of transmission that can affect any person. As the extent of the epidemic unfolded, misinformation about AIDS and how it is transmitted triggered widespread fear of contracting the disease. Some communities responded with hysteria that resulted in violence. In the United States, a Florida family with three HIV-positive sons who had become infected from blood transfusions were driven from their home when it was torched by an arsonist in 1987. In other communities, parents protested when HIV-infected children attended school. In many areas of the world, women in particular may face consequences if their HIV status is discovered. Reports indicate that many HIV-infected women are subject to domestic violence at the hands of their husbands—even if the husbands themselves are the source of infection. As a result, some women in developing nations fear being tested for HIV infection and cut themselves off from medical care and counseling.

In addition to social stigma, people infected with HIV must grapple with more immediate concerns—a daily struggle for basic medical care and other basic rights in the face of discrimination and fear because of their HIV status. In some places, nurses and other medical personnel who fear infection refuse to perform procedures on HIV-infected people. In 1998 the United States Supreme Court heard the case of Sidney Abbott, a young woman in Maine who sued dentist Randon Bragdon after he refused to treat her when he learned of her HIV-positive status. Basing its ruling on the Americans with Disabilities Act, the Supreme Court ruled in *Bragdon* v. *Abbott* that the woman's HIV infection constituted a disability, even though she suffered from no disease symptoms.

AIDS advocates expect this decision to protect the rights of many people with AIDS in the United States.

ACT UP Demonstration

The grassroots AIDS organization AIDS Coalition to Unleash Power, commonly known as ACT UP, uses nonviolent civil disobedience to protest against government and societal indifference to the AIDS epidemic.

ABCNews VideoSource

Some developing nations, such as Uganda, have met the AIDS crisis head-on, attempting to educate citizens and change high-risk behaviors in the population. However, other nations have been slow to even acknowledge the disease. In India, for example, the nation's prime minister did not speak publicly about the dangers posed by the epidemic until 1999.

In developed nations, some of the stigma attached to a diagnosis of AIDS has lessened in recent years, in part due to the admissions by public figures and celebrities, especially in the United States, that they were HIV-infected. The deaths from AIDS of actor Rock Hudson and tennis player Arthur Ashe, and the AIDS advocacy roles of basketball player Magic Johnson and Olympic diver Greg Louganis have personalized the disease and helped society come to terms with the enormity of the epidemic.

Ray Children

Left to right, Candy, Robert, Randy, and Richard Ray leave Memorial Elementary School in Arcadia, Florida, on August 24, 1987. It was the boys' first day at school after having been barred because they were infected with HIV. The three hemophiliac brothers acquired the disease from contaminated blood products. A federal judge ordered the school to admit the boys, but the family's home was burned by an arsonist one week after their return.

UPI/CORBIS-BETTMANN

To some scientists, the AIDS epidemic signals a troubling trend in humanity's future. Along with other deadly microbial threats of recent years—most notably Ebola virus, which has caused sporadic epidemics in Africa, and hantavirus, which broke out in the American Southwest in the early 1990s—AIDS is viewed by some as yet another in a series of emerging diseases that demonstrate how vulnerable humans are to newly encountered microbes. With population and land development increasing, humans have encroached farther into rain forests and other formerly wild areas, unleashing previously unknown disease agents. Meanwhile, global travel has become faster, more convenient,

and more accessible to many people. Some scientists are worried by these trends, fearing the potential for an as-yet-unknown pathogen to arise and spread quickly and lethally around the globe.

The social, ethical, and economic effects of the AIDS epidemic are still being played out, and no one is entirely certain what the consequences will be. Despite the many grim facts of the AIDS epidemic, however, humanity is armed with proven, effective weapons against the disease: knowledge, education, prevention, and the ever-growing store of information about the virus's actions.

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