HIV/AIDS Overview

Introduction

Human immunodeficiency virus has affected individuals worldwide since it first caused rare illnesses in a select group of individuals in 1980.\(^1\) First identified in 1983, human immunodeficiency virus (HIV) quickly spread, eventually becoming a worldwide pandemic. It has been estimated that approximately forty million people worldwide live with HIV,\(^4\) and one million of those with HIV reside in the United States. The disease had a significant impact on Africa, with the numbers peaking at 2.3 million in 2010. By 1983, HIV was discovered as the cause of a number of rare cases of Kaposi’s sarcoma and pneumocystis pneumonia in otherwise healthy individuals.\(^2\) In the first decade, the disease spread rapidly, destroying the immune systems of those infected. Health clinicians must understand the signs and symptoms of infection, as well as the various stages of HIV infection.

Overview Of Human Immunodeficiency Virus

Since it was first discovered, HIV has become a worldwide pandemic.\(^3\) Initially, HIV was considered a homosexual disease, but it was soon discovered to be a virus that infected anyone, regardless of race, sexual orientation, or socioeconomic status.\(^5\) HIV attacks, and eventually destroys, the immune system. During the early stages of infection, individuals can live symptom free.\(^6\) Progression of the disease varies by patient and can be impacted by a variety of factors. In the stage of the infection known as HIV, patients often exhibit few symptoms. When the disease transitions to acquired immune deficiency syndrome (AIDS) the patient often experiences an increase
in symptoms and severity of the disease and presents with one or more opportunistic infections.\textsuperscript{7,8}

**Origin of HIV**

When HIV emerged in the early 1980s scientists began trying to determine its origins. After years of research, scientists traced the virus to chimpanzees in Africa.\textsuperscript{9} These chimpanzees were infected with simian immunodeficiency virus (SIV), which is a retrovirus similar to HIV.\textsuperscript{9} While HIV did not spread significantly into the human population until the 1980s, evidence shows that SIV may have infected humans as early as 1884.\textsuperscript{10} While there are no documented cases of HIV from that time period, scientists did discover a documented case of HIV posthumously in a fifteen-year-old black male who died in 1968.\textsuperscript{11} There are various theories as to why the virus did not spread in earlier populations, but there is no definitive answer as to why. Regardless, something caused the virus to spread in the 1980’s, resulting in the pandemic that has affected society for the past decades.

Although there is evidence that HIV may have infected humans as early as 1884, the subtype of the virus that currently infects individuals has been traced to a more recent time period. Research shows that HIV most likely spread to humans at three different points in history, one for each subtype of HIV-1 (M, N, and O).\textsuperscript{12} The most common strain of HIV-1, the type that infects most patients today, is believed to have been transmitted by the Cameroon chimps to humans in the period shortly before 1931.\textsuperscript{10} This conclusion was made after extensive research, which examined the virus in samples of infected tissue that was collected over the past three decades. Upon examination of these samples, it was determined that an ancestral
form of HIV started to spread in the human population approximately 75 years prior. Therefore, it is assumed that the transmission from chimpanzees to humans occurred shortly before that.

**History of HIV Development**

In June of 1981, the Centers for Disease Control and Prevention (CDC) reported on five individual cases of a rare lung infection, Pneumocystis carinii pneumonia (PCP). All five individuals were homosexual men living in Los Angeles, and each patient had been healthy prior to the onset of infection. Upon further examination, it was determined that all five men were experiencing other illnesses as well. When the CDC report was released, other medical clinicians submitted reports of similar cases nationwide. In all cases, patients had been previously healthy and were presenting with similar infections. Among the infections were reports of a rare form of cancer, Kaposi’s sarcoma. A task force was formed to study the incidence of infections and to determine common causes among the patients. In 1981, there were 270 cases reported with 121 deaths. By 1982, there were a total of 452 reported cases from 23 states.

In the two years following the first reported cases, various initiatives were established to assist with the identification, management and care of the unknown disease. Initially, the disease was thought to be specific to homosexual men. In fact, in the beginning, many individuals referred to the disease as GRID (Homosexual-Related Immune Deficiency). While the virus was originally thought to be a disease only affecting homosexual men, it was soon discovered in other individuals, especially those who had received blood transfusions. In 1982, the term Acquired Immune Deficiency Syndrome (AIDS) was used to define the syndrome that was affecting
individuals throughout the country.\textsuperscript{19} Care centers were established to help the tens of thousands of patients who were infected with the disease.\textsuperscript{16}

By 1983, the CDC was able to identify the specific transmission modes of the disease as through sexual contact and exposure to blood and blood-borne pathogens.\textsuperscript{20} The CDC also discovered that the disease had infected homosexual men, women with male partners, infants and injection drug users.\textsuperscript{15} As a result, a public statement was released warning individuals to refrain from activities that would put them in contact with the disease.\textsuperscript{20} Scientists in France identified the specific virus strain suspected to be causing AIDS as Lymphadenopathy Associated Virus (LAV),\textsuperscript{21} while scientists in the United States identified the virus as the retrovirus HTLV-III.\textsuperscript{22} After comparing the findings, it was determined that the two strains were almost identical. It was also determined that they were most likely the cause of AIDS.\textsuperscript{10}

In 1985, the viral strain became known as Human Immunodeficiency Virus and was identified as the cause of AIDS.\textsuperscript{10} As a result, the CDC redefined the AIDS clinical definition to include HIV as the cause of the infection. Acquired Immune Deficiency Syndrome was determined to be an end result of HIV infection.\textsuperscript{3} While the disease is considered to have started in 1980, it is now understood that it must have originated years earlier as an individual can live for many years with HIV before progressing to the stage of AIDS.\textsuperscript{13}

In the years following the discovery of HIV, significant research focused on identifying the origin and causes of the virus, developing treatment, and attempting to find a cure.\textsuperscript{23} In the late 1980s and throughout the 1990s, when the virus reached its peak, numerous
organizations were founded to address the needs of those living with HIV and to help prevent the spread of the infection. During this time, the stigma associated with the virus impacted how people viewed and interacted with HIV positive individuals and educational campaigns aimed at eliminating the stigma were introduced. Social service and case management programs were developed to address non-HIV issues in patients and training for healthcare clinicians focused on the effective treatment and management of the virus.

Since the first reported case of AIDS the disease spread and grew to significant numbers. Human immunodeficiency virus has impacted individuals throughout the world and has resulted in a worldwide pandemic which required myriad initiatives to help infected individuals live with the disease and also to minimize the spread of the infection. However, by the early 2000s, public knowledge of the virus had increased. Due to educational programming and patient treatment strategies, the number of new cases began to decrease. In addition, HIV positive individuals began to live longer and remained relatively symptom-free for extended periods of time. Human immunodeficiency virus treatment strategies evolved and a multifaceted approach to disease management became standard protocol for working with HIV positive patients.

**Epidemiology Of HIV**

Over the past decades, HIV has become a worldwide pandemic. Since the epidemic began, approximately sixty million people worldwide have contracted the disease. Currently, there are approximately forty million people living with HIV. Of those, one million reside in the United States. Approximately 3 million of the current HIV cases are in
individuals under the age of fifteen. Since 1995, HIV has been one of the leading causes of death in persons age 25 to 44. The total number of deaths since the virus was first reported total approximately thirty million worldwide.

**Global Impact**

While the epidemic has had a significant impact on the United States, its impact has been even greater worldwide, with the most significant numbers occurring in Sub-Saharan Africa. More than two-thirds of the reported cases of HIV are in individuals living in Sub-Saharan Africa. Since the disease began spreading, it has utterly devastated the country, with the number of reported cases peaking at 2.3 million. Due to the lack of adequate care and prevention measures, the transmission rate of HIV in Sub-Saharan Africa is greater than in other areas.

The World Health Organization (WHO) monitors the disease on a global scale, and reports are issued annually which provide detailed statistics on the number of reported cases globally and by nation. According to the WHO, 34.0 million (31.4–35.9 million) people globally were living with HIV at the end of 2011. An estimated 0.8% of adults aged 15 to 49 years worldwide are living with HIV, although the burden of the epidemic continues to vary considerably between countries and regions. Sub-Saharan Africa remains most severely affected, with nearly 1 in every 20 adults (4.9%) living with HIV and accounting for 69% of the people living with HIV worldwide.

While HIV has affected individuals on a global scale, the disease has been reported as most prevalent in Sub-Saharan Africa, where 69% of
the population is currently HIV positive. HIV was reported to also be the leading cause of death in Africa. This region had the highest percentage of children who are HIV positive, which is 94%. In nine countries in this region, at least 10% or more of the population is HIV positive, and all the nations in the region have generalized HIV epidemics. The highest numbers of people worldwide who are HIV positive reside in South Africa, and Swaziland had the highest overall prevalence rate, reported as 26%. The remaining HIV cases were spread throughout the world, with a high concentration of cases in low and middle-income countries. International and national organizations responding to the HIV epidemic supported health team efforts to provide education and health aid to high-risk areas, such as the U.S. Peace Corps as well as other Africa and interurban initiatives.

<table>
<thead>
<tr>
<th>Region</th>
<th>Total No. (%) Living with HIV in 2011</th>
<th>Newly Infected in 2011</th>
<th>Adult Prevalence Rate 2011</th>
</tr>
</thead>
<tbody>
<tr>
<td>Global Total</td>
<td>34.0 million (100%)</td>
<td>2.5 million</td>
<td>0.8%</td>
</tr>
<tr>
<td>Sub-Saharan Africa</td>
<td>23.5 million (69%)</td>
<td>1.8 million</td>
<td>4.9%</td>
</tr>
<tr>
<td>South/South-East Asia</td>
<td>4.0 million (12%)</td>
<td>280,000</td>
<td>0.3%</td>
</tr>
<tr>
<td>Eastern Europe/Central Asia</td>
<td>1.4 million (4%)</td>
<td>140,000</td>
<td>1.0%</td>
</tr>
<tr>
<td>Latin America</td>
<td>1.4 million (4%)</td>
<td>86,000</td>
<td>0.4%</td>
</tr>
<tr>
<td>North America</td>
<td>1.4 million (4%)</td>
<td>51,000</td>
<td>0.6%</td>
</tr>
<tr>
<td>Western/Central Europe</td>
<td>900,000 (3%)</td>
<td>30,000</td>
<td>0.2%</td>
</tr>
<tr>
<td>East Asia</td>
<td>830,000 (2%)</td>
<td>89,000</td>
<td>0.1%</td>
</tr>
<tr>
<td>Middle East/North Africa</td>
<td>300,000 (1%)</td>
<td>37,000</td>
<td>0.2%</td>
</tr>
<tr>
<td>Caribbean</td>
<td>230,000 (0.7%)</td>
<td>13,000</td>
<td>1.0%</td>
</tr>
</tbody>
</table>
Since 2001, the number of new HIV infections has decreased by more than 20%. In low and middle-income countries, the rate of infection has declined by more than 50%. However, even with a decline, there are still new cases reported each year, and the risk of infection in low and middle-income countries is still high. In 2011, there were 2.5 million new infections reported, and 1.8 million of the infections were in Sub-Saharan Africa.

Between the years 2010 to 2014, the rate of HIV infection diagnosed for persons aged 25–29 years reportedly increased. The rates for children (aged less than 13 years) and persons aged 13–14, 15–19, 35–39, 40–44, 45–49, 50–54, 55–59, and 60–64 years were reported decreased. The rates of HIV infection for persons aged 20–24, 30–34, and 65 years and older remained stable. In 2014, the highest rate of diagnosed HIV infection was for persons aged 25–29 years, followed by the rate for persons aged 20–24 years. Young women are two times more likely to test positive for HIV than men of the same age. The virus also significantly impacts children under the age of fifteen. In 2011, there were 3.3 million children worldwide who tested positive for HIV. There are many international health organizations, such as UNICEF, World Camp for Kids, Save the Children, and others supporting volunteer efforts for children with HIV infections and AIDS.

### National Impact

To properly track the HIV epidemic in the United States, reporting of the virus has been required throughout the country since shortly after the virus was discovered. From 1981 through 1995, the virus spread...
rapidly, and although antiretroviral treatment helped reduce the number of cases, the virus peaked in the United States in the period from 1993 to 1995. By 1989, the number of reported cases in the United States reached 100,000, and by 1995 the numbers had exceeded half a million.

To accurately measure the impact of the virus in the United States, the CDC collects information about each reported HIV case. This information is compiled into surveillance reports that explain how and where the virus has spread. The reports examine factors such as risk group, age, gender, status, and geographic location to analyze trends in viral spread and progression.

The most recent HIV Surveillance Report, released in 2014 by the CDC, provided information on the period from 2010 to 2014. While the report itself is very detailed and includes extensive information on the epidemiology of the virus, the CDC also releases brief reports that summarize the information and provide basic trend information based on risk group. The following is the CDC’s most recent summary of HIV trends from 2010 through 2014.

**HIV Incidence (New Infections)**

The estimated incidence of HIV has remained stable overall in recent years. During the years 2010–2014, the CDC reported the annual estimated number and rate of HIV diagnoses in the U.S. as increased in some subgroups while decreased in others. Such variations in trends among groups were anticipated as a result of public education and testing outcomes in certain subgroups.
Some groups are affected more than others by HIV infection. Men who have sex with men (MSM) continued to bear the greatest burden of HIV infection; and, among races/ethnicities, while African Americans had been disproportionately affected, from 2010 through 2014, the rates for American Indians/Alaska Natives and Asians increased while the rates for blacks/African Americans, Native Hawaiians/other Pacific Islanders, and persons of multiple races decreased. The rates for Hispanics/Latinos and whites remained stable. In 2014, the rates were 49.4 for blacks/African Americans, 18.4 for Hispanics/Latinos, 15.4 for persons of multiple races, 10.6 for Native Hawaiians/other Pacific Islanders, 9.5 for American Indians/Alaska Natives, 6.2 for Asians, and 6.1 for whites.\(^\text{32}\)

**HIV Diagnoses**

In 2011, an estimated 49,273 people were diagnosed with HIV infection in the United States. In that same year, an estimated 32,052 people were diagnosed with AIDS. Since the epidemic began, an estimated 1,155,792 people in the United States have been diagnosed with AIDS.\(^\text{4}\) At the end of 2013, an estimated 516,401 persons in the United States were living with infection ever classified as stage 3 (AIDS).\(^\text{32}\)

**Deaths**

An estimated 15,529 people with an AIDS diagnosis died in 2010, and nearly 636,000 people in the United States with an AIDS diagnosis have died since the epidemic began.\(^\text{3}\) The deaths of persons with an AIDS diagnosis can be due to any cause — that is, the death may or may not be related to AIDS.
Risk Group

Homosexual, bisexual, and other men who have sex with men (MSM) of all races and ethnicities remain the population most profoundly affected by HIV.

- In 2010, the estimated number of new HIV infections in MSM cohorts was 29,800, a significant 12% increase from the 26,700 new infections with MSM in 2008.
- Although MSM represent about 4% of the male population in the United States, in 2010, MSM accounted for 78% of new HIV infections among males and 63% of all new infections. MSM accounted for 52% of all people living with HIV infection in 2009, the most recent year these data are available.
- In 2010, white MSM continued to account for the largest number of new HIV infections (11,200), by transmission category, followed closely by black MSM (10,600).
- The estimated number of new HIV infections was greatest with MSM in the youngest age group. In 2010, the greatest number of new HIV infections (4,800) with MSM occurred in young black/African American MSM aged 13–24. Young black MSM accounted for 45% of new HIV infections among black MSM and 55% of new HIV infections among young MSM overall.
- Since the epidemic began, almost 300,000 MSM with an AIDS diagnosis have died, including an estimated 6,863 in 2009.

Heterosexuals and injection drug users also continued to be affected by HIV.

- Heterosexuals accounted for 25% of estimated new HIV infections in 2010 and 27% of people living with HIV infection in 2009.
• Since the epidemic began, more than 85,000 persons with an AIDS diagnosis, infected through heterosexual sex, have died, including an estimated 4,003 in 2010.
• New HIV infections among women are primarily attributed to heterosexual contact (84% in 2010) or injection drug use (16% in 2010). Women accounted for 20% of estimated new HIV infections in 2010 and 24% of those living with HIV infection in 2009. The 9,500 new infections among women in 2010 reflect a significant 21% decrease from the 12,000 new infections that occurred among this group in 2008.
• Injection drug users represented 8% of new HIV infections in 2010 and 16% of those living with HIV in 2009.
• Since the epidemic began, more than 182,000 injection drug users with an AIDS diagnosis have died, including an estimated 4,218 in 2010.

The CDC 2014 surveillance report indicated that between the years 2010 - 2013, the rates of deaths for male and female adults and adolescents diagnosed with HIV infection decreased. The number of deaths among males with diagnosed HIV infection attributed to perinatal transmission increased. The number of deaths among males with infection attributed to injection drug use, male-to-male sexual contact and injection drug use, or heterosexual contact decreased. The number of deaths among males with diagnosed HIV infection attributed to male-to-male sexual contact remained stable. The number of deaths among females with infection attributed to injection drug use or heterosexual contact decreased. The number of deaths among female adults and adolescents with infection attributed to perinatal transmission remained stable.32
Race/Ethnicity

Blacks/African Americans were reported to experience the most severe burden of HIV, compared with other races and ethnicities.

- Blacks represent approximately 12% of the U.S. population, but accounted for an estimated 44% of new HIV infections in 2010. They also accounted for 44% of people living with HIV infection in 2009.
- Since the epidemic began, more than 260,800 blacks with an AIDS diagnosis have died, including 7,678 in 2010.
- Unless the course of the epidemic changes, at some point in their lifetime, an estimated 1 in 16 black men and 1 in 32 black women will be diagnosed with HIV infection.

HIV had also disproportionally affects Hispanics/Latinos. Data extracted from literature showed:

- Hispanics/Latinos represented 16% of the population but accounted for 21% of new HIV infections in 2010. Hispanics/Latinos accounted for 19% of people living with HIV infection in 2009.
- Disparities persist in the estimated rate of new HIV infections in Hispanics/Latinos. In 2010, the rate of new HIV infections for Latino males was 2.9 times that for white males, and the rate of new infections for Latinas was 4.2 times that for white females.
- Since the epidemic began, more than an estimated 96,200 Hispanics/Latinos with an AIDS diagnosis have died, including 2,370 in 2010.

As mentioned previously, those diagnosed with AIDS in the 2014 CDC surveillance report indicated that from 2010 through 2014, rates for all
race/ethnicity groups decreased. In 2014, the rates were 25.4 for blacks/African Americans, 12.6 for persons of multiple races, 7.7 for Hispanics/Latinos, 4.0 for American Indians/Alaska Natives, 3.5 for Native Hawaiians/other Pacific Islanders, 2.7 for whites, and 2.1 for Asians.32

**HIV Retrovirus And Types**

Human Immunodeficiency Virus (HIV) is a retrovirus that attacks the immune system. Retroviruses are viruses that contain DNA as part of their genetic material.34 When the virus enters the body, it attacks the CD4+ T cells (lymphocytes with a central role in cell-mediated immunity), thereby causing the production of antibodies. Once this process is initiated, HIV subsequently destroys the immune system by taking over the helper cells and reducing their ability to protect the body from other diseases.35 Over time, the body becomes unable to fight off infection and succumbs to a variety of secondary infections.36 Human Immunodeficiency Virus is often slow to progress, and individuals who test positive for HIV often exhibit no symptoms for long periods of time.34 Some individuals will go a number of years without seeing progression of the virus. In a select few, the virus never progresses.37

Human Immunodeficiency Virus has been categorized into two distinct subtypes: HIV-1 and HIV-2. Both types of HIV are transmitted the same way, but the impact of HIV-2 is less severe than that of HIV-1. In addition, HIV-2 is not transmitted as easily as HIV-1.35
**HIV Type 1**

Human Immunodeficiency Virus Type 1 (HIV-1) is the most common form of HIV and it makes up the majority of HIV cases worldwide. When people refer to HIV, they are often referring to HIV-1.\(^{38}\)

**HIV Type 2**

Human Immunodeficiency Virus Type 2 (HIV-2) is a newer classification of HIV. It is predominately found in West Africa and is not common amongst HIV cases.\(^{39}\)

**Subtypes**

Human Immunodeficiency Virus mutates rapidly, and there are a number of subtypes found in both HIV-1 and HIV-2.\(^{35}\) As the disease continues to evolve, more subtypes found are to be expected. Current testing methods are able to identify all types and subtypes of HIV.\(^{40}\)

Human Immunodeficiency Virus Type 1 can be separated into *four distinct groups*, with nine or more subtypes occurring among the four groups. Group M (“major”) is by far the most common group, accounting for over 90% of all HIV/AIDS infections. Group N (“non-M, non-O”), has only been seen in Cameroon. Group O (“Outlier”) is usually only seen in West-central Africa. Group P (“Pending”) is a new identified HIV sequence only seen in one women, and is pending additional discovery in other human cases. While various subtypes are present, over ninety percent of the infections belong to one group and subtype. The other subtypes are less prevalent and make up only a small percentage of HIV infections.\(^{35}\)
Acquired Immune Deficiency Syndrome

Acquired Immune Deficiency Syndrome (AIDS) is the end stage of HIV infection. AIDS occurs when the immune system has been destroyed and the individual is unable to fight off other infections.\(^7\) Acquired Immune Deficiency Syndrome is diagnosed when the patient presents one or more AIDS indicator illnesses or when the patient’s CD4+ T cell count drops below 200, where normal CD4+ counts range from 500 to 1600.\(^{41}\) Acquired Immune Deficiency Syndrome indicator illnesses, also known as opportunistic infections, are conditions that a healthy immune system is typically able to fight off. However, once the virus has destroyed the immune system, HIV positive patients are more susceptible to these infections.\(^{36}\) The CDC has identified more than twenty opportunistic infections that are considered AIDS Indicator Conditions.\(^{42}\) These are listed below, as:

- Candidiasis of bronchi, trachea, esophagus, or lungs
- Invasive cervical cancer
- Coccidioidomycosis
- Cryptococcosis
- Cryptosporidiosis, chronic intestinal (greater than 1 month's duration)
- Cytomegalovirus disease (particularly CMV retinitis)
- Encephalopathy, HIV-related
- Herpes simplex: chronic ulcer(s) (greater than 1 month's duration); or bronchitis, pneumonitis, or esophagitis
- Histoplasmosis
- Isosporiasis, chronic intestinal (greater than 1 month's duration)
- Kaposi’s sarcoma
- Lymphoma, multiple forms
- Mycobacterium avium complex
• Tuberculosis
• Pneumocystis carinii pneumonia
• Pneumonia, recurrent
• Progressive multifocal leukoencephalopathy
• Salmonella septicemia, recurrent
• Toxoplasmosis of brain
• Wasting syndrome due to HIV

Once an individual develops AIDS, HIV infection has progressed to a stage that is difficult to manage. Individuals with AIDS are at risk of life-threatening complications and death related to AIDS acquired infections.\(^{43}\)

**Transmission Of HIV**

Human immunodeficiency virus is transmitted when an individual comes in contact with certain body fluids or tissue of an infected person. For transmission to occur, the infected fluid must come into contact with a mucous membrane or open wound.\(^{44}\) Individuals who get infected fluid on their skin are not at risk, unless there is a break in the skin.

Another method of transmission is through direct injection of the virus into the bloodstream, which occurs when individuals share needles. Three conditions must be present for HIV to be transmitted:\(^{45}\)

1. There must be an HIV source.
2. There must be a sufficient dose of virus.
3. There must be access to the bloodstream of another person.

If all three conditions are not present, HIV transmission will not occur.
Human immunodeficiency virus is found in the following body fluids:\textsuperscript{46}  
- Blood  
- Vaginal secretions  
- Semen  
- Other body fluids containing blood  
- Breast milk  

Human immunodeficiency virus is transmitted through the following methods:\textsuperscript{46}  
- Sexual Intercourse  
- Injecting Drugs  
- Mother to Child  
- Blood Transfusions, blood products and organ/tissue donation  

The most common methods of transmission are through sexual intercourse (anal or vaginal) and sharing needles with an infected person.\textsuperscript{47} While other methods of transmission are also a risk, the rate of transmission is lower. Human immunodeficiency virus is not transmitted through feces, saliva, sweat, urine, or other bodily fluids. In addition, HIV is not spread through the air.\textsuperscript{48} Each method of transmission must be understood so that proper preventative measures can be taken.  

\textbf{Sexual Intercourse}  

Human immunodeficiency virus transmission rates are extremely high during sexual intercourse. Primary modes of transmission are through anal or vaginal intercourse.\textsuperscript{46} While there is a small risk of transmission during oral intercourse, it is not as common as through vaginal or anal intercourse.\textsuperscript{49}
Human immunodeficiency virus is transmitted during sexual contact as vaginal fluid, pre-semen and semen all contain HIV. Both partners are at risk of becoming infected with HIV during sexual intercourse.\(^4^6\) During anal sex, the skin lining of the rectum can tear easily, providing an opening for the infection to enter.\(^5^0\) The inside of the vagina is lined with mucous membranes that allow the virus to enter the body.\(^4^6\) During penetration, the lining of the vagina can tear, providing additional locations for the virus to enter the body.\(^4^4\) In the penis, the urethra provides another route for the infection to enter. Additionally, the penis may have small cuts or tears in the skin that provide a place for the virus to enter.\(^4^4\)

**Intravenous Drugs and Needle Sharing**

Along with sexual intercourse, sharing needles is the most common method of HIV transmission.\(^4^6\) When an individual injects drugs, blood enters the syringe. If another person uses the syringe after an infected individual, the infected blood enters the bloodstream of the non-infected individual.\(^5^1\)

Human immunodeficiency virus can also be transmitted through sharing other drug paraphernalia that has come into contact with an HIV positive person’s blood. This includes the tools used to cook or dissolve drugs, the water that is used to clean paraphernalia and other objects used during the drug preparation and injection process.\(^4^6\)

**Mother to Child**

Human immunodeficiency virus can be transmitted from a positive mother to her child during pregnancy, delivery, and breastfeeding. Transmission occurs when the infant is exposed to the mother’s
vaginal secretions or blood that is present in the amniotic fluid. Additionally, the virus can be transmitted to the child during breastfeeding as breast milk also contains trace amounts of HIV.

The risk of transmission depends on the viral load of the infected mother. The HIV viral load is ordered in conjunction with the CD4 cell count; high viral load can be anywhere from 5,000 to 10,000 copies/mL. Mothers with a high viral load have a higher chance of transmitting the virus to their infants during pregnancy, delivery or breastfeeding.

In the early 1990s, the use of antiretroviral agents to interrupt HIV transmission were initiated and studied in the U.S. and other wealthy countries. The avoidance of breastfeeding and improved comprehensive pregnancy health services led to significantly reduced perinatal transmission of HIV, and it was estimated that only 69 HIV-infected infants were born in 2013.

Efforts in less wealthier countries to introduce antiretroviral agents for perinatal prevention also led to a decrease in perinatal (mother to child) HIV transmission from over 570,000 in 2003 to an estimated 110,000 in 2015 within the sub-Saharan Africa. Transmission from mother to child is less common than transmission during sexual intercourse or from sharing needles. However, the risk is still present. With no medical interventions, the risk of transmission from mother to child is significant.
Blood Transfusions, Blood Products and Organ/Tissue Donation

Human immunodeficiency virus is highly concentrated in blood. Therefore, blood transfusions and receipt of blood products and organ/tissue donation can directly transmit HIV from an infected individual to a non-infected person.53

While HIV is transmitted most easily through direct entrance into the bloodstream, there is minimal risk of acquiring the virus through blood transfusions, blood products and organ/tissue donation. An extensive screening and testing process ensures that these products are HIV free prior to being given to an individual.46

Probability of Infection

Although HIV has become a worldwide pandemic over the last thirty years, it is actually more difficult to acquire HIV than it is other diseases, such as Hepatitis.54 Most cases of HIV are transmitted through direct sexual intercourse or sharing needles.47 An increase in the use of preventative measures has had an impact on the probability of infection after contact with an HIV positive individual.55

The following table from the CDC shows the probability of infection based on different activities.
**Estimated Per-Act Probability of Acquiring HIV from an Infected Source, by Exposure Act**

<table>
<thead>
<tr>
<th>Type of Exposure</th>
<th>Risk per 10,000 Exposures</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Parenteral</strong></td>
<td></td>
</tr>
<tr>
<td>Blood Transfusion</td>
<td>9,000</td>
</tr>
<tr>
<td>Needle-sharing during injection drug use</td>
<td>67</td>
</tr>
<tr>
<td>Percutaneous (needle-stick)</td>
<td>30</td>
</tr>
<tr>
<td><strong>Sexual</strong></td>
<td></td>
</tr>
<tr>
<td>Receptive anal intercourse</td>
<td>50</td>
</tr>
<tr>
<td>Receptive penile-vaginal intercourse</td>
<td>10</td>
</tr>
<tr>
<td>Insertive anal intercourse</td>
<td>6.5</td>
</tr>
<tr>
<td>Insertive penile-vaginal intercourse</td>
<td>5</td>
</tr>
<tr>
<td>Receptive oral intercourse</td>
<td>Low</td>
</tr>
<tr>
<td>Insertive oral intercourse</td>
<td>Low</td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td></td>
</tr>
<tr>
<td>Biting</td>
<td>Negligible</td>
</tr>
<tr>
<td>Spitting</td>
<td>Negligible</td>
</tr>
<tr>
<td>Throwing body fluids (including semen or saliva)</td>
<td>Negligible</td>
</tr>
<tr>
<td>Sharing sex toys</td>
<td>Negligible</td>
</tr>
</tbody>
</table>

**Vulnerable Populations**

While HIV can infect anyone who comes into contact with the virus, there are certain populations that have a higher risk of acquiring the disease than others. These are defined as vulnerable populations. Populations most vulnerable to HIV infection are sex workers, drug users, men who have sex with men, partners and those living with an HIV infected individual, and prisoners. Additional education and
prevention measures are necessary to help these populations avoid becoming infected with HIV.

**Co-Infection with Other Sexually Transmitted Disease’s**

Individuals who engage in the type of risky behaviors that can transmit HIV are often co-infected with other sexually transmitted diseases (STDs) and infections. Individuals who are already infected with other STDs are at an increased risk of developing HIV because their immune systems are already compromised. Some STDs cause lesions or other breaks in the skin that make it easier for HIV to enter the bloodstream. Others cause an increase in pus and bleeding at the site, which provides a source for infection. In addition, these individuals are more at risk because they are engaging in the type of behaviors that regularly transmit STDs and other infections, such as Hepatitis C.

Approximately one-third of HIV positive individuals in the United States are also infected with Hepatitis C. Co-infection poses problems in the management and treatment of HIV, as the disease tends to progress rapidly and cause more complications. Since the liver is already damaged from Hepatitis C, antiretroviral treatment for HIV poses a greater risk of permanently destroying the liver.

**Workplace Exposure**

Individuals who work in occupations that put them at risk of coming in contact with the body fluids of infected individuals are considered to have an occupational risk of acquiring the disease. The occupations that pose the greatest risk for exposure to HIV include: healthcare
workers, emergency personnel, law enforcement officials, mental health workers and correctional employees. Ultimately, anyone who has the potential to come in contact with the bodily fluids of an infected individual is at risk. Healthcare workers are at greatest risk of acquiring HIV as they often work directly with the body fluids of infected individuals.

The most common cause of transmission in healthcare workers is by needle stick. While individuals are at risk of acquiring HIV, occupational transmission rates are very low. The chance of getting HIV from a needle stick is less than 1%. However, individuals who work in occupations that put them in contact with the bodily fluids of infected individuals should still take the necessary precautions to prevent the spread of infection.

**Prevention Of HIV**

Proper prevention strategies help to reduce the spread of HIV. Since HIV is transmitted through sexual intercourse, sharing needles, contact with infected blood and blood products, and from mother to child, a variety of methods should be employed to prevent the spread of infection. An important step in preventing transmission of HIV is to properly identify active cases. Therefore, regular testing and diagnosis of new HIV infections is crucial. In the United States alone, approximately twenty percent of people who are infected with HIV do not know that they have the virus.

Individuals who do not know that they are HIV positive do not take the same precautions as those who do know their status, thereby increasing the chances of transmitting the virus to someone else.
Specific prevention measures should be utilized for each method of transmission, which will ensure universal precaution.

**Sexual Intercourse**

*Abstinence*

The most reliable way to prevent HIV transmission is to abstain completely from sexual activities. This method of prevention is 100% effective. However, few individuals are receptive to this form of prevention, so other prevention strategies must be introduced and encouraged.\(^65\)

*Monogamy*

Monogamy is the practice of having only one sexual partner. This strategy only works if each person has a confirmed negative status prior to committing to a monogamous relationship.\(^66\) Individuals who practice complete monogamy can engage in all forms of sexual activity with each other because the risk of transmitting HIV is non-existent. The exception to this is if one partner is an intravenous drug user, as he or she is at risk of acquiring the disease through needle sharing and then passing it to his or her sexual partner.\(^65\) Another strategy involves limiting sexual partners to minimize the potential of transmission. However, this strategy does not reduce the risk as greatly as abstinence or monogamy.\(^66\)

Individuals who choose to engage in sexual intercourse with a variety of partners can take precautions to prevent the transmission of HIV. These strategies are discussed further below.
Condoms

Latex and polyurethane condoms are an effective means of preventing the transmission of HIV when used correctly. In recent studies, female condoms have also been proven to prevent the transmission of HIV. Condoms can be used during penetration and also to prevent transmission of HIV during oral sex on a man. To work properly, all condoms must be stored and used properly. Condoms should be kept in a cool dry place. Condoms should not be stored in a wallet or other place that could cause the material to break down, thereby resulting in tears that could allow the virus to get through the barrier.

Non-Penetrative Sexual Activity

Minimizing penetration during sexual activities is one method that helps reduce transmission of HIV. With this method, individuals refrain from anal or vaginal penetration during intercourse, engaging in other sexual activities instead. Through this prevention strategy, individuals are less likely to transmit bodily fluids that may contain HIV.

Dental Dams

Dental dams are thin pieces of latex that can be used as a barrier during oral sex on a woman. Dental dams cover the surface of the vagina and reduce contact with vaginal secretions.

Injection Drug Use

Individuals who inject drugs can prevent transmission of HIV by reducing the amount they come into contact with the blood of other users. Other than refraining completely from using injection drugs, the best way to prevent HIV transmission during injection drug use is to
never share needles or other drug paraphernalia.\textsuperscript{51} For injection drug users who cannot ensure a clean, new needle during each injection, there are two strategies that will help prevent the spread of infection.

\textit{Needle Sterilization}

Injection users who share needles with others should clean needles and all syringe parts between uses. Syringes and needles should be cleaned using water and bleach. The syringe should first be rinsed with water to remove any traces of blood, followed by full strength bleach. The bleach should remain in the syringe for thirty seconds or longer and should be followed by a rinse with clean water.\textsuperscript{51} While cleaning needles and paraphernalia with bleach can be effective in preventing the spread of HIV, success is dependent on the individual properly following the guidelines. Therefore, there is a large margin of error and many individuals still become infected with HIV even after sterilizing paraphernalia.\textsuperscript{68}

\textit{Needle Exchange}

The most effective method of preventing the spread of HIV among injection drug users is through needle exchange programs.\textsuperscript{68} Injection drug users can exchange their dirty needles and syringes for new, clean paraphernalia at registered needle exchange centers. Individuals can be assured that the sites are safe and secure and they will not be penalized for using illegal substances. These programs are meant as a way to help prevent the spread of HIV, not as a means of catching illicit drug users.\textsuperscript{68}
**Mother to Child**

A mother infected with HIV is at risk of passing the infection on to her child during pregnancy, delivery and through breastfeeding if appropriate preventative measures are not taken.\(^{46,52}\) With proper prevention strategies, the risk of transmission from mother to child is lower than five percent.\(^{52}\)

Mothers who are treated with antiretrovirals during pregnancy significantly reduce the risk of transmitting HIV to the child. Antiretroviral therapy has been shown to reduce the rate of transmission during pregnancy and delivery from approximately 25% to 5%.\(^{52,69}\) A woman who is HIV positive and pregnant should start antiretroviral therapy immediately and should be monitored closely throughout her pregnancy.\(^{69}\) Special precautions should be taken during delivery to minimize the infant’s contact with the mother’s blood and vaginal secretions. A cesarean may be recommended, but should be done so only after careful consideration by the attending physician.\(^{52}\) Human immunodeficiency virus is present in breast milk. Therefore, a mother who is HIV positive should not breastfeed her child. During treatment, an HIV positive mother should be given information regarding breastfeeding and HIV transmission and she should be encouraged to refrain completely from breastfeeding.\(^{52}\)

**Blood Transfusions, Blood Products and Organ/Tissue Donation**

Blood transfusions, blood product donation and organ/tissue donation pose a great risk for HIV transmission if not monitored closely. In 1985, new requirements were instituted for screening blood and blood products in the United States. All blood and blood products are tested for HIV prior to use and infected blood is discarded immediately.
Human immunodeficiency virus testing is also done on all organ and tissue donations to ensure that HIV is not transmitted during the donation process.\textsuperscript{70}

**Healthcare Workers**

Proper prevention strategies ensure that healthcare workers who regularly come into contact with bodily fluids do not acquire HIV from infected patients. The rate of transmission of HIV in healthcare workers is extremely low. Since 2001, there have been no reported cases of HIV transmission in healthcare workers.\textsuperscript{62} Healthcare workers have been expected to follow standard precautions to ensure that they do not acquire HIV from infected patients, which has resulted in relatively low rates of transmission. Healthcare workers are expected to adhere to the following standards when working with all patients, whether or not they are confirmed HIV positive.

*Universal/Standard Precaution*

Healthcare workers are required to treat all patients as potentially infected, and to take all preventative measures. The CDC has issued the following recommendations for healthcare workers to practice universal precaution:\textsuperscript{71}

- routinely use barriers (such as gloves and/or goggles) when anticipating contact with blood or body fluids
- immediately wash hands and other skin surfaces after contact with blood or body fluids
- carefully handle and dispose of sharp instruments during and after use
Universal precaution was standard protocol until 1996, when the terminology changed to standard precaution. When healthcare providers practiced universal precaution, the main goal was to utilize protective measures to prevent themselves from coming into contact with blood borne pathogens and other disease that could result in infection. Universal precaution focused on infectious agents present in blood. Standard precaution expanded the definition to include protecting other patients and individuals in the clinical setting. Standard precaution also treats all bodily fluids, with the exception of sweat, as potential disease carriers.

*Personal Protective Equipment*

Healthcare workers are required to use personal protective equipment when working with patients to minimize the spread of infection. Personal protective equipment should be worn whenever there is a chance that the provider will come in contact with a patient’s blood or other bodily fluids. Standard protective equipment includes gloves and masks, as well as face shields and protective eyewear when appropriate.

*Sharps Disposal*

Sharps needles, scalpel blades and any other sharp objects must be disposed of properly to prevent the possibility of accidental needle sticks or punctures. Proper disposal requires that the items be immediately removed from the utensils and placed directly in properly labeled sharps containers. Needles and other sharp tools must not be left on counters or disposed of in standard trash containers as this increases the risk of accidental sticks and cuts.
Post-Exposure Precautions

When an individual has been exposed to HIV, either occupationally or through sexual activity or needle sharing, immediate precautions can help reduce the likelihood that the individual will become HIV positive. When an individual comes into contact with the bodily fluids of an HIV positive individual, a standard set of procedures is initiated. These procedures are known as post-exposure prophylaxis. Post-exposure prophylaxis is specific to the individual exposure, but often include immediate first aid, counseling and testing services. In some cases, a 28-day course of antiretrovirals is prescribed to prevent HIV from spreading throughout the body. Post-exposure prophylaxis is standard protocol for healthcare workers who have come into contact with blood or other bodily fluids. However, the use of post-exposure prophylaxis is expanding to other individuals who have been exposed to the virus, including victims of sexual assault and those who have engaged in high risk activities with HIV positive individuals.

Vaccine

Since HIV was first discovered, researchers have attempted to develop a vaccine to prevent the spread of the infection. However, due to the unique nature of the virus and the way it attacks the immune system, this has been difficult. Over the years, numerous vaccine trials have been performed using animal subjects. While these trials have helped scientists identify potential vaccine options, they have not resulted in the successful development of an effective vaccine.

Currently, no vaccine exists for HIV. However, scientists continue to conduct trials and are much closer to developing a vaccine than they were in the past. In 2009, a trial in Thailand showed a protection rate
of thirty one percent with a trial vaccine study. This has been the most significant result thus far. Since 2009, research has focused on improving the results and determining exactly how the vaccine worked. In 2011, after further research and development, a vaccine was approved to begin trials on humans. While no vaccine currently exists, there is the potential that one will be developed in the near future.

**Diagnosis Of HIV**

Early diagnosis of HIV is imperative to ensure that the illness does not progress beyond the early stages. If HIV is diagnosed while it is still in the early stages, the potential for the patient to remain symptom and complication free is increased significantly. Once the disease progresses, treatment is less successful and further complications can develop.

**Signs and Symptoms**

In the early stages of HIV infection, an individual may present very few symptoms. However, there are some signs that may indicate infection. Within the first two months of infection, individuals might experience flu like symptoms such as fever, fatigue, headache, muscle soreness, rash and other typical flu symptoms. Once the virus progresses, an individual can remain symptom free for ten or more years, which can make it difficult to diagnose the disease. Providers must rely on information obtained from the patient regarding sexual activity, drug use, and high risk behaviors and encourage patients to undergo testing to determine if they are HIV positive.
Once HIV progresses to a more severe stage, it will produce more symptoms and will make it easier for healthcare providers to identify and diagnose the disease.\textsuperscript{82} HIV itself does not produce symptoms, but in the later stages of infection, individuals are more susceptible to other infections because of their compromised immune systems.\textsuperscript{82} As individuals present these symptoms, healthcare providers can screen for HIV and begin treatment.

Some of the symptoms that patients may present as the illness progresses include:\textsuperscript{36}

\begin{itemize}
  \item diarrhea
  \item unexplained weight loss
  \item persistent fever
  \item persistent cough
  \item persistent vaginal candidiasis (women)
  \item thrush/oral candidiasis
  \item enlarged lymph nodes or other swollen glands
\end{itemize}

Since many of the symptoms present in HIV positive individuals mirror symptoms of other illnesses, it is difficult to identify and diagnose HIV. Healthcare providers should discuss these symptoms with their patients and inquire about past and current risky behavior as part of the diagnosis process.\textsuperscript{63} HIV testing should be recommended as part of this process.

Once an individual has transitioned from HIV to AIDS status, more symptoms will be present. AIDS is characterized by an increase in opportunistic infections, most of which cause specific symptoms. The
The immune system of an AIDS patient has been destroyed by HIV, which results in more pronounced illness.\(^\text{83}\)

**Diagnostic Testing**

Since HIV does not produce concrete signs and symptoms in the early stages of infection, it is imperative to counsel all patients to undergo regular testing any time they engage in high-risk behavior.\(^\text{84}\) Early diagnosis and treatment can minimize the impact of HIV on the immune system and can enable a patient to live with the illness for a long time without progressing to later stages of infection, such as AIDS.\(^\text{83}\) Any individual who engages in behaviors that can transmit the infection should regularly be tested for HIV. There are two different testing options:

**Confidential**

With confidential testing, patients provide their full name and medical information and consent to having the testing information recorded in their medical records. Even though their information is provided, the results of the test are kept confidential and are only given to the patient. All confidential testing results are reported to the Department of Public Health for tracking purposes, but the patient’s name is not attached to the report.\(^\text{85}\)

**Anonymous**

Anonymous testing is completely anonymous. Patients do not provide their names or medical information. Results are not linked to a patient’s name or medical record.\(^\text{85}\)
**Informed Consent**

In both confidential and anonymous testing, the patient is required to give informed consent. Testing cannot occur if the patient does not consent to the procedure.\(^{85}\)

**Counseling**

Pre- and post-test counseling is recommended for all patients. Counseling can be administered by the testing provider or through direct referral to a provider. While counseling is recommended, it is not mandatory. Patients have the option to opt out of pre- and post-test counseling without being denied the right to test.\(^{84}\)

*Pre-Test Counseling*

Counseling prior to testing should focus on behavior expectations and change. Patients should be encouraged to consider risky behaviors and identify strategies for reducing future risks. Patients should also be encouraged to discuss the potential effects a positive result will have and identify strategies for coping with the result.\(^{86}\)

*Post-Test Counseling*

Individuals who are negative may opt not to have any post-test counseling. If they do consent to post-test counseling, the discussion should focus on how to change future behaviors to minimize the potential of acquiring the virus.\(^ {84}\) Individuals who test positive will require more in-depth counseling. In most instances, the testing provider will provide the post-test counseling.\(^ {85}\) However, there are occasions when the patient will need to be referred to someone else for counseling. Post-test counseling for HIV positive individuals must
include information on reporting requirements and partner notification services.\(^\text{86}\)

Post-test counseling for positive individuals must also include referrals to appropriate services, including mental health counselors, medical providers, drug and alcohol counselors and other appropriate personnel.\(^\text{84}\) Counseling should also include discussions of prevention and treatment strategies, as well as strategies for notifying friends and family members.\(^\text{86}\)

**Types of Testing**

HIV is diagnosed using either screening or confirmatory tests. In all cases, tests screen for HIV antibodies, not the virus itself.\(^\text{40}\)

*Screening Tests*

Initial HIV testing is done through the use of a screening test. This is the first option for testing because it is less expensive than confirmatory testing and easier to perform.\(^\text{87}\) However, screening tests are also less reliable than confirmatory tests, so a positive test result should always be verified using a confirmatory test.\(^\text{40}\) The primary form of screening test is the ELISA (enzyme-linked immunosorbent assay) test. The ELISA test is done to screen for HIV antibodies in a serum specimen taken from the individual.\(^\text{40}\) ELISA tests can detect HIV antibodies in the following specimens:
Blood

The majority of ELISA tests screen for HIV antibodies using a patient’s blood sample. Blood can be extracted using venipuncture or a fingerstick.87

Oral Fluid

Some test kits allow patients to use samples collected from the oral mucosal transudate (mucous membrane of the mouth). A common misconception is that these tests detect antibodies in the saliva of the patient, however the antibodies are actually detected in the lining of the mucous membrane. These tests use a special collection instrument to gather cells from the lining of the mouth. The sample is then sent to a lab for testing.87

Urine

Human Immunodeficiency Virus antibodies are present in the urine of infected patients. New screening tests are now available that can detect these antibodies using standard sample of urine from the patient. These tests are typically conducted in a doctor’s office. However, while screening tests can detect antibodies in the urine, there is currently no confirmatory test that can test urine. Therefore, a confirmatory test will still need to be done using a blood sample.40

Confirmatory Tests

Once a patient has had an initial positive result from a screening test, a confirmatory test must be conducted to verify the positive result.87 Confirmatory tests are more expensive than screening tests, so they should only be used to confirm a positive result, not as an initial
screening for a patient who suspects he or she may be infected with the virus. Most screening tests are conducted in a laboratory. The sample is collected and sent to the laboratory for testing. When a sample is positive, a confirmatory test is conducted on the same sample. Although screening tests are highly accurate, some screening tests can produce a false positive because the enzyme reacts to specific proteins present in the sample. These proteins are often a result of other autoimmune diseases.

The use of a confirmatory test following a positive result on a screening test will ensure proper diagnosis of HIV infection. The most common confirmatory test is the Western Blot; sometimes called the protein immunoblot, it is a widely approved method to detect specific proteins. It uses gel electrophoresis to isolate specific proteins by their length. These proteins are then transferred to a membrane and are attached to antibodies that react to the protein being tested.

**Rapid Testing**

Although most samples are sent to laboratories for testing, there is the option to have patients screened using a rapid serologic test. These tests provide results in approximately thirty minutes and do not require the sample to be sent to a laboratory. Rapid tests differ from ELISA tests in that they measure antibodies using different mechanisms. Rapid test kits are less sensitive than ELISA tests, but they are easier to use and are quite accurate. Test results from a rapid test kit still require validation from a confirmatory test as rapid tests are only screening tests.
Home Test Kits

Some patients choose to conduct their own HIV testing using a Federal Drug Administration (FDA) approved home test kit. Home test kits provide patients with the option of testing without having to utilize the services of a health clinic or testing center. Home test kits require the patient to provide a small blood sample, which is sent to the testing company via mail. The sample is mailed in packaging that is provided with the test kit and which adheres to appropriate mailing standards for the transfer of bodily fluids. The testing company conducts the test and positive results are confirmed using an on-site Western Blot confirmatory test. Home test kits provide another option for individuals, but they do not ensure appropriate pre- and post-test counseling.

Additional HIV Tests

Traditional screening and confirmatory tests are recommended for individuals to determine their HIV status. However, additional testing methods do exist and can be used to determine HIV infection levels in specific populations, such as healthcare workers who are exposed to the infection occupationally. These tests are expensive and are not recommended as initial screening tests.

p24 Antigen Test

The p24 Antigen Test detects core protein of HIV, which is present in the early stages of HIV infection. Core protein levels drop and eventually disappear once the body produces antibodies to the virus. Therefore, the p24 antigen test should only be used immediately following exposure to an infected individual.
Plasma HIV RNA Test

Viral load can be determined through the Plasma HIV RNA test, which can detect levels of the virus in a person’s blood approximately nine days after infection occurs. Since this tests levels of the virus, there is no chance of a false positive. Plasma RNA HIV tests are not used as screening tests in the general population, but can be used to determine infection in individuals who know they have had direct exposure to the virus. This test is often used on healthcare workers who receive a needle stick from an infected patient.

The p24 Antigen Test and the Plasma HIV RNA Test listed above are not used as primary screening tests for individuals because most people who request testing have passed the window phase of infection. The window phase of infection is the stage when no antibodies have been produced in response to the infection. Therefore, traditional screening tests will easily diagnose an HIV positive status. The above tests are best used in patients who have been exposed to the bodily fluids of an infected individual through sexual intercourse, needle sharing or accidental needle stick and need to determine status immediately following the exposure so that appropriate treatment can begin.

Test Results

During the screening process, test results can be negative, positive, and indeterminate. Depending on time that has elapsed since infection, negative results may not be accurate.
Window Period

When an individual is infected with HIV, there is a window period during which no antibodies are present. Since screening tests measure the antibodies present in the individual, test results may come back negative even though the individual is infected. Some people may produce enough antibodies within a few weeks of becoming infected, but others can take up to twelve weeks. Therefore, the window period is defined as three months to ensure antibodies have time to develop. If an individual receives a negative test result while in the window period, it is recommended that another test be conducted once the window period has ended to ensure accuracy.

Negative Results

Negative test results verify that there are no antibodies present in the specimen. Unless an individual is still in the window period, these results can be considered accurate. There are no false-negative results once an individual has passed the window period.

Positive Results

A positive screening result confirms that the screening test has reacted positively to antibodies in the specimen. Positive results are quite accurate. However, the test occasionally reacts positively to antibodies produced by other autoimmune disorders. Therefore, a confirmatory test is required to ensure accuracy. A positive confirmatory result verifies that a person is HIV positive.
**Indeterminate Results**

Although rare, a confirmatory test will sometimes provide an indeterminate result, meaning there is not enough evidence to conclude that an individual is HIV positive or negative. Indeterminate results can occur when a patient is newly infected and has not produced enough antibodies. Indeterminate results can also be caused by other factors, including recent vaccination, pregnancy and the presence of other autoimmune disorders.

If an individual is considered high risk, further testing can be done, including p24 antigen testing or HIV RNA testing. However, these tests should only be used if an individual is thought to be in the window period. For individuals whose risk is low, no additional testing is recommended.

**Reporting Test Results**

Once an individual is determined to be HIV positive, the information should be disseminated to the appropriate parties. It minimum, this includes basic reporting to the CDC. However, infected individuals are encouraged to notify those they might have exposed to the virus as well.

**Reporting Requirements**

As of 2008, confidential, name based reporting of HIV cases is conducted in the United States. This information is used to compile surveillance data for the Centers for Disease Control. Prior to 2008, various methods were used for data collection and reporting, which negatively impacted the effectiveness of surveillance reports.
Partner Notification

To prevent the transmission of HIV through early testing and diagnosis, individuals are encouraged to notify their past and current sexual partner and/or those they have shared needles with during drug use. Post-test counseling provides information regarding partner notification. Patients can notify their partners themselves, or they can use a partner notification service. This is a free service that is provided by testing and healthcare centers. When partner notification occurs, the individual receives notification that he or she may have been exposed to HIV through an individual who has been confirmed as HIV positive. The name and identifying information of the infected individual is not revealed. The recipient of the information is given instructions regarding testing options and counseling services available.

Early diagnosis and treatment is imperative in helping prevent the spread of the infection to other individuals. Partner notification services allow individuals to inform past and current partners of the potential risk without having to identify themselves as HIV positive.

The Clinical Stages of HIV Infection

To truly understand how HIV progresses, an understanding of the biology of the virus and the functions of the immune system is necessary. HIV uses the immune system to replicate itself and increase the viral load in the body. Therefore, it is essential to understand both systems and how they function together.

Human immunodeficiency virus belongs to a group of viruses known as retroviruses. Retroviruses are unique because they store their genetic
material on long strands of Ribonucleic Acid (RNA). Almost all organisms, including most viruses, store their genetic material on long strands of DNA. While the structures of DNA and RNA are similar, the two molecules do have some differences that make it more complicated for HIV to replicate than those viruses that store their genetic material on strands of DNA. HIV cannot live outside of a human host and it relies on CD4 cells to replicate.

Once HIV enters the body, it immediately begins to attack the immune system as it seeks a host for the replication process. Any virus that
cannot enter a human body dies within hours.\textsuperscript{98} Since HIV cannot replicate in the absence of a human host, there is no increase of infectiousness. However, as soon as HIV enters the body, it begins the process of replicating and taking over the host’s immune system.\textsuperscript{100}

The virus is able to quickly and efficiently replicate using the attributes of its own genetic makeup combined with those of the host cell.\textsuperscript{101} The human immune system is the ideal breeding ground for HIV and the viral load rapidly increases within the first few weeks of infection.\textsuperscript{97} Meanwhile, the healthy immune system becomes depleted as CD4 cells are destroyed during the replication process.\textsuperscript{99}

\textbf{The Biology of HIV}

Human immunodeficiency virus is a spherical shaped virus, comprised of an outer coat, known as a viral envelope. The viral envelope is made up of two layers of lipids that are hijacked from the membrane of a human cell after the formation of a new virus particle, known as a virion.\textsuperscript{99} There are proteins embedded within the viral envelope that came from the host cell, along with approximately 72 copies of a complex HIV protein.\textsuperscript{102} The HIV protein, which is called \textit{Env}, protrudes from the surface of the virus. Env is comprised of molecules called glycoprotein 120 (gp120) and glycoprotein 41 (gp41), which secure the molecule in the viral envelope.\textsuperscript{99} The inside of the nucleoid contains Viral Genomic RNA and the associate enzyme called reverse transcriptase (RT).\textsuperscript{98} Two proteins known as Transmembrane Glycoprotein and Envelope Glycoprotein surround the outer layer, or envelope. These proteins enable HIV to bind and fuse with another target cell.\textsuperscript{99}
The core of the virus is bullet-shaped and contains approximately 2,000 copies of the viral protein, p24. Within the core are two strands of HIV RNA, both of which contain complete copies of the viral genes. The information needed to make the structural proteins for new virus particles exist within the virus’s structural genes: gag, pol, and env. The core also contains the HIV nucleocapsid protein p7. Between the viral core and the viral envelope is the HIV matrix protein called p17.

HIV uses regulatory genes to aid in infecting a cell. There are six genes total (tat, rev, nef, vif, vpr, and vpu), and they all contain the necessary information that will enable the virus to produce the proteins that will control the ability of HIV to infect a cell, produce new copies of virus, or cause disease. The virus also contains three enzymes that it uses to take over a cell and complete the replication process, thereby increasing the amount of virus in the body. The three enzymes are: reverse transcriptase, integrase, and protease. At the end of the strand of HIV RNA is the long terminal repeat (LTR), which is able to control the production of new viruses by acting as a switch. Proteins from HIV or the host cell activate the LTR.

**The Immune System**

The immune system is complex and has myriad ways of fighting off foreign agents. When a virus enters the body, the immune system responds by initiating specific processes that work together to defend the body from the invader. The first stage of defense involves recognition of the foreign agent and delivery of the agent to the lymph system. Once in the lymph system, a macrophage acts quickly to ingest and eliminate the agent.
Once the macrophage ingests the agent, it processes it and displays the antigens for the virus on its exterior. The antigen acts as a signal for the helper T-cells. Once a helper T-cell recognizes and deciphers the signal, it sounds an alarm for the rest of the immune system to respond. The first responder is the B-cell, which reads the antigen from the surface of the macrophage and is activated to produce antibodies that are antigen specific. The released antigens then spread throughout the body and attach to the virus particles. The antibodies assist the immune system during the invasion as the virus attempts to outnumber the immune cells. The antibodies attach to the antigens and send signals to the macrophages and immune cells to destroy the antibody and whatever it has captured. Once the level of agents has decreased significantly, and the infection has been eliminated, the suppressor T-cell sends a signal to other cells so that they can stop acting against the agent.

**HIV Replication**

Human immunodeficiency virus cannot replicate without an appropriate host. It relies on cells within the human body to complete its lifecycle and will die if it does not locate a host within a short period of time. Once HIV enters the body, it immediately begins its replication process. HIV relies on CD4+ T cells for the replication process. When HIV enters a body, it seeks out CD4 cells and attaches to them. The spiky surface enables the virus to attach to the CD4 cell, after which the viral envelope fuses with the cell membrane. Once fusion occurs, the HIV particle releases its contents into the cell and leaves the empty envelope behind.
After the virus releases its particles into the cell, the reverse transcriptase enzyme begins its conversion process. During this process, the enzyme converts viral RNA into DNA, which is recognized and accepted by the human genetic material.\textsuperscript{101} The converted DNA is transported to the cell’s nucleus. From there, it is converted to human DNA by the HIV enzyme integrase.\textsuperscript{97} Once the integration is complete, the converted DNA becomes a provirus.\textsuperscript{99} 

Once the virus becomes a provirus, it can lie dormant for an extended period of time. It will not begin the next phase of the replication process until the cell is activated.\textsuperscript{99} Once the cell is activated, it treats the HIV genes as if they are human genes.\textsuperscript{97} The first stage of replication involves using human enzymes to convert the HIV genes into messenger RNA, which are removed from the nucleus.\textsuperscript{98} The messenger RNA is then used as a blueprint for the production of HIV proteins and enzymes.\textsuperscript{99}

The strands of messenger RNA contain complete copies of HIV genetic material.\textsuperscript{99} When these copies come together with the newly formed HIV proteins and enzymes, they produce new viral particles. The new particles are released from the cell as part of a process called “budding”.\textsuperscript{105} At this point in the HIV lifecycle, the enzyme protease takes on a crucial role. Protease works by chopping the long strands of protein into smaller pieces. These smaller pieces of protein are then used to construct mature viral cores.\textsuperscript{99} 

The mature viral cores are the result of a complete HIV lifecycle and are ready to begin the process with new CD4 cells.\textsuperscript{101} These new cells
seek out CD4 cells and begin to replicate. This process enables HIV to spread very quickly and eventually destroy the immune system.\textsuperscript{97}

**Stages of HIV Infection**

Human immunodeficiency virus is a progressive illness. Once HIV enters an individual’s body, it goes through seven stages of infection.\textsuperscript{97} Healthcare providers should be familiar with the various stages of infection so that they can best treat and manage the illness in their patients. The first three stages of infection are all part of the window period, during which an individual might not test positive for HIV.\textsuperscript{40} Once a person passes through the first three stages, he or she will have enough antibodies present to cause a positive reaction on a screening test.\textsuperscript{92}

**Viral Transmission**

Viral transmission is the first stage of HIV infection and refers to the period during which the virus enters the body from an infected source. Viral transmission occurs immediately, and the disease quickly transitions to the next stage of infection.\textsuperscript{98}

**Primary HIV Infection**

The first few weeks after viral transmission are known as the period of primary HIV infection. During this time, individuals may experience flu-like symptoms such as a sore throat, fever, rash, swollen lymph nodes, and fatigue.\textsuperscript{82} However, many patients will experience no symptoms at all. During this stage, patients have a high viral load and can already transmit the virus to others.\textsuperscript{107} However, since the body is still responding to the virus, antibodies might not yet be present.\textsuperscript{40}
Seroconversion

Seroconversion is the technical term for the primary stage of the window period. Seroconversion is the period of time between initial infection and the development of adequate antibodies. During this stage, individuals will often test negative for HIV because there are not enough antibodies present in their system. Patients rarely experience symptoms during this stage, but they are still contagious to others.

Asymptomatic HIV Infection

The asymptomatic stage of infection is the period that follows the window period. During this stage of infection, an individual has enough antibodies present and will produce a positive test result. However, at this stage, the patient does not present any symptoms. Individuals can remain in the asymptomatic stage of infection for ten years or more. Individuals who have not been tested for HIV will not be aware of their positive status while they are in this stage of infection. This poses a great risk, as individuals will continue to engage in risky behavior during this time while being unaware that they are potentially transmitting the virus to others.

Symptomatic HIV Infection

This is the period during which a patient begins to exhibit symptoms associated with HIV. Symptomatic HIV infection occurs prior to the disease transition to AIDS. At this point in the illness, HIV has destroyed the immune system to a point that it is unable to fight off other infections. Patients in the symptomatic stage of infection will often present the following symptoms.
• Diarrhea
• Fever or night sweats
• Enlarged glands
• Oral infections
• Skin problems

Many patients do not discover their HIV positive status until they enter the symptomatic stage of infection. Patients can live for ten or more years with the virus without experiencing any symptoms. If a patient is not tested for HIV during the asymptomatic stage of infection, he or she will have no indication of the illness. However, when a patient begins experiencing symptoms during this later stage of infection, presence of the virus is suspected and the patient is often tested and diagnosed. This presents a problem for caregivers as patients who are unaware of their HIV status until they reach the symptomatic stage of infection often experience more complications than those who know their status early on. HIV is managed well with antiretroviral treatment and patient care. This is difficult in patients that are unaware of their status.

*Acquired Immune Deficiency Syndrome (AIDS)*

Acquired Immune Deficiency Syndrome is the final stage of HIV infection and eventually results in death. In this stage, the immune system of the patient is almost completely destroyed, leaving the patient susceptible to a range of infections. AIDS is diagnosed using two separate criteria:

• CD4 levels <200 cells/µL
• Presence of one or more AIDS defining conditions
During clinical management of HIV, patient CD4 counts are regularly monitored. Once a patient’s CD4 count drops below 200, he or she is considered to have moved into the final stage of infection. A CD4 count below 200 indicates that the virus has destroyed the immune system and the patient will have difficulty fighting off infection.

Patients are considered to have AIDS when they present with one or more of the AIDS defining conditions, also known as opportunistic infections, listed below:

- Bacterial infections, multiple or recurrent
- Candidiasis of bronchi, trachea, or lungs
- Candidiasis of esophagus
- Cervical cancer, invasive
- Coccidioidomycosis, disseminated or extrapulmonary
- Cryptococcosis, extrapulmonary
- Cryptosporidiosis, chronic intestinal (>1 month's duration)
- Cytomegalovirus disease (other than liver, spleen, or nodes), onset at age >1 month
- Cytomegalovirus retinitis (with loss of vision)
- Encephalopathy, HIV related
- Herpes simplex: chronic ulcers (>1 month's duration) or bronchitis, pneumonitis, or esophagitis (onset at age >1 month)
- Histoplasmosis, disseminated or extrapulmonary
- Isosporiasis, chronic intestinal (>1 month's duration)
- Kaposi sarcoma
- Lymphoid interstitial pneumonia or pulmonary lymphoid hyperplasia complex
- Lymphoma, Burkitt (or equivalent term)
- Lymphoma, immunoblastic (or equivalent term)
• Lymphoma, primary, of brain
• Mycobacterium avium complex or Mycobacterium kansasii, disseminated or extrapulmonary
• Mycobacterium tuberculosis of any site, pulmonary, disseminated, or extrapulmonary
• Mycobacterium, other species or unidentified species, disseminated or extrapulmonary
• Pneumocystis jirovecii pneumonia
• Pneumonia, recurrent
• Progressive multifocal leukoencephalopathy
• Salmonella septicemia, recurrent
• Toxoplasmosis of brain, onset at age >1 month
• Wasting syndrome attributed to HIV

Patients often experience a variety of symptoms once they progress to AIDS. These symptoms are not caused by HIV, but rather by the opportunistic infections that the individual is susceptible to as the result of a suppressed immune system.\textsuperscript{36}

Proper management of AIDS is necessary for patient comfort and longevity. With appropriate treatment, the affects of AIDS can be minimized. Patients who receive regular care are able to reduce the number and severity of opportunistic infections, thereby ensuring fewer symptoms and illness-related complications.\textsuperscript{112}

While a patient may reduce the impact of AIDS through proper care, the patient’s status does not change. Once a patient is diagnosed with AIDS, he or she maintains that diagnosis, even if the patient begins to feel better and experiences less symptoms.\textsuperscript{36}
Patients who receive adequate care during this stage have an increased likelihood of living longer than those that do not receive adequate care.\textsuperscript{113} The typical life expectancy of an individual with AIDS is 10 – 12 months.\textsuperscript{112} However, some patients can live four or more years with AIDS if the disease is managed properly.\textsuperscript{113} Patient morbidity is not a direct result of HIV. It is the result of complications from HIV, typically as the result of opportunistic infections.\textsuperscript{111}

**Classification Systems**

There are currently two classification systems in place to track and monitor HIV worldwide. These classification systems define stages of infection and are used to monitor patient progress and provide information for surveillance purposes. The two official classifications are the U.S. Centers for Disease Control and Prevention (CDC) classification system and the World Health Organization (WHO) Clinical Staging and Disease Classification System. The CDC classification system determines stages based primarily on CD4+ T-cell counts, which requires regular laboratory testing and frequent monitoring to assess. In later stages of infection, the CDC does incorporate documentation of AIDS-defining conditions as additional criteria.\textsuperscript{7,37} However, primary classification is based on CD4+ T-cell counts. The WHO classification system determines stages based on clinical manifestations that can be assessed and evaluated without the use of laboratory testing. The WHO classification system is used primarily to assess and classify patients who do not have access to appropriate diagnostic testing methods. \textsuperscript{7,37}

*CDC Classification System*
The CDC Classification system has three clinical stages that are defined by CD4+ T-cell count. The follow are the clinical stages of HIV as defined by the CDC:

HIV infection, stage 1:
No AIDS-defining condition and either CD4+ T-lymphocyte count of ≥500 cells/µL or CD4+T-lymphocyte percentage of total lymphocytes of ≥29.

HIV infection, stage 2:
No AIDS-defining condition and either CD4+ T-lymphocyte count of 200–499 cells/µL or CD4+ T-lymphocyte percentage of total lymphocytes of 14-28.

HIV infection, stage 3 (AIDS):
CD4+ T-lymphocyte count of <200 cells/µL or CD4+ T-lymphocyte percentage of total lymphocytes of <14, or documentation of an AIDS-defining condition. Documentation of an AIDS-defining condition supersedes a CD4+ T-lymphocyte count of ≥200 cells/µL and a CD4+ T-lymphocyte percentage of total lymphocytes of ≥14.

HIV infection, stage unknown:
No information available on CD4+ T-lymphocyte count or percentage and no information available on AIDS-defining conditions.

World Health Organization Classification System
The World Health Organization uses the following stages for HIV infection.

Clinical stage 1 (Asymptomatic):
- Asymptomatic
- Persistent generalized lymphadenopathy

Clinical stage 2 (Mild disease):
- Moderate unexplained weight loss (<10% of presumed or measured body weight)
- Recurrent respiratory tract infections (sinusitis, tonsillitis, otitis media, pharyngitis)
- Herpes zoster
- Angular cheilitis
- Recurrent oral ulceration
- Papular pruritic eruptions
- Seborrhoeic dermatitis
- Fungal nail infections

Clinical stage 3 (Moderate disease):
- Unexplained severe weight loss (>10% of presumed or measured body weight)
- Unexplained chronic diarrhea for longer than one month
- Unexplained persistent fever (intermittent or constant for longer than one month)
- Persistent oral candidiasis
- Oral hairy leukoplakia
- Pulmonary tuberculosis
• Severe bacterial infections (i.e., pneumonia, empyema, pyomyositis, bone or joint infection, meningitis, bacteremia)
• Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis
• Unexplained anemia (<8 g/dl), neutropenia (<0.5 x 10^9 /L) and or chronic thrombocytopenia
• (<50 X 10^9 /L)

Clinical stage 4 (Severe disease):
• HIV wasting syndrome
• Pneumocystis pneumonia
• Recurrent severe bacterial pneumonia
• Chronic herpes simplex infection
• Esophageal candidiasis (or candidiasis of trachea, bronchi or lungs)
• Extrapulmonary tuberculosis
• Kaposi's sarcoma
• Cytomegalovirus infection (retinitis or infection of other organs)
• Central nervous system toxoplasmosis
• HIV encephalopathy
• Extrapulmonary cryptococcosis including meningitis
• Disseminated non-tuberculous mycobacteria infection
• Progressive multifocal leukoencephalopathy
• Penicilliosis
• Chronic cryptosporidiosis
• Chronic isosporiasis
• Disseminated mycosis (extrapulmonary histoplasmosis, coccidiomycosis)
• Recurrent septicemia (including non-typhoidal Salmonella)
• Lymphoma (cerebral or B cell non-Hodgkin)
• Invasive cervical carcinoma
• Atypical disseminated leishmaniasis
• Symptomatic HIV-associated nephropathy or HIV-associated cardiomyopathy

**Proper Diagnosis and Early Intervention**

Proper care and management of HIV infected patients is of the utmost importance in reducing the impact of the disease and preventing patient morbidity. HIV can progress rapidly, especially in the absence of treatment. Proper diagnosis and early intervention help prevent the infection from progressing from the asymptomatic stage to the symptomatic stage of infection. Patients who receive adequate care early and regularly may not ever progress to AIDS. Treatment and care of HIV infected patients is discussed in Part II of this course series.

**Summary**

Human immunodeficiency virus is a disease that affects over forty million people worldwide and one million people in the United States. During the early stages of infection, individuals can live symptom free. Progression of the disease varies by patient and can be impacted by a variety of factors. Healthcare providers must understand the signs and symptoms of infection, as well as the various stages of HIV infection. Proper treatment can prevent the infection from progressing beyond the asymptomatic stage. Therefore, providers must work closely with patients to develop a treatment plan that minimizes progression. Different therapies and strategies can have differing effects on patients.
and an understanding of the adverse affects of antiretroviral drugs is imperative in disease management. In the stage of the infection known as HIV, patients often exhibit few symptoms. When the disease transitions to Acquired Immune Deficiency Syndrome (AIDS) the patient often experiences an increase in symptoms and severity of the disease and presents with one or more opportunistic infections. Appropriate treatment and management of HIV is imperative to prevent the infection from causing irreversible effects on the patient.

Through the use of highly effective antiretroviral therapy, case management services and prevention programs, the spread of the disease in the U.S., has slowed in recent years. In low to middle income countries, the number of individuals infected annually is still significant. However, new initiatives aimed at reducing the spread of HIV in these areas are starting to improve prevention rates. There is no cure for HIV. HIV positive individuals require care from onset of infection and through the remainder of the patient’s life. However, through the use of antiretroviral therapy and a comprehensive treatment plan, the disease can remain a manageable, chronic illness for 10 – 20 years. Treatment for an HIV positive individual is a complex process that requires the provider to work with the patient to develop a treatment plan that is able to address the individual patient’s needs and minimize the progression of the virus.

References Section
http://www.sciencedaily.com/releases/2012/12/121218143029.htm
31. Hamouda O. Global Epidemiology of HIV. Sexually Transmitted Infections and Sexually Transmitted Diseases 2011: 249-270.
34. HIV Types. Available at http://www.avert.org/hiv-types.htm.
48. Hall HI, Holtgrave DR, Maulsby C. HIV transmission rates from persons living with HIV who are aware and unaware of their infection. AIDS. 2012;26:893-896.


76. Smith DK et al. Antiretroviral Postexposure Prophylaxis After Sexual, Injection-Drug Use, or Other Nonoccupational Exposure to HIV in the United States. Recommendations from the U.S.
Department of Health and Human Services. MMWR Recommendations and Reports. January 21, 2005/54(RR02);1-20.

77. Robb ML et al. Risk behaviour and time as covariates for efficacy of the HIV vaccine regimen ALVAC-HIV (vCP1521) and AIDSVAX B/E: a post-hoc analysis of the Thai phase 3 efficacy trial RV 144. Lancet. 2012; (12)7: 531-537.


91. Hecht FM et al. HIV RNA level in early infection is predicted by viral load in the transmission source. AIDS. 2010 April 24; 24(7): 941–945.


94. CDC. Data Security and Confidentiality Guidelines for HIV, Viral Hepatitis, Sexually Transmitted Disease, and Tuberculosis Programs: Standards to Facilitate Sharing and Use of Surveillance Data for Public Health Action. Atlanta, Georgia: Centers for Disease Control and Prevention; 2011.


100. Pinney JW, Dickerson JE, Fu W, Sanders-Beer BE, Ptak RG, Robertson DL. HIV-host interactions: a map of viral perturbation of the host system AIDS. 2009; (23) 5: 549-554.


APPENDIX A: HELPFUL HIV/AIDS RESOURCES

2. Aids.org. CD4 (T-CELL) TESTS. http://www.aids.org/topics/aids-factsheets/aids-background-information/what-is-aids/hiv-testing/cd4-t-cell-tests/
APPENDIX B: HIV/AIDS SUPPORT GROUPS & EDUCATION

The following websites provide the clinician with some helpful education tools and referrals for individuals and families seeking support after being diagnosed HIV positive and/or having AIDS in the U.S. and internationally.


9. UNICEF. Join our Fight Against AIDS. http://www.unicefusa.org/work/hivaid/