

PART ONE

HIV BASICS AND SOCIAL WORK PRINCIPLES

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Chapter One

HIV HISTORY, ILLNESS, TRANSMISSION, AND TREATMENT

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INTRODUCTION

HIV disease—a condition caused by infection with the human immunodeficiency virus—is a complex, incurable illness that can lead to a life-threatening condition called *Acquired Immune Deficiency Syndrome* (AIDS). Since the first documented AIDS-related deaths in 1981, HIV disease has grown into a global epidemic—known as a *pandemic*—that profoundly affects individuals and their interpersonal relationships throughout the human life cycle. In addition to being a serious biological disease, HIV creates social, political, and economic problems that highlight international injustices. HIV disease brings global attention to homophobia, oppression of women, racism, poverty, and health care disparities.

Early in the pandemic, it was clear that people could reduce HIV transmission if they had access to the tools to do so, such as condoms, clean needles, and reproductive care. Advances in medication treatments have made HIV disease more manageable and much less deadly, but millions of people worldwide still do not have access to adequate medical care and treatment. A person with access to skilled HIV care in New York City might perceive and experience HIV disease quite differently than a working-class single mother in the rural southern United States. Epidemiological data illuminate how HIV disease disproportionately affects marginalized people throughout the world: Women, African Americans, Latinos, those in poverty, sex workers, injecting drug users, and men who have sex with men. While advances have been made in the medical treatment of HIV, social and political actions have fallen behind.

Health care and social service professionals can have a powerful impact on the effects of HIV. Basic knowledge about the science of HIV disease—how it is transmitted, prevented, and treated, as well as its sociopolitical history—is an important foundation for any human services practitioner. This chapter provides basic historical, epidemiological, biological, immunological, medical, and prevention information so that social service providers can be prepared to provide information and support to persons with HIV and those at risk for HIV infection. Some information found in this chapter is knowledge that will remain relatively stable over time (for example, information about biology, transmission, and history). Facts about treatment, prevention, and epidemiology change more frequently, and those working in HIV services should monitor these changes regularly.

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THE EMERGENCE OF HIV IN THE UNITED STATES

The First 20 Years

From June to August 1981, the Centers for Disease Control and Prevention (CDC) published three reports documenting two rare conditions—a form of cancer called *Kaposi's sarcoma* (KS) and a pulmonary condition called *Pneumocystis carinii pneumonia* (PCP)—in previously healthy men living in New York and California (CDC, 1981a, 1981b, 1981c). Of the 108 documented cases, 95 percent were 25 to 49 years of age and 43 of the men had died. The mysterious link between these rare fatal illnesses and the subjects' histories of same-gender sexual behavior confounded public health investigators. Because physicians treating these cases associated the illness with men who identified as gay, names like *gay-related immunodeficiency disease* (GRID) and *gay cancer* were assigned to the condition. The CDC—a branch of the government public health service that monitors and intervenes in existing and emerging diseases—sent researchers to investigate the possible causes of this emerging public health crisis. Through months of extensive interviews, medical examinations, and analyses of social networks, researchers speculated that the mysterious illness was likely caused by an infectious microorganism transmitted between people through sexual contact.

Gay men were not the only population being affected by this newly discovered disease. In the first half of 1982, the CDC had documented cases among people with hemophilia, injection drug users, heterosexuals, babies, and Haitians. Because the disease was no longer considered to be limited to gay men, and because it was transmitted not only through sex but also blood contact, the CDC identified the illness more broadly as *acquired immune deficiency syndrome*, or AIDS (Harris et al., 1983).

In 1983, a French virologist Dr. Luc Montagnier and his research team at the Pasteur Institute isolated HIV, the virus that causes AIDS. By mid-1985 this pivotal discovery led to the development of an antibody test which could detect HIV in the blood supply and human infection well before an AIDS diagnosis. The HIV antibody test remains the gold standard for diagnosing HIV infection to this day.

In the absence of a clear scientific understanding of AIDS, the disease readily became a metaphor for the “immoral” behavior of gay men and drug users. The pandemic's emergence during Ronald Reagan's presidency, backed by social and religious conservatives, resulted in a lack of federal governmental attention to the public health emergency. President Reagan did not make any reference in his speeches to AIDS until 1987, six years after the first reports of a fatal infectious disease. That same year, Republican senator Jesse Helms introduced a bill that refused federal funding to groups that “promote” homosexuality in their education and literature, creating a significant barrier to public funding of gay-related AIDS organizations (Levine, Nardi, & Gagnon, 1997).

Gay communities in New York City and San Francisco, responding to political and social inaction, organized grassroots political action and community advocacy groups such as AIDS Coalition to Unleash Power (ACT UP), Gay Men's Health Crisis (GMHC), and AIDS Project Los Angeles (APLA). ACT UP's primary mission was to bring attention to the absence of a public health response to the AIDS crisis; the slogan “Silence = Death” (see Figure 1.1), accompanied by a pink triangle that the Nazis used to identify homosexuals, became a symbol of AIDS activism. The coalition sponsored highly effective, nonviolent demonstrations at locations deemed critical to combating the public health response and institutionalized homophobia (a 1990 demonstration at the National Institutes of Health is a good example of their tactics). Over several years, ACT UP uncovered inherent disparities in U.S. health care delivery, not just for gay men living with HIV, but also for women and people of color, and broadened their message to “health



Figure 1.1 Silence = Death

Source: Silence = Death Project (1986).

care is a right.” ACT UP is credited for significant changes in the ways pharmaceutical companies and the FDA research and approve medications through the clinical trial process, as well as bringing national attention to the AIDS crisis and discrimination.

AIDS gained greater media attention when public figures affected by HIV entered the spotlight, leading to widespread awareness, controversy, and fear. Rock Hudson, a prominent Hollywood star who was a leading man in romantic roles, began showing signs of illness and deterioration and publicly announced in 1985 that he had AIDS. He died shortly thereafter. Some describe this as “giving AIDS a face,” which simultaneously signified a pivotal moment in gay and lesbian recognition. Never had such a prominent Hollywood icon openly and publicly acknowledged being gay, and AIDS awareness spurred a powerful gay and lesbian movement. Olympic medalist Greg Louganis and basketball star Magic Johnson are two professional athletes whose HIV status created controversy in the sports world, and both have become public advocates for HIV awareness and prevention.

In 1984, Ryan White, a 13-year-old Indiana boy with hemophilia, was diagnosed with AIDS. Ryan’s diagnosis drew national attention due to the stigma he experienced in his public school. Initially the superintendent barred Ryan from attending school, and after that was reversed, a group of parents sued to keep him out. Despite the confirmation of his right to attend school by the courts, the daily verbal and emotional assaults that he experienced forced him and his family to move to another community and school. After Ryan White’s death in 1990, Congress passed the Ryan White Comprehensive AIDS Resources Emergency (CARE) Act, the first legislative initiative to provide comprehensive care funds for people with AIDS (PWAs). The act provided emergency relief grants to cities with more than 2,000 AIDS cases to provide care for people with AIDS and funding for prevention and intervention for at risk groups. In 2006, the CARE Act was renamed the Ryan White HIV/AIDS Treatment Modernization Act, which placed greater emphasis on funding medical care–related programs and services. In fiscal year 2008, \$2.1 billion of federal funds were allocated toward the Ryan White HIV/AIDS program.

The number of HIV infections and deaths peaked in the 1990s. This was partly attributed to the introduction of a 1993 revised case definition for AIDS that not only measured the disease through clinical manifestations (that is, symptoms or opportunistic illnesses), but also through the measurement of cells critical to immune function, called CD4, or T cells (Castro, Ward, & Slutsker, 1992). Levels of the CD4 marker helped determine

disease progression. A CD4 count below 200 signified an infected person's acute risk for AIDS-related illnesses and death. The revision also shifted AIDS diagnoses among women by including cervical cancer and other diseases specific to HIV-infected women in the new criteria (Castro et al., 1992). Case definition revisions influenced important changes in U.S. HIV-related health policies during the 1990s.

The Clinton administration, taking office in 1992, made notable advances in HIV funding, increasing allocations to the CARE act by 200 percent, targeting funds to research, prevention, and housing. President Clinton also developed the Office of AIDS Research, responsible for overseeing efficient allocation of HIV research funds, and passed an AIDS disaster bill that provided up to \$4 billion for research.

A highly significant HIV-related development was the introduction of uniquely effective medication treatments. A 1996 cover story for the *New York Times Magazine* titled "When Plagues End" (Sullivan, 1996, November 10) captured a powerful, though misguided, optimism for an imminent HIV cure. Dr. David Ho, a principal researcher at the Aaron Diamond AIDS Research Center was *Time* magazine's 1996 Man of the Year for his role in developing a promising new drug class called *protease inhibitors* and a highly effective HIV-inhibiting triple-drug treatment (called "combination therapy"). New technologies developed to measure HIV levels in blood led to Ho's discovery that HIV was never, in fact, latent; rather, billions of HIV particles were being produced daily, slowly wearing down the immune system. Presumably, medications that inhibited HIV replication in blood would prevent the onset of AIDS.

Use of these new medication combination regimens (popularly known as drug cocktails) controlled HIV replication in infected people, often reducing the virus to undetectable levels. People with usually life-threatening AIDS-related illnesses were recovering at unprecedented rates, AIDS diagnoses began to plummet, and hospitals burdened by the number of HIV cases witnessed significant reductions of AIDS cases and deaths. A phenomenon called the *Lazarus syndrome* referred to people with AIDS who, expecting to die soon, living on disability, and having taken cash payments for insurance policies, suddenly found themselves leaving their sickbeds and returning to life. Hopes that these medications could eradicate HIV—essentially a cure for AIDS—were high, but continued attempts to do so have so far failed.

EPIDEMIOLOGY: STATISTICS AND POPULATIONS IN THE TWENTY-FIRST CENTURY

In 2006—the last year for data collection by the CDC—the estimated number of AIDS-related deaths was 14,627, and the total number of people who have died of AIDS since the beginning of the pandemic reached 565,927 (CDC, 2006). Approximately 56,300 people in the United States became newly infected with HIV in 2006 (Hall et al., 2008). Research suggests that the number of new HIV infections per year peaked in the 1990s and has remained stable since the year 2000. Men who have sex with men (MSM) of all races comprise the majority of these new annual infections (53%), followed by heterosexual transmission (31%), injection drug users (IDU) (12%), and both MSM and IDU (4%). At the end of 2003, it was estimated that 1.1 million people were living with HIV infection (Glynn & Rhodes, 2005). Approximately a quarter of those HIV-infected do not know that they have HIV, and recent research suggests that the number of people living with HIV has been significantly underestimated (Hall et al., 2008).

Rates of infection among young men who have sex with men in the United States continue to rise. In the five years between 2001 and 2006, researchers observed an 8.6%

increase in new HIV infections among MSM, and a 33% increase among MSM under 30 years of age (CDC, 2008). Men who have sex with men represent the only group that experienced an increase in HIV or AIDS diagnoses during this time. More alarming are statistics showing disparities in race and HIV transmission among youth: During 2006, more than 90 percent of newly infected MSM under 20 years of age identified as African American or Latino. HIV and AIDS disproportionately affect people of color in all categories. African Americans experienced approximately 45% of new HIV infections from 2001 to 2006; African Americans and Latinos had infection rates 7 and 3 times the rate of Whites, respectively (Hall et al., 2008).

Women represented 27% of AIDS diagnoses in 2000, compared to 8% in 1985, and HIV incidence has remained stable since it peaked in the late 1980s. African American women are disproportionately affected by HIV or AIDS: Those older than 13 represent 66% of AIDS cases among women and the majority of new HIV infections, while representing 12% of all women in the general population. All women are primarily infected through heterosexual sex. Black men and women have the highest mortality rates.

The global HIV pandemic is staggering. UNAIDS (2008) estimated that at the end of 2007 there were 33 million people living with HIV worldwide, a dramatic increase from the estimated 8 million reported in 1990. Following are other significant statistics about the pandemic:

- Approximately 67% of people living with HIV reside in sub-Saharan Africa.
- More than 2.5 million adults and children were infected with HIV in 2007.
- More than 25 million people have died from AIDS since 1981.
- There are approximately 11 million children orphaned by HIV in Africa.
- People under age 25 account for almost half of all new infections.
- Women represent half of all HIV infections.
- 31% of people in low- and middle-income countries who need antiretroviral treatment, receive it. Children are one-third as likely to have access to these life-saving drugs.
- Less than 40% of people under age 15 know basic information about HIV.

BIOLOGICAL ASPECTS OF HIV

HIV is a retrovirus. Retroviruses, like other viruses, require a host to survive, but they differ in how they replicate and function. HIV, using an enzyme called *reverse transcriptase*, converts viral RNA into DNA, which is then integrated into the genetic coding of certain human immune cells crucial for the body's defense against illness. (This reverse action is where *retro* viruses get their name.) HIV's ability to encode itself in immune cells makes HIV treatment challenging and eradication of the virus virtually impossible. Viral suppression or elimination while simultaneously preserving the immune system is a formidable task; medications have shown much success in suppressing viral replication, but not in complete eradication of HIV. Vaccine development has presented an even greater challenge, with little prospect of a successful HIV vaccine on the horizon.

There are two genetic types, HIV-1 and HIV-2, which are essentially the same virus, transmitted and causing illness in similar ways. The vast majority of infections in the world are caused by HIV-1. HIV-2 is more common in Western Africa. There is some evidence that HIV-2 may not be as easily transmitted as HIV-1, and the time from infection to illness is longer (CDC, 2007). Differences between the two types of HIV have

greater implications for detection (a specific test exists to detect antibodies to HIV-2) and treatment. Current antiviral medications are developed to treat HIV-1 subtypes, and less is known about effective antiviral treatment for HIV-2 infection.

HIV and the Immune System

HIV targets an infected person's immune system. The immune system is a complex system of specialized organs, tissues, cells, and proteins whose primary task is to defend the body against infection, illness, and death. The immune system relies on White blood cells called *leukocytes* to perform central functions of immunity: identifying foreign substances in the body, initiating an immune response, and destroying or inhibiting that substance's function. Among the many different types of White blood cells, a particular category called *lymphocytes* is critical in understanding how HIV disease works.

Two types of lymphocytes, B and T lymphocytes, are generated in a person's bone marrow, later mature in bone marrow and lymphoid tissue (such as the lymph nodes, thymus, and spleen), respectively, and circulate throughout the body in blood and lymphatic fluids. B cells, upon encountering a foreign substance in the body, generate *antibodies* that bind to receptors on that substance, marking it for attack by other cells of the immune system. T cells are responsible for cell-mediated immunity: That is, they identify "self" cells in the body that have been infected and alert the immune system to attack and destroy those cells. One subtype of T cell—commonly referred to as a CD4 cell or a *helper cell*—helps orchestrate an immune response when it identifies an *antigen* (a marker identifying a foreign substance). Using a protein on its surface called CD4, the helper cell binds to the antigen and activates certain immune responses to begin their attack. (Figure 1.2 shows a representation of the HIV life cycle.)

HIV essentially hijacks a person's immune system to reproduce copies of itself. After HIV is transmitted, HIV seeks out the CD4 molecules. Given the abundance of this molecule on helper cells, HIV attaches to this cell, inserts its genetic coding, integrates itself in the cell's DNA, and changes that cell's function into an HIV "factory." Eventually this process wears down and destroys the CD4 cell, while generating thousands of new copies of HIV from one single cell. Without a sufficient number of CD4 cells, a person's immune system cannot orchestrate an adequate response against pathogens, resulting in severe vulnerability to certain forms of cancer and viral, bacterial, parasitic, and fungal infections that normally do not affect people with healthy immune systems. These conditions are known as *opportunistic infections and cancers* that comprise the condition called AIDS.

Course of HIV Disease

Without anti-HIV medication (called antiretrovirals), the number of years from infection to AIDS ranges from 7.7 to 11 (Babiker, Darby, De Angelis, Ewart, & Porter, 2000). A small number of HIV-infected persons (less than 5 percent) can be described as *long-term nonprogressors*—those who naturally mount an effective immune response against HIV, demonstrating significant viral suppression and elevated CD4 counts without treatment for longer than 10 years. When a person has less than 200 CD4 cells (people with normally functioning immune systems have anywhere from 500 to 1,800 CD4 cell counts), or if a person has an AIDS-defining opportunistic infection, that person meets the criteria for an AIDS diagnosis.

The course of HIV disease can be divided into four major categories: primary or acute infection, asymptomatic, symptomatic, and AIDS. There is not a single test that can be used to diagnose a person with AIDS; rather, a combination of diagnostic procedures is used to determine an AIDS diagnosis.

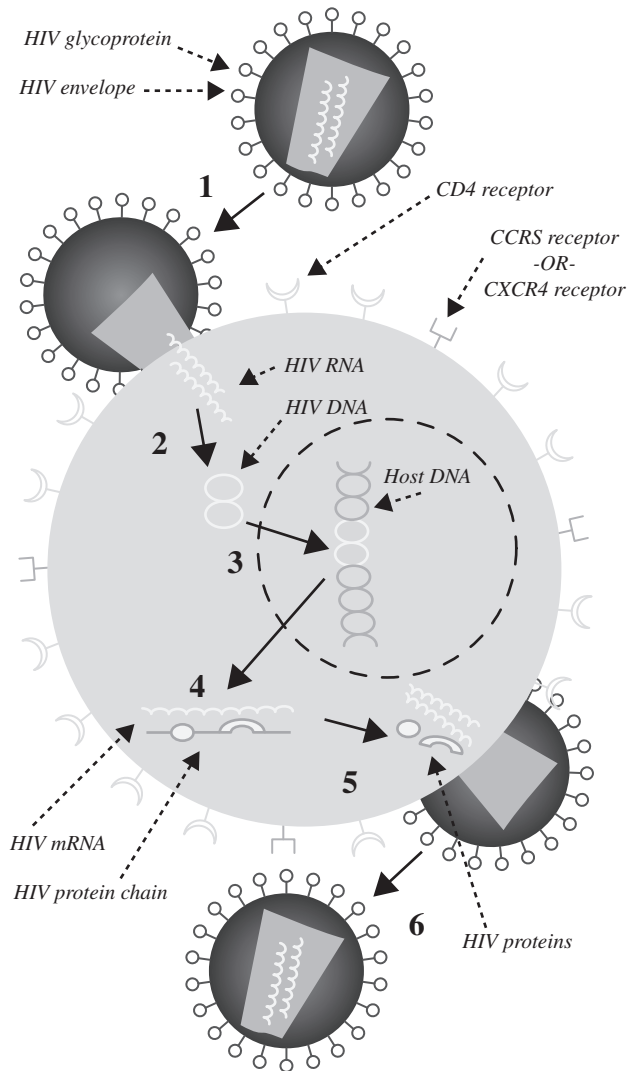


Figure 1.2 Stages of HIV life cycle

Source: http://aidsinfo.nih.gov/contentfiles/HIVLifeCycle_FS_en.pdf

Progression of HIV disease is determined through clinical manifestations of HIV-related symptoms and illnesses and through routine blood tests to monitor diagnostic markers, like CD4 counts and levels of virus in the blood (viral load). The CDC defines the progression from one disease stage to another by (1) measuring CD4 counts and/or (2) diagnosis of medical symptoms.

The stages are not rigid and exist on a continuum; they serve as a map for understanding disease progression, for deciding when to think about particular treatment interventions, for collecting data for epidemiological studies, and for the provision of certain entitlements.

Primary or Acute Infection

When a person is infected with HIV, the retrovirus travels to nearby lymph nodes where it begins replicating and infecting CD4 cells over the course of two to three days. HIV levels peak within weeks of infection (25 days on average). It is estimated that 87% of people

who are at this stage of infection will develop a set of symptoms described as *acute retroviral syndrome* (ARS), or primary HIV infection. A cardinal symptom of ARS is a high fever, generally accompanied by a number of other symptoms, including joint and muscle pain, fatigue, swollen lymph glands, and a rash on the trunk of the body. This transient condition has symptoms similar to those of influenza or mononucleosis and lasts an average of 14 days. Identifying the acute period is critical, because at that stage people are simultaneously highly infectious and unlikely to be aware of their HIV status. Some practitioners advocate for antiretroviral medication treatment during this period, as it might provide long-term advantages to the immune system. Health care professionals aware of a person's risk for HIV infection and of the symptoms involved in primary infection can play an important role in early treatment intervention and the prevention of transmission to others.

As the immune system identifies and targets HIV, antibody production begins. This process is called *seroconversion*, at which point a person is considered antibody-positive or HIV-positive (more on testing positive later). The time between the transmission of HIV and the production of antibodies that can be detected by standard antibody tests is called the *window period* (see section on testing). Even though HIV does attack and eventually weaken a person's immune system, the body does mount an immune response, and following the acute phase, HIV levels are generally reduced to low, and sometimes undetectable, levels. The level of virus in a person's blood at the end of the acute phase is identified as the *viral set point*.

Asymptomatic

For many years it was believed that HIV remained inactive or dormant in a person's body for a number of years until an unknown factor activated the virus, thus beginning replication and compromising the immune system. It is now clear that HIV remains active throughout the course of infection, slowly wearing away a person's immune system for an average of 10 years without resulting in any overt symptoms. An HIV-infected person in this stage has a 500 or greater CD4 count and has no or few HIV-related or AIDS-related symptoms.

HIV Symptomatic

During this period, a person has a range of 200 to 499 CD4 cells and may begin to manifest certain symptoms that do not qualify as AIDS-defined illnesses. This period can be critical in initiating certain medical treatments to address symptoms, as well as anticipating prophylactic treatment to prevent the onset of an opportunistic infection. If antiviral treatment has not been initiated, it is likely to be recommended and/or initiated if CD4 counts drop below 350. Some conditions that may present during this period are thrush of the mouth, throat, or vagina (candidiasis), diarrhea, shingles, and peripheral neuropathy (pain and tingling sensations in extremities).

Late-Stage Disease: AIDS

HIV-infected persons are identified as having AIDS when they have CD4 counts below 200 and/or they have two or more AIDS-related opportunistic infections or cancer. Antiretroviral treatment is prescribed during this period. For classification purposes, even if a person experiences remission of opportunistic infections and returns to a CD4 count above 200, that person is still classified as having AIDS. When a person's CD4 count drops below 200, physicians will likely offer to begin prophylactic treatments to prevent the onset of certain opportunistic infections, such as *Pneumocystis carinii* (PCP) or *mycobacterium avium* complex (MAC).

The multiple conditions that can affect a person who has HIV in every area of the body—brain, eyes, mouth and throat, lungs, gastrointestinal system, skin, and extremities—signifies the profound impact that HIV has on immune function. Approximately 33 conditions have been identified as being AIDS-related. The symptoms, conditions, and treatments are diverse and complex.

HIV TESTING

Diagnosing HIV infection is a critical tool in both prevention and treatment. People who know that they are HIV-infected are less likely to engage in high-risk behavior and more likely to seek treatment (MacKellar et al., 2005; Marks, Crepaz, Senterfitt, & Janssen, 2005). One study estimated that if all people in the United States became aware of their HIV status, unprotected anal and vaginal sex could decrease by 57% and yearly HIV incidence attributed to sex could be reduced by 31% (Marks, Crepaz, & Janssen, 2006).

The usual method for diagnosing HIV infection is an HIV antibody test. Testing technologies have changed and improved since the identification of HIV and methods used to detect infection. Antibodies produced in response to HIV, like most other antibodies that are generated, persist in a person's body throughout his or her life. For this reason, when a person is infected with HIV, that person is often characterized as being "HIV-positive," which refers to the fact that a person has shown the presence of antibodies to the virus. While tests exist (PCR or viral load tests) for detecting HIV in the body, antibody tests are technically less demanding, are more cost efficient, and have higher accuracy.

The process of antibody testing is supposed to begin with a pretest interview by a trained counselor. The purpose of the session is to discuss risk factors, explain the testing process, assess risk for HIV infection, and get informed consent to perform the test. Following the interview, fluid is collected for testing. Blood is standard, while oral fluid tests have been increasing in popularity. Oral fluid tests are cost efficient, do not require a phlebotomist, and are easier to administer in venues other than hospitals and clinics. Once fluid is collected, an enzyme immunoassay (EIA) test is performed. The EIA sacrifices *specificity* for *sensitivity*: For this reason, a negative result outside of the window period is highly accurate, and no further testing is necessary. If an EIA comes back positive, a test that is less sensitive but more specific, the Western blot test, is used to confirm the presence or absence of HIV antibodies. The Western blot test is highly accurate. In some cases, an indeterminate result might occur, where the test cannot be interpreted as either positive or negative; this most often occurs when someone is tested during the process of seroconversion.

Standard tests involve drawing a small amount of blood that will be tested for antibodies in a lab. Tests that use oral fluid (sometimes called saliva tests) are less invasive. Oral tests are subjected to the same testing process as blood. The FDA has also approved rapid tests: A significant barrier to HIV testing is associated with the psychological stress people experience between specimen collection and receiving their results, which is one week to ten days. Rapid tests produce results within an hour (if the result is negative), can be obtained in clinics, labs, and doctor's offices, and have similar accuracy to other methods. A disadvantage is that the test is similar to the EIA; while a negative result is accurate, a positive result requires an additional test, like the Western blot, to confirm results.

Since there is delay between infection with HIV and antibody production, called the *window period*, it is important that antibody tests are performed after the window period has ended. Most people develop a detectable level of antibodies within a few weeks of infection (within 25 days, on average). With rare exceptions, HIV-infected people will

have a detectable level of antibodies by three months, and a test performed at this point is usually considered accurate. To allow room for error, the CDC suggests that six months elapse before a test is considered accurate; it is reasonable for people with high-risk exposures to wait six months for testing, or be retested after a negative result at three months.

HIV-1 and HIV-2 are the only known types of HIV in the world, and two tests exist to detect the different types. Since HIV-1 accounts for the vast majority of infections worldwide, HIV-1 tests are typically used. HIV-1 antibody tests will detect the antibodies for HIV-1 with greater than 99% accuracy and will detect HIV-2 antibodies about 70% of the time. HIV-2 antibody tests should be used in cases where people have had high-risk exposures in endemic areas (West African countries). A combination HIV-1/HIV-2 test is used to test the U.S. blood supply and in many national labs.

HIV TRANSMISSION

Armed with accurate information about the dynamics of HIV transmission, social service and health professionals will be equipped to educate people in preventing the spread of HIV infection and reducing unrealistic fears of infection. Concerns about HIV infection can be psychologically and interpersonally debilitating, and many people are understandably anxious about their risk for HIV infection. Education about the basics of transmission can calm people's fears and help them feel in greater control of their health.

Communicating accurately about HIV transmission requires the language of odds and probability. Claiming that HIV can never be transmitted in a particular situation is inaccurate; scientists cannot claim that HIV cannot be transmitted in a particular situation with 100% certainty. What needs to be emphasized is the *probability* of transmission in any given circumstance. It is theoretically possible that an airplane will crash the next time you fly; the probability that it will crash in any given flight is about 250,000 in 1. Since the odds are extremely low, and assuming a vacation is very important to you, you might take a *calculated risk* and fly regardless of the small dangers involved. People make similar decisions when engaging in sexual activity.

Unique and bizarre situations arise that scientists cannot predict; discussion about transmission does not account for extremely rare circumstances. The CDC has been monitoring the ways that HIV is transmitted since the beginning of the pandemic, and epidemiological data strongly establishes how HIV is and is not transmitted:

- Unprotected vaginal or anal sexual intercourse
- Oral sex (rarely)
- Blood contact: primarily sharing syringes or needles for injection drug use, and much less frequently through occupational exposures and blood transfusions
- Mother-to-infant transmission: in the uterus, during vaginal delivery, or through breast-feeding

Reported transmission is also broken down into population categories that imply routes of transmission: men who have sex with men (MSM), injection drug users (IDU), MSM who also use injection drugs, and heterosexuals. (See Table 1.1.) The CDC annually monitors cases of HIV infections and AIDS diagnoses.

A phenomenon called the *masking effect* influences the accuracy of identifying transmission routes. When a person engages in more than one sexual behavior (for example, oral and vaginal sex) with partners, researchers cannot firmly establish the route of

Table 1.1. HIV Transmission Estimates Involving Sex and Injection Drug Use in the United States

	2006 Incidence	Incidence per Year (2003–2006)
MSM	20,100	31,200
IDU	4,900	5,900
MSM/IDU	1,400	1,600
Heterosexual	13,100	16,400

Source: *JAMA*, August 6, 2008

transmission and therefore attribute transmission to the higher-risk category (in this case, vaginal sex). If HIV was in fact transmitted through oral sex, this is *masked* in the documentation. Research studies that control for these variables (for example, studies that look at people who engage *only* in oral sex) better establish the odds of transmission through a particular behavior, since people often engage in more than one type of sex with their partners.

How HIV Is Transmitted

A person can become infected with HIV when certain fluids containing HIV come into direct contact with a person's mucous membranes or bloodstream. Mucous membranes are tissue that line cavities in the body: Those that are implicated in HIV transmission line the mouth and throat, rectum, urethra, and vagina. Damage to the mucous membranes or the existence of any inflammation or lesions (such as due to sexually transmitted infections) increases the risk for infection. Mucous membranes in certain areas of the body are more susceptible to transmission than others: Rectal mucous membranes are more prone to damage during sex and also contain higher numbers of cells that HIV targets.

Coming into contact with concentrated HIV-infected fluids (blood, semen, vaginal or cervical secretions) does not inevitably mean that infection will occur. Intact skin is an effective barrier against HIV, so where contact occurs is significant. Many variables that can and cannot be observed determine the likelihood of transmission during any exposure: (1) the type of fluid, (2) the concentration of HIV in that fluid, (3) the type and location of exposure, (4) the presence of sexually transmitted infections, and (5) the immune response of the exposed person all influence the likelihood of infection.

Introduction of HIV-infected blood into one's bloodstream poses the greatest risk for transmission, since it contains the highest concentration of HIV in people who are infected (Levy, 1998). Other body fluids that usually contain enough concentration of HIV to cause transmission include semen, cervical and vaginal secretions, and breast milk. HIV can be isolated in pre-ejaculatory fluid in much smaller concentrations. HIV can also be isolated in other areas of the body, such as cerebrospinal fluid, but risk of transmission from other fluids is generally a concern only for health care and first response workers. HIV can be infrequently isolated, in trace amounts, in an HIV-infected person's saliva and tears, but there is no evidence that people get infected through contact with these fluids. HIV has not been found in sweat.

Sexual Transmission

Approximately two-thirds of all cases of HIV infections worldwide are attributed to sexual transmission, particularly anal or vaginal sex without condoms. When describing sexual transmission, partners can be identified as *insertive* or *receptive*. The insertive partner refers to the person who is inserting his penis into another person's mouth, vagina,

or anus. The receptive person is the one whose vagina, anus, or mouth is in contact with the penis. The receptive partner, regardless of gender, is considered to be at significantly greater risk for infection than the insertive partner when having sex without condoms if ejaculation occurs inside the body. Epidemiology has revealed a high variability in the insertive partner's risk around the world; insertive partners in the United States are at much lower risk for infection compared to men in other regions of the world, for reasons that are not fully known (Padian, Shiboski, Glass, & Vittinghoff, 1997). One explanation is that in any population with a high prevalence of sexually transmitted infections (STIs), the incidence of HIV transmission through sex seems to be much higher (Fleming, 1999). Research also demonstrates that uncircumcised men are at greater risk for HIV infection than circumcised ones (Auvert et al., 2001). The lining of the foreskin in uncircumcised men has been found to contain cells vulnerable to HIV infection; in circumcised men, transmission could occur only through a much smaller area, the urethra. African countries where circumcision practices are highly dependent on cultural and religious practices show that those that do practice circumcision have much lower rates of transmission to the male than in those communities where it is not practiced (Auvert et al., 2001; Auvert et al., 2005; Williams et al., 2006).

Research demonstrates that a person is 18 to 43 times more likely to transmit HIV to a partner during the acute phase compared to the asymptomatic phase of HIV infection (Pinkerton, 2007). When someone is initially infected, there are fluctuating high levels of HIV in that person's body. A person usually does not know that he or she is infected during this period because standard HIV tests may not detect infection in the early weeks of infection.

Controversy persists regarding transmission through oral sex. Since many people engage in oral sex under the assumption that it is safer than anal and vaginal sex, it is important to ascertain the probability of transmission. Transmission risk through receptive oral sex (meaning those who are performing oral sex on another person, potentially getting fluids in their mouth) is low compared to the risks associated with vaginal and anal sex without condoms. When comparing the different kinds of oral sex people engage in (fellatio, cunnilingus, and anilingus), receptive fellatio carries the most risk, while there is little to no evidence that people have been infected with HIV while performing cunnilingus or anilingus. A small number of cases have been attributed to oral-vaginal contact and one case of oral-anal contact, and the presence of blood in those cases potentially increased that risk. Studies examining the risk for transmission during fellatio have been most effectively studied among men who have sex with men, due to the capacity to control for other variables of transmission.

Characteristics of the oral cavity that reduce the likelihood of HIV transmission include a thicker mucous membrane, fewer cells that are targeted by HIV, and certain proteins in saliva that inhibit HIV's function and infectivity (Campo, 2006). Additionally, antibodies against HIV have been detected in HIV-infected people, reducing the likelihood that HIV will be transmitted to another person through saliva. An oral cavity that is healthy—no tears, lesions, STIs, or oral disease—is an excellent barrier against infections by bacteria and viruses, including HIV.

A systematic review of the existing studies that examine oral sex risk concluded that there is insufficient data to determine the precise probability of transmission, but confirmed that the risk is extremely low (Baggaley, White, & Boily, 2008). A study identifying 102 men having sex with men who had recently seroconverted suggested that eight of them (7.8 percent) were probably infected through oral sex (Dillon et al., 2000). The presence of oral ulcers, contact with ejaculate or pre-ejaculate, and frequent exposures were

associated with some of these infections. This study estimated the route of transmission for only a small group of recently infected people and does not suggest the probability of transmission through oral sex in the general population. Another study of heterosexual couples of mixed HIV status that engaged only in oral sex resulted in no cases of HIV transmission (del Romero et al., 2002). An additional study of men having sex with men who engaged only in receptive oral sex with partners of known and unknown HIV status resulted in no transmissions (Page-Shafer et al., 2002). In order to more accurately determine oral transmission risk, larger and costlier studies need to be conducted.

Blood Transmission

Transmission through contact with blood occurs mostly when people share injection equipment: needles or syringes. Sharing injection needles or syringes accounts for approximately one-third of all HIV cases in the United States, although the incidence of HIV infection in this category has decreased by 80 percent since the beginning of the pandemic (Hall et al., 2008). It is likely that increased education and access to needle-exchange and syringe-exchange programs has had an impact on transmission in this category.

HIV transmission to health care workers exposed in the health care setting, called *occupational exposure*, is very rare. As of December 2001, only 57 reports of infections through occupational exposure have been reported (CDC, 2003). Six people who were infected (seemingly accidentally) by their HIV-infected dentist during surgery received much attention in the 1980s, but this is the only reported incident of provider-to-patient transmission (Rom, 1997).

The United States has one of the safest blood supplies in the world. Through the end of 2001, approximately 14,262 AIDS diagnoses were attributed to blood transfusion, with the vast majority of infections occurring before 1985 (CDC, 2003). The introduction of antibody screening in 1985 increased the safety of the blood supply, and in 1996, p24 antigen tests were included in the screening method, which reduces the window period by about a week. The risk of receiving a blood transfusion containing HIV is 1 in 676,000.

Vertical/Perinatal Transmission

An HIV-infected mother can transmit HIV to her infant at three different stages, all described as vertical or perinatal transmission: gestation (in the uterus), labor and vaginal delivery, and breast-feeding. Vaginal delivery poses the greatest risk of transmission to the infant due to increased exposure to maternal fluids. Without medical interventions, such as anti-HIV treatment to the mother and/or newborn or cesarean delivery, an HIV-infected mother has a 25 to 30% chance of transmitting HIV to her infant (CDC, 2008a). In the United States, medical interventions have reduced the rate of transmission to less than 2%, with a 95% reduction in AIDS cases due to vertical transmission since 1992. In 2006, only 115 children diagnosed with HIV or AIDS were infected perinatally, with 92% of all pediatric cases being associated with this route of transmission.

While the rates of vertical transmission have radically declined in the United States, education about prevention of perinatal transmission is still necessary and screening for HIV among pregnant women has become more widespread. From 2001 to 2004, approximately 7% of documented HIV-infected women were unaware of their status at time of delivery. The CDC has recommended *universal voluntary routine* screening for all pregnant women, with counseling and consent, and the availability of rapid tests increases the feasibility of testing pregnant women during labor.

During the first months of an infant's life, he or she carries maternal antibodies, so an infant will be HIV-positive by standard antibody tests (if the mother is HIV-infected) regardless of the presence of HIV in his or her body. Maternal antibodies

are eventually replaced by the infant's own antibodies, but antibody tests can have false positives up to 18 months after birth. Tests that detect HIV itself are more accurate in determining the HIV status of a newborn when used repeatedly in the first six months after birth.

No Evidence for Other Transmission Routes

Numerous studies have examined the possibility of transmission through the major routes of transmission. The following are examples of ways that HIV is *not* transmitted:

- *Casual contact.* Several epidemiological studies early in the pandemic examined households where those who were uninfected had daily contact with an HIV-infected family member, and no cases of transmission through casual contact were detected (Fischl et al., 1987; Friedland et al., 1986; Lusher et al., 1991) through activities such as sharing kitchen utensils or bathroom facilities or kissing.
- *Inanimate objects.* HIV is fragile when exposed to the environment outside the human body. HIV requires a host—a living human cell—to survive. Laboratory studies have allowed fluids that contain high concentrations of HIV to dry and have found that infectiousness is reduced significantly within several hours (by about 95 percent). These studies do not replicate real-life situations, and there is no documented evidence that someone has been infected through contact with inanimate objects (<http://www.cdc.gov/HIV/resources/qa/qa35.htm>).
- *Accidental injury with injection needles outside of health care settings.* Since the beginning of the pandemic, anecdotes of people being exposed to HIV through accidental injury by a needle (for example, in a movie theater) have not been verified.
- *Insects.* There is no evidence that HIV is transmitted by insects, such as mosquitoes or ticks. In areas where there is a high prevalence of HIV infection and large populations of insects, there have been no documented cases of transmission through this route. Insects inject their own saliva as a lubricant to assist feeding (malaria and yellow fever are transmitted through insect saliva). They do not inject their own or a previously bitten person's blood. Also, HIV does not survive or reproduce in insects; HIV does not survive long enough outside of its host to be spread by the insect's mouth area; and insects also do not generally feed on two people in immediate succession.

TREATMENT

The development of effective medication regimens that radically reduce HIV-associated illness and death alters psychological and social perceptions of HIV disease. For people who have access to anti-HIV medication and expert medical care, HIV has largely become a manageable, chronic disease instead of a fatal one. Unfortunately, disparities in access to quality medication and treatment illuminate the complicated interplay of socioeconomic class, oppression, political and economic ideologies, and health care delivery. In 2007, approximately 31% of people in low- or middle-income countries in need of anti-HIV medication received it (WHO, 2007). While these numbers are unacceptably low—less than a third of those who need medications are getting them—there have been notable advancements in providing access to treatment in the twenty-first century, and international public health initiatives are gaining greater attention and funding.

Medications used to treat an HIV-infected person can be broken down into five categories:

1. Those that suppress HIV replication, called *antiretrovirals* (ARVs), *antiretroviral treatment* (ART), or *highly active antiretroviral treatment* (HAART)
2. Those that treat or prevent opportunistic infections (such as antibiotics)
3. Those that treat or manage HIV symptoms
4. Those that treat or manage the side effects of other medications
5. Psychotropic medication for psychiatric symptoms related to HIV infection

In addition, some HIV-infected people choose to use supplements, such as vitamins, herbal and homeopathic preparations, and alternative treatments such as massage, Reiki, and acupuncture. However, given the lack of rigorous research and regulatory control over their production, alternative treatments need to be used with caution and under the guidance of a medical professional. People with HIV often take a number of different medications, and potentially harmful interaction between different substances needs to be closely monitored by a medical professional. This section focuses primarily on antiretroviral treatment (ART or ARVs).

Antiretroviral Treatment

The development of and access to a new class of antiretrovirals called *protease inhibitors* in the mid-1990s marked a turning point in HIV treatment. Protease inhibitors, used in combination with other classes of medications, reduced HIV to undetectable levels in many HIV-infected persons, resulting in decreasing mortality rates and AIDS diagnoses (see Figure 1.3). While protease inhibitors represent just one class

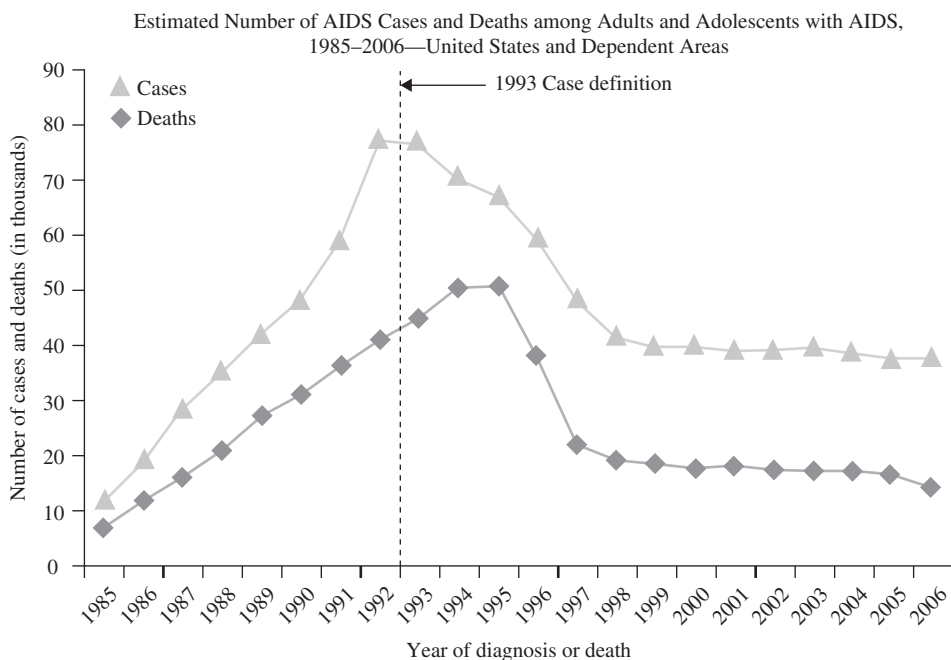


Figure 1.3 Impact of Combination Therapy

Source: http://www.cdc.gov/HIV/topics/surveillance/resources/slides/epidemiology/slides/EPI-AIDS_1.pdf

of medications that are now used to treat HIV disease, their development and success gave medicine a sophisticated understanding of how to medically intervene in HIV disease progression.

There are now more than 30 FDA-approved HIV antiretroviral medications. The largest groups of anti-HIV medications that are prescribed can be broken down into three classes: nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs, or “nukes”), non-nucleoside reverse transcriptase inhibitors (NNRTIs, or “non-nukes”), and protease inhibitors (PIs). There are three other classes of medication—entry inhibitors, integrase inhibitors, and maturation inhibitors—which are newer medications that are less frequently used or are still considered experimental. The classes are named in reference to where they act in *inhibiting* the life cycle of HIV in a CD4 cell. By disrupting certain HIV replication processes—fusion and entry into the cell, reversing HIV RNA into DNA, integrating itself into the cell’s DNA, and assembling new replications of HIV—ART can attack HIV’s Achilles’ heel: its need to use CD4 cells to produce replications of itself.

Antiretroviral treatments are always prescribed in certain combinations—called *combination therapy*—most often using three drugs from two different classes of medication. Treatment with only one particular drug, called *monotherapy*, is likely to fail by encouraging a drug-resistant mutation of HIV to develop. Prescribing different types and classes of medications attacks the virus at different stages of its life cycle, reducing its capacity to develop resistance against the drugs. Consistent suppression of HIV replication is crucial, since the development of drug-resistant strains of HIV can render a particular medication treatment ineffective. Drug-resistant HIV strains can also be transmitted to another person, in whom the same medications would likely be ineffective, which is a public health concern.

The primary aim of ART is to reduce and maintain HIV at undetectable levels. Undetectable *does not mean that there is no HIV!* Even if HIV is not detected by standard viral load tests, that does not mean that HIV is not present in a person’s blood or body. The virus can be present in amounts too small to be detected by current tests, in a CD4 cell, or in areas of the body called *reservoirs* (for example, in semen or cervical fluid or lymphoid tissue). While there is strong evidence that a person who has undetectable HIV levels in his or her blood has a much lower chance of transmitting HIV than someone who has a detectable level, that person on treatment is still infected and can still transmit the virus to another person. Given the impossibility of knowing the amount of HIV present in a person’s body at any given time, experts are reluctant to say that HIV-infected people on ART cannot transmit HIV to a partner.

Anti-HIV treatment has dramatically reduced rates of mother-to-infant transmission in the United States and other countries where adequate medical treatment exists. Without medication, an HIV-infected mother has a 20% to 30% chance of transmitting HIV to her infant. Administration of anti-HIV medication during pregnancy and/or delivery, performing cesarean sections in women with high viral loads, and providing medication to newborns has reduced the rate of vertical transmission to less than 2% (Cooper et al., 2002). Another study demonstrated 90% effectiveness in preventing HIV transmission to infants among a cohort (European Collaborative Study, 2005). These reductions reflect statistics in areas where there is access to adequate prenatal and HIV care. Mother-to-child HIV transmission accounts for the vast majority of the estimated 700,000 new annual HIV infections in children worldwide. These data emphasize how education, treatment, and increased access to prenatal care in resource-challenged areas can dramatically reduce HIV transmission to infants.

The Challenges of Taking HIV Medication: Side Effects

Medications to fight HIV could be considered blunt instruments; they effectively debilitate HIV, but in the process can also produce unwanted and unintended side effects in the people who take them. As people live longer with HIV, and as the field sees people living longer on ART, greater understanding is developing about the long-term effects on HIV-infected persons, leading to efforts to fine-tune medications.

Side effects that people on HIV treatment experience should always be taken seriously. If short-term side effects can be managed and tolerated until they subside, that is preferable to changing an already effective treatment. If side effects are too difficult to manage, alternative treatment regimens should be explored with the physician. Intolerable side effects that a person experiences can lead to not taking the medicine correctly or stopping treatment altogether, and effective ongoing communication and interaction with caregivers can help prevent this.

The cause of physical and psychological symptoms can be difficult, and sometimes impossible, to accurately identify. While certain side effects are relatively easy to identify and diagnose, others can be attributed to multiple factors: for example, lifestyle, unidentified illness, and nutrition. If the initiation of a particular antiretroviral medication coincides with the development of depressive symptoms, the task of identifying the cause of symptoms can be daunting. One antiretroviral, called Sustiva, has been reported to result in depressive symptoms in some people. However, it is not unusual for a person who is struggling with being HIV-infected and having to take medication to experience depression. Determining what is causing a symptom in a person taking ART is an inexact science that requires thorough biopsychosocial assessment, different levels of intervention, and the willingness of caretakers to take concerns seriously and to be flexible, and sometimes creative, in their approaches to treatment. A thorough assessment of a person's way of life and psychological status can also illuminate factors that can contribute to, and possibly improve, side effects of medication.

Most people can tolerate short-term side effects to continue their medication regimen; rarely are side effects severe enough to merit changing a medication regimen, but all adverse reactions should be taken seriously. The most common short-term side effects are gastrointestinal symptoms (diarrhea, nausea, vomiting), headache, rash, fatigue, dry mouth, and psychological symptoms (depression, anxiety, and nightmares). As people live longer with HIV on antiretroviral treatments, long-term side effects are only recently being observed and studied. Longer-term health problems could be associated with the anti-HIV medications themselves, the dynamics of HIV infection, older age, or unidentified risk factors. Some of the long-term side effects associated to ART are:

- **Fat redistribution.** Lipodystrophy is an abnormal distribution of fat (lipids) in the body. Lipohypertrophy refers to abnormal fat accumulation, usually seen in the abdomen, breasts, or upper back. Fat loss (lipoatrophy) usually occurs in the face, arms, legs, and buttocks. These symptoms may be associated with other metabolic abnormalities and often result in distressing psychological reactions. Some treatments that replace or remove fat in affected areas exist.
- Higher levels of cholesterol and triglycerides, which are associated with increased risk for heart attack, stroke, and pancreatitis.
- Diabetes as a result of increased glucose and insulin levels.
- Bone loss and weakening of bones (osteoporosis and osteopenia).
- Liver and kidney damage.

Certain medications are implicated in the risks of the development of some of these long-term side effects, and understanding the risks associated with particular medications, as well as thorough assessments of other health factors, nutrition, and lifestyle, can all have an impact on these conditions.

Medication Adherence

A critical determinant of successful antiretroviral treatment—and a considerable challenge for many people taking ART—is adherence (sticking to) to medication regimens. When antiretrovirals are not taken in accordance with how they are prescribed, HIV can mutate and develop *resistance* to that medication, possibly resulting in *cross-resistance*—a resistance to other drugs in a particular class of medication—leading to failure in that particular treatment. Adherence to regimens can be particularly difficult when there are multiple drugs that need to be taken multiple times every day, sometimes with particular dietary restrictions, dosage, and timing requirements. Advancements in drug formulations have greatly reduced the amount of pills that a person may need to take; medications continue to be developed that combine different drugs within and across classes into one dose.

Research suggests that poor adherence is a widespread problem (Murphy et al., 2001; Nieuwkerk et al., 2001), though few long-term studies exist. It is believed that 95% adherence is needed for the best results, or the person with HIV risks increased viral replication and development of drug-resistant virus (Paterson et al., 2000). However, there is evidence that levels of adherence needed to achieve sufficient viral suppression is dependent on the class of medication taken. One study demonstrates that regimens of protease inhibitors require greater adherence (greater than 95%) than NNRTI regimens (greater than 54%), a significant finding since protease inhibitors are commonly prescribed in treatment regimens (Bangsberg, 2006). While more research needs to be conducted on medication-taking behaviors among HIV-infected populations, the importance of adhering as closely as possible to a medication regimen is vital to treatment success.

Researchers and clinicians study and observe varying psychosocial factors that predict medication adherence, such as socioeconomic status, race, gender, psychiatric conditions and cognitive functioning, family and social support networks, attitudes toward treatment, physician-patient relationships and rapport, and the complexity of treatment regimens (Ammassari et al., 2002; Stone et al., 2001; van Servellen, Chang, Garcia, & Lombardi, 2002). While research studies have attempted to identify personality traits, behaviors, and environmental conditions that contribute to suboptimal medication adherence, providers should be cautious about drawing premature conclusions about a person's likelihood to adhere to medication. Individual readiness to begin medication, recognizing potential barriers to adherence, effective provider-client communication, and ongoing monitoring and assessment are all critical in supporting medication adherence. It can be difficult for service providers who are not on complicated medication regimens to understand why a person would risk his or her health by not taking medications correctly, and active empathic engagement with persons with HIV is a vital tool to support adherence.

When to Start Treatment

Since the development of effective antiretroviral treatment, debates have persisted about when to treat a person who is infected with HIV. With the advent of protease inhibitors and combination therapies, a “hit early, hit hard” approach was endorsed, with the hope that early, intensive treatment would offer the possibility of viral eradication. When the hope for eradication was never realized, physicians and researchers began to think

more critically about when was the most effective time to initiate treatment. The debates have been vigorous, involving an intersection of different principles, ethics, and values, along with a lack of thorough enough understanding of the mechanics of antiretroviral treatment and disease progression.

From a medical standpoint, researchers have conflicted opinions about whether early intervention actually demonstrates long-term advantages for survival rates and viral suppression, though the tide seems to be turning, with the support of important research, toward suggesting earlier medication interventions. Dr. Anthony Fauci, a central figure in the study of anti-HIV medication research, recently suggested that early intervention has the promise of a “functional cure” of HIV. The arguments against treating early involve starting someone on medication that cannot be stopped once started, that causes long-term physical side effects, that puts financial and psychological burdens on the person with HIV, and that raises the risk of developing resistance to the medication due to difficulties involved in long-term adherence. Ethically, one should be treated only when benefits outweigh costs. Given the long-term side effects of long-term treatment, the person with HIV and his or her physician must weigh these decisions carefully.

The U.S. Department of Health and Human Services has set, and continues to revise, guidelines on when a person should begin ART. (See Table 1.2.) Physicians, as well as HIV-infected persons and those who provide services to them, need to stay abreast of these changing guidelines.

HIV has a tendency to mutate quite rapidly, creating slightly different variations of itself, which has resulted in a genetic diversity of HIV that can present challenges to treatment. Given the number of different medications and mutations of HIV that are resistant to particular medications, choosing a good treatment regimen requires specialized medical testing

Table 1.2 Indications for initiating ART therapy

Clinical Condition and/or CD4 Count	Recommendations
<ul style="list-style-type: none"> History of AIDS-defining illness (AI) CD4 count <200 cells/mm³ (AI) CD4 count 200–350 cells/mm³ (AII) Pregnant women* (AI) Persons with HIV-associated nephropathy (AI) Persons coinfectd with hepatitis B virus (HBV), when HBV treatment is indicated (Treatment with fully suppressive antiviral drugs active against both HIV and HBV is recommended.) (BIII) 	Antiretroviral therapy should be initiated.
<ul style="list-style-type: none"> Patients with CD4 count >350 cells/mm³ who do not meet any of the specific conditions listed above 	<p>The optimal time to initiate therapy in asymptomatic patients with CD4 count >350 cells/mm³ is not well defined. Patient scenarios and comorbidities should be taken into consideration.</p> <p>(See box below and text regarding risks and benefits of therapy in patients with CD4 count >350 cells/mm³).</p>

Source: <http://www.aidsinfo.nih.gov/Guidelines/GuidelineDetail.aspx?MenuItem=Guidelines&Search=Off&GuidelineID=7&ClassID=1>

and expertise. Laboratory analysis (called *genotyping* and *phenotyping*) of the specific characteristics of HIV with which a person is infected can anticipate medications the virus might be resistant to, which drugs will more likely work, and at what dosage and combinations. Resistance testing is recommended for all HIV-infected people, especially for those newly infected (even if they don't plan on starting treatment), before a medication regimen is decided upon, and those for whom medication regimens fail or are not working well.

Similar to diabetics who need to closely monitor and manage glucose levels, people with HIV need to closely monitor viral levels and CD4 counts to determine how effective a particular drug regimen is and to prevent disease progression. Drug-resistant mutations of HIV are most commonly attributed to poor medication adherence, problems with how the medication is absorbed into the bloodstream, and adverse drug interactions. When medications fail to suppress HIV replication sufficiently, HIV-infected persons need to make informed decisions with their doctors about changing treatment regimens.

HIV PREVENTION

In the absence of effective medical interventions to prevent HIV transmission and cure infection, educational and behavioral interventions have been the cornerstone of HIV prevention since the early years of the pandemic. Assuming that people cannot take the steps to promote and protect their health unless they have an understanding of the risks involved in engaging in certain behaviors, a central piece of HIV prevention has been educating people about how HIV is transmitted, how to prevent transmission of the virus, and how to get tested. With the advent of effective anti-HIV treatments, cultural attitudes have changed in accordance with access to the medications. Prevention experts express concern that, especially among populations that are at significant risk for HIV infection, people have become complacent about HIV transmission and safer sex and drug behavior. Recent research on continued high rates of HIV transmission among certain populations suggests that prevention efforts are not effective enough and need to be closely examined and revised.

Early in the pandemic, when scientists began to realize that HIV was an infectious agent that could be transmitted through *behaviors* like sex and sharing syringes, there were ideological debates about funding prevention efforts toward those who engaged in risky behavior. The "Just Say No to Drugs" campaign of the Reagan administration was in vogue, and in many ways the message was applied to sex: Abstinence is the best way to prevent HIV infection. Conservatives did not want to support and fund explicit messages about condom use and needle sharing to prevent HIV transmission for fear of appearing to condone promiscuous or drug-using behavior. Implicit in this position was a fundamental rejection of homosexuality, drug use, and any behavior that was deemed deviant. Prevention advocates urged that preventing the spread of a fatal disease took precedence over moral messages.

Safer sex education began in the private sector. The initial strategies started by community organizers in the gay community involved disseminating explicit information about HIV transmission and distributing condoms throughout community venues. Materials that were unapologetic about using frank and culturally appropriate language to describe the realities of sexual behavior and HIV transmission were considered to be more effective than information that was euphemistic or omitted information that might be "offensive." Attitudes toward sex in the United States made transparent and accurate transmission of information difficult.

HIV prevention efforts through federal government funding in the United States have been fueled primarily by politically conservative and religious principles, focused

primarily on abstinence-based education. Federal funding to schools has been strictly prohibitive of comprehensive sex education to students, restricting funds to abstinence-only education models. A meta-analysis of the existing empirical research on the effectiveness of abstinence-only programs in the United States found that the programs showed no consistent beneficial effect on HIV infection rates, the incidence of sexual behaviors, including sexual initiation, unprotected or frequency of vaginal sex, amount of partners, or condom use (Underhill, Operario, & Montgomery, 2007).

Federal funding of needle-exchange or syringe-exchange programs—services where people can exchange used needles for new ones or have access to clean needles without a prescription—has also proven controversial, because opponents argue that it will increase or condone illegal drug use. Injection drug users share needles due to limited access to clean needles, and not supplying them with clean needles perpetuates the HIV pandemic. Since cleaning needles requires knowledge about the process, access to supplies, and careful attention after each use, programs that provide clean needles to users increase the odds that they will not need to share needles. In 1992, Connecticut decriminalized possession of syringes or needles without a prescription, which made them available for sale through pharmacies for nonmedical use. The amount of needles or syringes purchased for nonmedical use increased significantly (Valleroy et al., 1995). New Haven, Connecticut, also implemented legal needle-exchange programs in 1990. Studies demonstrated that this intervention decreased the incidence and prevalence of HIV among injectors in the area and increased referrals to drug treatment programs (Heimer, Kaplan, Khoshnood, Jariwala, & Cadman, 1993; Vlahov & Junge, 1998). Despite the evidence, the United States has steadfastly refused, on ideological grounds, to federally fund needle-exchange and clean-needle programs.

A harm-reduction model of prevention presumes that complete abstinence from risk-taking behavior is unrealistic for many people and that there are ways to reduce harm when taking risks. Methadone maintenance programs are based on the harm-reduction model; a less harmful drug, methadone, is administered in a controlled fashion for heroin addicts to prevent the more harmful effects of illegal heroin use. The harm-reduction approach respects the reality of the person's psychological preparedness for change, emphasizes the importance of avoiding judgment of people's behaviors, and places the value of individual and collective health over moral and ideological arguments.

When condoms are used correctly for anal and vaginal sex, they are very effective in preventing the transmission of HIV and many other STIs. Male condoms are latex, polyurethane, or animal membrane sheaths that are placed on an erect penis to prevent the receptive partner in vaginal or anal sex from coming into contact with semen or pre-ejaculate. While animal-membrane condoms are effective as birth control, they should never be used to prevent HIV transmission because they contain pores that HIV can pass through, while latex and polyurethane condoms have pores smaller than the virus. Water- or oil-based lubricants can be used with polyurethane condoms, while one should exclusively use water-based lubricant with latex condoms. Nonoxynol-9, a spermicide that is in some lubricants, should not be used for disease prevention, as allergic reactions and irritation to the substance have been shown to increase the risk for HIV transmission when exposed, and spermicides do not kill retroviruses.

Since the data show that condoms should be used for vaginal and anal sex consistently, we need to educate people how to use condoms correctly. The CDC has set forth the following guidelines for using male condoms:

- Use a new condom for each act of intercourse.
- Put on the condom as soon as erection occurs and before any sexual contact (vaginal, anal, or oral).

- Hold the tip of the condom and unroll it onto the erect penis, leaving space at the tip of the condom, yet ensuring that no air is trapped in the condom's tip.
- Adequate lubrication is important, but use only water-based lubricants, such as glycerin or lubricating jellies (which can be purchased at any pharmacy). Oil-based lubricants, such as petroleum jelly, cold cream, hand lotion, or baby oil, can weaken the condom.
- Do not use lubricants with nonoxynol-9 (a chemical that inhibits sperm from causing pregnancy) for HIV prevention, as it can cause an allergic reaction that increases a person's risk for HIV infection.
- Withdraw from the partner immediately after ejaculation, holding the condom firmly to keep it from slipping off.

The FDA approved a female condom in 1993. Statistics reflecting increasing rates of HIV infection among women through heterosexual sex raised concerns about their ability to negotiate condom use with their partners. The female condom is a polyurethane pouch with two rings on each end, and one opening. A removable flexible ring at the closed end is inserted into the vagina, and the ring on the opened end stays outside the vulva, which prevents it from slipping or bunching up. The fact that women can wear the condom for up to eight hours prior to sex, or use it if their partner refuses to wear a condom, empowers them to have more control during sex. Female condoms are more expensive than male condoms and can be difficult to use and negotiate, so it is still widely unavailable around the world. Female condoms can be used for anal intercourse as well, whether the insertive partner is male or female.

CONDOM EFFECTIVENESS

There is some confusion about the research on condom effectiveness, due to both the methodological complexity of this research, misinterpretation of findings, and ideological debates. Theoretically, a condom should be 100 percent effective in preventing the transmission of HIV based on laboratory studies, since HIV cannot permeate condoms (Carey et al., 1992). Epidemiologic studies have demonstrated that condoms are highly effective in preventing the transmission of HIV, as well as preventing the transmission of certain STIs—such as chlamydia, gonorrhea, and trichomoniasis (Weller & Davis, 2003). It has been incorrectly presumed that condoms do not work because they do not prevent the transmission of all STIs 100% of the time; some STIs, like herpes, syphilis, and genital warts (HPV), are transmitted by lesions on the skin that may not be shielded by the condom. Reviews of existing literature show that condoms are effective in preventing HIV transmission 80 to 95% of the time, with considerable limitations in some of the research to account for correctness of use (Pinkerton & Abramson, 1997; Weller & Davis, 2003). In a longitudinal four-year study of mixed-HIV-status couples, all 124 couples who used condoms every time prevented transmission of HIV, while 12 partners of 121 couples who did not consistently use condoms became infected (De Vincenzi, 1994). Other studies of serodiscordant couples where consistent versus inconsistent use was closely examined yielded similar results (Allen et al., 1992; Guimarães, Muñoz, Boschi-Pinto, & Castilho, 1995; Laurian, Peynet, & Verroust, 1989; Nicolosi, Leite, Musicco, Arici, et al., 1994; Saracco et al., 1993).

Studies conducted about condom failure among sexual partners have shown widely different rates, with most failures resulting from incorrect use and not with the condom itself. Condom breakage during intercourse is estimated to be anywhere from 1 to 8%. One study of couples using condoms over a period of time showed that 62% of them experienced no condom failure (meaning breakage or slippage), 29% had one to three failures, and 9% had four or more failures. Most studies show that higher rates of condom failure happen among a small percent of the general population (some have estimated as low as 4 to 6%), depending on aspects of condom use like technical skill, experience using condoms, prior episodes of breakage, condom fit, and amount of lubrication. Commercial sex workers, presumably due to their experience in using condoms, have demonstrated the lowest condom breakage or slippage rates.

Medical Approaches to Prevention

Two interventions use existing antiretroviral treatments to attempt to prevent HIV infection prior to exposure and immediately after exposure. Postexposure prophylaxis (meaning prevention), or PEP, was first conceived in health care settings following occupational exposures to HIV-infected blood among health care workers. Theoretically, if anti-HIV medication is used shortly after exposure, long-term infection could be prevented. The effectiveness of PEP in nonoccupational exposures has not been studied. One study did demonstrate a 81% reduction in HIV infection among health care workers treated with PEP compared to those who remained untreated following an occupational exposure (Cardo et al., 1997). PEP has subsequently become available to the general public, usually through clinics or emergency rooms, for sexual exposures that present a high-risk for transmission. For example, it has been routine to offer PEP to victims of sexual assault when there is the possibility of transmission, or among serodiscordant (one is HIV-positive and one is HIV-negative) couples when there is an incident that poses significant risk for infection.

In order for PEP to be effective, treatment needs to be initiated within 32 hours of exposure, and some suggest that administration within 12 hours is optimal. Beginning PEP has several complications. First, access to medication in the short time period following exposure is unrealistic for most people. Also, a person has to commit to taking medication daily for about one month; these medications are typically not covered by health insurance for PEP, so it can be expensive, and adherence to the medication can be complicated by side effects and adverse psychological reactions.

PrEP, or preexposure prophylaxis, is a more recent area of investigation, and works on the same principles as PEP, except medication is administered to an HIV-negative person *prior* to being exposed to HIV. PrEP can be especially useful for women around the world who experience cultural barriers to negotiating condom use, active injection drug users, or men who have sex with men engaging in unprotected intercourse. Animal studies among nonhuman primates have demonstrated that administration of PrEP to an uninfected animal resulted in zero transmissions when repeatedly exposed to the primate equivalent of HIV, called *simian immunodeficiency virus* (SIV), compared to an untreated control group that resulted in significant levels of infection (Garcia-Lerma et al., 2006). While human research trials in Africa are under way, there is no evidence that PrEP will be effective in humans.

Microbicides are creams or gels that are applied inside the rectum or vagina to protect against HIV and other STI transmission. Research on microbicides was initiated and designed to provide more control to people, especially women, in preventing HIV transmission when condom use is sporadic or unavailable. There are many experimental microbicides that have shown effectiveness in animal studies, but human studies have been unsuccessful so far, and more need to be conducted to determine the effectiveness of microbicides.

Ultimately, a vaccine would be the most effective way to prevent transmission, and potentially eradicate HIV transmission around the world. Vaccines work by stimulating antibody production against a particular pathogen before someone is exposed to it, providing resistance to infection when exposed in the future. Vaccine trials to date have been limited due to ethical and programmatic difficulties, and none of the vaccine trials have yielded successful results. The high genetic variability of HIV and its capacity to mutate and evolve at a rapid pace makes the development of an effective vaccine against all strains of HIV a formidable task.

Personal Perspective

Living with HIV, by Chris

I tested HIV-positive on October 28, 1992. I was an active alcoholic and cocaine addict at the time, and my life was already a train wreck. The HIV diagnosis just felt like the final nail in the coffin. My HIV diagnosis co-occurred with a case of Hepatitis A. I continued to drink and do drugs throughout this time.

In 1992, being HIV-positive was still very much a death sentence. I was in show business in New York City, and many people in my world were getting sick and dying. The first time I got blood work done, my CD4 count was 424. AZT was the only approved treatment, and it wasn't thought of as being great. They said it might prolong your life for a little while. I took it briefly in 1993, but it made me dizzy and nauseated and I soon gave up. So from the end of 1992 through the beginning of 1995, I just kind of waited to get sick.

In February of 1995, I heard about a new drug called Epivir (3TC) that was shown to be effective in combination with AZT. I went on it right away, and three months later my CD4 count had doubled from 267 (the lowest it's ever been) to 545. I also got sober in July of that year, and know that that helped strengthen my immune system as well.

In December of 1995, I was prescribed Invirase, one of the first protease inhibitors, to add to my regimen. I was one of the very first people on combination therapy, called "the triple cocktail." Over the next nine years my CD4-cells went up and stayed up (at one time topping 1,500) while my viral load was most often undetectable. When it wasn't, my doctor changed my medication. And yet I still felt that my life was only really being increased in three-month increments, from doctor's appointment to doctor's appointment. I kind of waited for what I thought would be the inevitable fall. Side effects could be bad too: rash, nausea, kidney stones, and stomach problems. Some I was able to deal with. Some of the medications I simply couldn't take. Lypodystrophy also occurred. I lost fat in my face and gained it in the back of my neck.

In August of 2004, after almost nine years of antiviral therapy, I wanted a break. I was tired of Sustiva and the resulting horrible dreams that often woke me

up feeling terrified. I had done so well for so long; I wanted to see how I could do without medication. And I must admit I sort of wanted to see if the virus would “still be there” untreated.

Under the supervision of an HIV specialist, at first my treatment vacation was quite liberating. It was a relief not to have to take pills anymore. At first my counts remained stable. Then over the course of the next 19 months, my T cells slowly decreased while my viral load slowly increased. It became increasingly demoralizing. I was reminded that I “still had it.”

In March of 2006, with my T cells back down to 426 and my viral load at about 10,000, my doctors advised that I resume antiretroviral treatment and I agreed. The vacation was over and that was okay. Since then I’ve been on a very good combination of Reyataz and Truvada (three pills a day) that I’ve tolerated quite well. My counts are great, and I have other options should this “cocktail” lose its efficacy. Thankfully, the fat deposits on my neck—known as lypodystrophy—have been surgically removed and the areas of my face that have lost fat—lipoatrophy—have been filled in with a treatment called Sculptra.

It’s only been in the past couple of years that I’ve really come to believe that I’m not going to die from HIV. Sixteen years after my diagnosis, I remain grateful and pretty astounded that my story has played out as it has.

CONCLUSIONS

The HIV pandemic continues to have a profound impact on people around the world, and it is crucial that social workers and other professionals in the human services are prepared to meet the needs of those confronted with the disease. While people in the helping professions are not required to be medical experts on HIV, being aware of the basics of HIV disease can have a significant impact among individuals and communities affected by HIV and AIDS. Armed with basic knowledge about transmission, treatment, policy, and prevention, we can listen intelligently and compassionately to people with HIV and their caregivers, provide support in seeking treatment and adhering to medication, reduce barriers to safer sex or access to clean needles and syringes, and reduce people’s anxieties about the risks associated with HIV disease.

REFERENCES

- Allen, S., Tice, J., Van de Perre, P., Seruflira, A., Hudes, E., Nsengumuremyi, F., et al. (1992). Effect of serotesting with counselling on condom use and seroconversion among HIV discordant couples in Africa. *British Medical Journal*, 304(6842), 1605–1609.
- Ammassari, A., Trotta, M. P., Murri, R., Castelli, F., Narciso, P., Noto, P., et al. (2002). Correlates and predictors of adherence to highly active antiretroviral therapy: Overview of published literature. *Journal of Acquired Immune Deficiency Syndromes*, 31(Suppl. 315), S123–S127.
- Auvert, B., Buvé, A., Lagarde, E., Kahindo, M., Chege, J., Rutenberg, N., et al. (2001). Male circumcision and HIV infection in four cities in sub-Saharan Africa. *AIDS*, 15, S31–S40.
- Auvert, B., Taljaard, D., Lagarde, E., Sobngwi-Tambekou, J., Sitta, R., & Puren, A. (2005). Randomized, controlled intervention trial of male circumcision for reduction of HIV infection risk: The ANRS 1265 Trial. *PLoS Medicine*, 2(11), 1112–1121.

- Babiker, A., Darby, S. C., De Angelis, D., Ewart, D., & Porter, K. (2000). Time from HIV-1 seroconversion to AIDS and death before widespread use of highly active antiretroviral therapy: A collaborative reanalysis. *Lancet*, 355, 1131–1137.
- Baggaley, R. F., White, R. G., & Boily, M.-C. (2008). Systematic review of orogenital HIV-1 transmission probabilities. *International Journal of Epidemiology*, 37(6), 1255–1266.
- Campo, J., Perea, M. A., del Romero, J., Cano, J., Hernando, V., & Bascones, A. (2006). Oral transmission of HIV, reality or fiction? An update. *Oral Diseases*, 12(3), 219–228.
- Carey, R. F., Herman, W. A., Retta, S. M., Rinaldi, J. E., Herman, B. A., & Athey, T. W. (1992). Effectiveness of latex condoms as a barrier to human immunodeficiency virus-sized particles under conditions of simulated use. *Sexually Transmitted Diseases*, 19(4), 230–234.
- Castro, K. G., Ward, J. W., & Slutsker, L. (1992). 1993 revised classification system for HIV infection and expanded surveillance case definition for AIDS among adolescents and adults. Centers for Disease Control and Prevention: *Morbidity and Mortality Weekly Report MMWR*, 41, 961–962.
- Centers for Disease Control and Prevention. (1981a). Follow-up on Kaposi's sarcoma and Pneumocystis pneumonia. *Morbidity and Mortality Weekly*, 30(33), 409–410.
- Centers for Disease Control and Prevention. (1981b). Kaposi's sarcoma and Pneumocystis pneumonia among homosexual men—New York and California. *Morbidity and Mortality Weekly*, 30, 305–308.
- Centers for Disease Control and Prevention. (1981c). Pneumocystis pneumonia—Los Angeles. *Morbidity and Mortality Weekly*, 30, 250–252.
- Centers for Disease Control and Prevention. (2003). Preventing occupational HIV transmission to health care workers. Retrieved March 31, 2009, from <http://www.cdc.gov/HIV/resources/Factsheets/hcwprev.htm>
- Centers for Disease Control and Prevention. (2006). *HIV/AIDS Surveillance Report, Volume 18*. Atlanta: Department of Health and Human Services, Centers for Disease Control and Prevention. Retrieved March 31, 2009, from <http://www.cdc.gov/HIV/topics/surveillance/resources/reports/2006report/default.htm>
- Centers for Disease Control and Prevention. (2008). Trends in HIV/AIDS diagnoses among men who have sex with men—33 States, 2001–2006. *Morbidity and Mortality Weekly*, 57(25), 681–686.
- Cooper, E. R., Charurat, M., Mofenson, L., Hanson, I. C., Pitt, J., Diaz, C., et al. (2002). Combination antiretroviral strategies for the treatment of pregnant HIV-1-infected women and prevention of perinatal HIV-1 transmission. *Journal of Acquired Immune Deficiency Syndromes*, 29(5), 484–494.
- del Romero, J., Marincovich, B., Castilla, J., García, S., Campo, J., Hernando, V., et al. (2002). Evaluating the risk of HIV transmission through unprotected orogenital sex. *AIDS*, 16(9), 1296–1297.
- De Vincenzi, I. (1994). A longitudinal study of human immunodeficiency virus transmission by heterosexual partners. *New England Journal of Medicine*, 331(6), 341–346.
- Dillon, B., Hecht, F. M., Swanson, M., Goupil-Sormany, I., Grant, R. M., Chesney, M. A., et al. (2000, January 30). Primary HIV infections associated with oral transmission. Paper presented at the 7th Conference on Retroviruses and Opportunistic Infections.
- Fischl, M. A., Dickinson, G. M., Scott, G. B., Klimas, N., Fletcher, M. A., & Parks, W. (1987). Evaluation of heterosexual partners, children, and household contacts of adults with AIDS. *JAMA*, 257(5), 640–644.
- Fleming, D. T. (1999). From epidemiological synergy to public health policy and practice: the contribution of other sexually transmitted diseases to sexual transmission of HIV infection. *Sexually Transmitted Infections*, 75(1), 3–17.
- Friedland, G. H., Saltzman, B. R., Rogers, M. F., Kahl, P. A., Lesser, M. L., Mayers, M. M., et al. (1986). Lack of transmission of HTLV-III/LAV infection to household contacts of patients

- with AIDS or AIDS-related complex with oral candidiasis. *New England Journal of Medicine*, 314(6), 344–349.
- Garcia-Lerma, J., Otten, R., Qari, S., Jackson, E., Luo, W., & Monsour, M. (2006). Prevention of rectal SHIV transmission in macaques by tenofovir/FTC combination. *PLoS Med* 5(2), e28. doi:10.1371/journal.pmed.0050028, 0291–0299.
- Glynn, M., & Rhodes, P. (2005, June 12). Estimated HIV prevalence in the United States at the end of 2003. Paper presented at the National HIV Prevention Conference, Atlanta, GA.
- Guimarães, M. D. C., Muñoz, A., Boschi-Pinto, C., & Castilho, E. A. (1995). HIV infection among female partners of seropositive men in Brazil. *American Journal of Epidemiology*, 142(5), 538–547.
- Hall, H. I., Song, R., Rhodes, P., Prejean, J., An, Q., Lee, L. M., et al. (2008). Estimation of HIV incidence in the United States. *JAMA*, 300(5), 520–529.
- Harris, C., Small, C. B., Klein, R. S., Friedland, G. H., Moll, B., Emeson, E. E., et al. (1983). Immunodeficiency in female sexual partners of men with the acquired immunodeficiency syndrome. *New England Journal of Medicine*, 308(20), 1181–1184.
- Heimer, R., Kaplan, E. H., Khoshnood, K., Jariwala, B., & Cadman, E. C. (1993). Needle exchange decreases the prevalence of HIV-1 proviral DNA in returned syringes in New Haven, Connecticut. *American Journal of Medicine*, 95(2), 214–220.
- Laurian, Y., Peynet, J., & Verroust, F. (1989). HIV infection in sexual partners of HIV-seropositive patients with hemophilia. *New England Journal of Medicine*, 320(3), 183.
- Levine, M. P., Nardi, P. M., & Gagnon, J. H. (1997). *In changing times: Gay men and lesbians encounter HIV/AIDS*. Chicago: University of Chicago Press.
- Levy, J. A. (1998). *HIV and the Pathogenesis of AIDS*. Washington, DC: ASM Press.
- Lusher, J. M., Operskalski, E. A., Aledort, L. M., Dietrich, S. L., Gjerset, G. F., Hilgartner, M. W., et al. (1991). Risk of human immunodeficiency virus type 1 infection among sexual and nonsexual household contacts of persons with congenital clotting disorders. *Pediatrics*, 88(2), 242–249.
- MacKellar, D. A., Valleroy, L. A., Secura, G. M., Behel, S., Bingham, T., Celentano, D. D., et al. (2005). Unrecognized HIV infection, risk behaviors, and perceptions of risk among young men who have sex with men: Opportunities for advancing HIV prevention in the third decade of HIV/AIDS. *Journal of Acquired Immune Deficiency Syndromes*, 38(5), 603–614.
- Marks, G., Crepaz, N., & Janssen, R. S. (2006). Estimating sexual transmission of HIV from persons aware and unaware that they are infected with the virus in the USA. *AIDS*, 20(10), 1447–1450.
- Marks, G., Crepaz, N., Senterfitt, J. W., & Janssen, R. S. (2005). Meta-analysis of high-risk sexual behavior in persons aware and unaware they are infected with HIV in the United States: Implications for HIV prevention programs. *Journal of Acquired Immune Deficiency Syndromes*, 39(4), 446–453.
- Murphy, E. L., Collier, A. C., Kalish, L. A., Assmann, S. F., Para, M. F., Flanigan, T. P., et al. (2001). Highly active antiretroviral therapy decreases mortality and morbidity in patients with advanced HIV disease. *Annals of Internal Medicine*, 135(1), 17–26.
- Nicolosi, A., Leite, M. L. C., Musico, M., Arici, C., Gavazzini, G., & Lazzarin, A. (1994). For the Italian Study Group on HIV Heterosexual Transmission. The efficiency of male-to-female and female-to-male sexual transmission of the human immunodeficiency virus: A study of 730 stable couples. *Epidemiology*, 5(6), 570–575.
- Nieuwkerk, P. T., Sprangers, M. A. G., Burger, D. M., Hoetelmans, R. M. W., Hugen, P. W. H., Danner, S. A., et al. (2001). Limited patient adherence to highly active antiretroviral therapy for HIV-1 infection in an observational cohort study. *Archives of Internal Medicine*, 161(16), 1962–1968.
- Padian, N. S., Shiboski, S. C., Glass, S. O., & Vittinghoff, E. (1997). Heterosexual transmission of human immunodeficiency virus (HIV) in northern California: Results from a ten-year study. *American Journal of Epidemiology*, 146(4), 350–357.

- Page-Shafer, K., Shiboski, C. H., Osmond, D. H., Dilley, J., McFarland, W., Shiboski, S. C., et al. (2002). Risk of HIV infection attributable to oral sex among men who have sex with men and in the population of men who have sex with men. *AIDS*, 16(17), 2350–2352.
- Paterson, D. L., Swindells, S., Mohr, J., Brester, M., Vergis, E. N., Squier, C., et al. (2000). Adherence to protease inhibitor therapy and outcomes in patients with HIV infection. *Annals of Internal Medicine*, 133(1), 21–30.
- Pinkerton, S. D. (2007). Probability of HIV transmission during acute infection in Rakai, Uganda. *AIDS and Behavior*, 12(5), 677–684.
- Pinkerton, S. D., & Abramson, P. R. (1997). Effectiveness of condoms in preventing HIV transmission. *Social Science & Medicine*, 44(9), 1303–1312.
- Saracco, A., Musicco, M., Nicolosi, A., Angarano, G., Arici, C., Gavazzeni, G., et al. (1993). Man-to-woman sexual transmission of HIV: Longitudinal study of 343 steady partners of infected men. *Journal of Acquired Immune Deficiency Syndromes*, 6(5), 497–502.
- Stone, V. E., Hogan, J. W., Schuman, P., Rompalo, A. M., Howard, A. A., Korkontzelou, C., et al. (2001). Antiretroviral regimen complexity, self-reported adherence, and HIV patients' understanding of their regimens: Survey of women in the HER study. *Journal of Acquired Immune Deficiency Syndromes*, 28(2), 124–131.
- Sullivan, A. (1996, November 10). When plagues end: Notes on the twilight of an epidemic. *New York Times Magazine*, pp. 52–62, 76–57, 84.
- Underhill, K., Operario, D., & Montgomery, P. (2007). Abstinence-only programs for HIV infection prevention in high-income countries (Review). *Cochrane Database of Systematic Reviews*, 4. Article CD005421. DOI: 10.1002/14651858.CD005421.pub2. Retrieved April 7, 2009.
- Valleroy, L. A., Weinstein, B., Jones, T. S., Groseclose, S. L., Rolfs, R. T., & Kassler, W. J. (1995). Impact of increased legal access to needles and syringes on community pharmacies' needle and syringe sales—Connecticut, 1992–1993. *Journal of Acquired Immune Deficiency Syndromes and Human Retrovirology*, 10(1), 73–81.
- van Servellen, G., Chang, B., Garcia, L., & Lombardi, E. (2002). Individual and system level factors associated with treatment nonadherence in human immunodeficiency virus-infected men and women. *AIDS Patient Care and STDs*, 16(6), 269–281.
- Vlahov, D., & Junge, B. (1998, June). The role of needle exchange programs in HIV prevention. *Public Health Reports*, 113, 75–80.
- Weller, S., & Davis, K. (2002). Condom effectiveness in reducing heterosexual HIV transmission. *Cochrane Database of Systematic Reviews*, 1, Article CD003255. DOI: 10.1002/14651858.CD003255. Retrieved April 7, 2009, from <http://mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD003255/frame.html>
- Williams, B. G., Lloyd-Smith, J. O., Gouws, E., Hankins, C., Getz, W. M., Hargrove, J., et al. (2006). The potential impact of male circumcision on HIV in sub-Saharan Africa. *PLoS Med*, 3(7), e262. Retrieved April 7, 2009, from <http://www.plosmedicine.org/article/info:doi/10.1371/journal.pmed.0030262>