HIV / AIDS: A COMPREHENSIVE REVIEW

Jassin M. Jouria, MD

Dr. Jassin M. Jouria is a medical doctor, professor of academic medicine, and medical author. He graduated from Ross University School of Medicine and has completed his clinical clerkship training in various teaching hospitals throughout New York, including King’s County Hospital Center and Brookdale Medical Center, among others. Dr. Jouria has passed all USMLE medical board exams, and has served as a test prep tutor and instructor for Kaplan. He has developed several medical courses and curricula for a variety of educational institutions. Dr. Jouria has also served on multiple levels in the academic field including faculty member and Department Chair. Dr. Jouria continues to serves as a Subject Matter Expert for several continuing education organizations covering multiple basic medical sciences. He has also developed several continuing medical education courses covering various topics in clinical medicine. Recently, Dr. Jouria has been contracted by the University of Miami/Jackson Memorial Hospital’s Department of Surgery to develop an e-module training series for trauma patient management. Dr. Jouria is currently authoring an academic textbook on Human Anatomy & Physiology.

Abstract

As a result of advanced treatment options and increased access to care, the number of people diagnosed with HIV is decreasing. With proper diagnosis and treatment, people can live symptom-free for a significant length of time. Advances in testing and treatment options have improved the care and management of HIV. Comprehensive prevention strategies and widespread education are important in ensuring that the spread of the disease is minimized. The management of HIV in infected individuals is complex and must be assessed on a case-by-case basis. This article will provide comprehensive review for the primary care provider, in identifying and treating patients with HIV.
Continuing Nursing Education Course Director & Planners
William A. Cook, PhD, Director, Douglas Lawrence, MS, Webmaster,
Susan DePasquale, CGRN, MSN, FPMHNP-BC, Lead Nurse Planner

Accreditation Statement
This activity has been planned and implemented in accordance with the policies of NurseCe4Less.com and the continuing nursing education requirements of the American Nurses Credentialing Center's Commission on Accreditation for registered nurses.

Credit Designation
This educational activity is credited for 12 hours. Pharmacology content 2 hours. Nurses may only claim credit commensurate with the credit awarded for completion of this course activity.

Course Author & Planner Disclosure Policy Statements
It is the policy of NurseCe4Less.com to ensure objectivity, transparency, and best practice in clinical education for all continuing nursing education (CNE) activities. All authors and course planners participating in the planning or implementation of a CNE activity are expected to disclose to course participants any relevant conflict of interest that may arise.

Statement of Need
Different therapies and strategies can have differing effects on patients and its imperative that nurses have an understanding of HIV and AIDS disease progression, treatment options and the adverse affects of antiretroviral drugs is imperative in disease management.
**Course Purpose**

To provide nursing professionals with knowledge HIV and AIDS disease progression, treatments and complications.

**Learning Objectives**

1. Understand the history and evolution of HIV.
2. Recognize the importance of HIV as a public health issue.
3. Understand the impact of HIV worldwide.
4. Identify the different stages of HIV infection.
5. Identify the methods of transmission of HIV.
6. Identify the signs and symptoms of HIV infection.
7. Understand the importance of proper diagnosis and identification of HIV.
8. Differentiate between screening and confirmatory tests used in HIV diagnosis.
9. Understand and describe how to conduct pre and post-test counseling with patients undergoing HIV testing.
10. Identify methods of HIV prevention for all risk groups.
11. Understand and differentiate between HIV and AIDS.
12. Identify and understand opportunistic infections.
13. Identify different HIV and AIDS treatment options.
14. Identify the types of antiretroviral drugs and the adverse effects of these drugs.
15. Understand the social and cultural dimensions of HIV.
**Target Audience**
Advanced Practice Registered Nurses, Registered Nurses, Licensed Practical Nurses, and Associates

**Course Author & Director Disclosures**
Jassin M. Jouria, MD, William S. Cook, PhD, Douglas Lawrence, Susan DePasquale, CGRN, MSN, FPMHNP-BC – all have no disclosures

**Acknowledgement of Commercial Support:**
There is no commercial support for this course.

**Activity Review Information:**
Reviewed by Susan DePasquale, CGRN, MSN, FPMHNP-BC

**Release Date:** 1/1/2015    **Termination Date:** 5/10/2016

Please take time to complete the self-assessment Knowledge Questions *before* reading the article. Opportunity to complete a self-assessment of knowledge learned will be provided at the end of the course.
1. The most common strain of HIV-1 infecting most patients today is believed to have been transmitted by:
   a. Humans in Africa
   b. Cameroon chimps to humans
   c. Insects to humans
   d. West African parrots

2. True or False. In both confidential and anonymous testing, the patient is required to give informed consent.
   a. True
   b. False

3. In 2011, there were __________ children worldwide who tested positive for HIV.
   a. 1.5 million
   b. 2.5 million
   c. 3.3 million
   d. none of the above

4. Post-test counseling regarding partner notification allows patients to:
   a. notify their partners themselves
   b. use a free-standing partner notification service
   c. have their name and identifying information kept confidential
   d. all of the above

5. True or False. Latex and polyurethane condoms are an ineffective means of preventing the transmission of HIV when used correctly.
   a. True
   b. False
6. The CDC 2011 Surveillance Report showed about _________new HIV infections per year.
   a. 50,000
   b. 37,000
   c. 25,000
   d. 125,000

7. True or False. HIV 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.
   a. True
   b. False

8. The WHO Classification System lists stage 1 symptoms as:
   a. moderate unexplained weight loss
   b. persistent generalized lymphadenopathy
   c. herpes zoster
   d. recurrent oral ulceration

9. The primary form of HIV screening is the:
   a. Complete blood count
   b. Sputum test
   c. ELISA (enzyme-linked immunosorbent assay) test
   d. Chest X-Ray

10. The common confirmatory test for HIV is the:
    a. Elisa test
    b. Western blot
    c. Chest X-Ray
    d. none of the above
11. The World Health Organization recommends *Clinical Stage Management* for Stage 1 to include:
   a. patient follow up every 6 – 12 months
   b. check for clinical signs of progression
   c. total lymphocyte count or CD4 cell count if available
   d. answers a and b above

12. Seroconversion is the period of time:
   a. between initial infection and the development of adequate antibodies
   b. when individuals often test positive for HIV
   c. when symptoms are experienced
   d. none of the above

13. True or False. In patients with a CD4 cell count below 200, an immunization vaccination will not work properly.
   a. True
   b. False

14. Early antiretroviral therapy (ART) commonly included:
   a. the use of a singular drug to treat the virus
   b. use of antiretroviral drug zidovudine or azidothymidine
   c. dual drugs to combat infection
   d. answers a and b above

15. True or False. The strength of ART recommendation varies on the basis of pre-treatment CD4 cell count.
   a. True
   b. False
16. True or False. Patients who experience lipodystrophy often have low insulin levels.
   a. True
   b. False

17. The CCR5 antagonist:
   a. was first approved by the FDA in 2007
   b. is used as a new line of defense against viral replication
   c. helps prevent cellular fusion between the virus and host cell
   d. all of the above

18. Treatment for patients co-infected with HIV/HBV include:
   a. ART with ABV treatment irrespective of CD4 cell count
   b. ART with ABV treatment irrespective of clinical stage
   c. Tenofovir Disoproxil Fumarate and lamivudine, epivir or emtricitabine antiretroviral regimens
   d. All of the above

19. True or False. There is a direct link between HIV and sexually transmitted diseases.
   a. True
   b. False

20. True or False. HIV-infected women should receive evaluation and appropriate prophylaxis for opportunistic infections (OIs), however, vaccinations indicated for persons with HIV infection should be avoided until after childbirth.
   a. True
   b. False
Introduction

Human Immunodeficiency Virus (HIV) has affected individuals worldwide since it first caused rare illnesses in a select group of individuals in 1980.\textsuperscript{1} HIV was first identified in 1983 and quickly spread, eventually becoming a worldwide pandemic. Approximately forty million people worldwide are living with HIV, with one million of those residing in the United States. The disease has 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 pneumosystis pneumonia in otherwise healthy individuals.\textsuperscript{2} In the first decade, the disease spread rapidly, destroying the immune systems of those infected. Since it was first discovered, HIV has become a worldwide pandemic.\textsuperscript{3} Approximately forty million people worldwide are living with HIV, with one million of those residing in the United States.\textsuperscript{4} 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.\textsuperscript{5}

HIV attacks, and eventually destroys, the immune system. During the early stages of infection, individuals can live symptom free.\textsuperscript{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} 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 effects of antiretroviral drugs is imperative in disease management. Appropriate treatment and management of HIV is necessary to prevent the infection from causing irreversible effects on the patient.\(^8\)

With the development of antiretroviral therapy and advancements in HIV management and care, the virus is now easily managed and can remain a chronic condition for more than ten years.\(^6\) However, the virus is complex and impacts each patient differently. Therefore, it is necessary for providers to work closely with patients to develop a treatment plan that will address the individual patient’s needs and minimize the progression of the virus.

**Overview**

**Origin**

When HIV emerged in the early 1980’s scientists began trying to determine its origins. After years of research, scientists traced the virus to chimpanzees in Africa.\(^9\) These chimpanzees were infected with simian immunodeficiency virus (SIV), which is a retrovirus similar to HIV.\(^9\) While HIV did not spread significantly into the human population until the 1980’s, evidence shows that SIV may have infected humans as early as 1884.\(^10\) 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.\(^11\) 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 thirty years.

Although there is evidence that HIV may have infected humans as early as 1884, the sub-type 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). The most common strain of HIV-1, the type that infects most patients today, is believed to have transmitted by the Cameroon chimps to humans in the period shortly before 1931. 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 ago. Therefore, it is assumed that the transmission from chimpanzees to humans occurred shortly before that.

**History**

In June of 1981, the Center for Disease Control 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 doctors 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 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. Care centers were established to help the tens of thousands of patients who were infected with the disease.

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. The CDC also discovered that the disease had infected homosexual men, women with male partners, infants and injection drug users. As a result, a public statement was released warning individuals to refrain from activities that would put them in contact with the disease. Scientists in France identified the specific virus strain suspected to be causing AIDS as Lymphadenopathy Associated Virus (LAV), while scientists in the United States identified the virus as the retrovirus HTLV-III. 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. AIDS 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 1980’s and throughout the 1990’s, 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.\textsuperscript{3} 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.\textsuperscript{16} Social service and case management programs were developed to address non-HIV issues in patients and training for healthcare providers focused on the effective treatment and management of the virus.\textsuperscript{16}

In the thirty years since the first reported case of AIDS, the disease has spread and swelled to significant numbers.\textsuperscript{10} HIV 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 2000’s, 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. HIV treatment strategies evolved and a multi-faceted approach to disease management became standard protocol for working with positive patients.

**Epidemiology**
Over the past thirty years, 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 – 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.\textsuperscript{26}

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 case 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 15-49 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.\textsuperscript{29}

While HIV has affected individuals on a global scale, the disease is most prevalent in Sub-Saharan Africa, where 69% of the population is currently HIV positive.\textsuperscript{26} HIV is currently the leading cause of death in Africa. This region has 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 of the nations in the region have generalized HIV epidemics.\textsuperscript{31} The highest numbers of people worldwide who are HIV positive reside in South Africa, and Swaziland has the highest overall prevalence rate, which is 26%. The remaining HIV cases are spread throughout the world, with a high concentration of cases in low and middle-income countries.\textsuperscript{32} International and national organizations responding to the HIV epidemic support health team efforts to provide education and health aid to high risk areas; examples include the U.S. Peace Corps (http://www.peacecorps.gov/learn/whatvol/hivaids/) as well as other
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.

Young people between the ages of 15 – 24 make up approximately 40% of the new HIV cases worldwide. 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 – 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 – 95 (28). 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 Center for Disease Control (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, which was released in 2011, provides information on the period from 2008 – 2011. 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 bulleted summary of HIV trends from 2008 – 2011.

**CDC Surveillance Report – 2011**

*HIV in the United States: At a Glance*

**HIV incidence (new infections):**
The estimated incidence of HIV has remained stable overall in recent years, at about 50,000 new HIV infections per year. Within the overall estimates, however, some groups are affected more than others. MSM (men who have sex with men) continue to bear the greatest burden of HIV infection, and among races/ethnicities, African Americans continue to be disproportionately affected.

**HIV diagnoses (new diagnoses, regardless of when infection occurred):**
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.³

**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.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.
By 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.\(^2\) 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 continue 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.

By race/ethnicity
Blacks/African Americans continue 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 also disproportionately affects Hispanics/Latinos. Data extracted from literature is included below:

- 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.

**Human Immunodeficiency Virus (HIV)**

Human Immunodeficiency Virus (HIV) is a retrovirus that attacks the immune system. Retroviruses are viruses that contain DNA as part of their genetic material. 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. Over time, the body becomes unable to fight off infection and succumbs to a variety of secondary infections. HIV is often slow to progress, and individuals who test positive for HIV often exhibit no symptoms for long periods of time. Some individuals will go a number of years without seeing progression of the virus. In a select few, the virus will never progress.
HIV 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-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-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**

HIV 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

HIV-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
Acquired Immune Deficiency Syndrome (AIDS)

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. AIDS 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. AIDS 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. The CDC has identified more than twenty opportunistic infections that are considered AIDS Indicator Conditions. 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 sarcomav
- 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. Most individuals die from complications related to AIDS acquired infections.⁴³

**Transmission**

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.
HIV is found in the following body fluids:  
- Blood  
- Vaginal secretions  
- Semen  
- Other body fluids containing blood  
- Breast milk

HIV is transmitted through the following methods:  
- 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. While other methods of transmission are also a risk, the rate of transmission is lower. HIV is not transmitted through feces, saliva, sweat, urine, or other bodily fluids. In addition, HIV is not spread through the air. Each method of transmission must be understood so that proper preventative measures can be taken.

Sexual intercourse
Human immunodeficiency virus transmission rates are extremely high during sexual intercourse. Primary modes of transmission are through anal or vaginal intercourse. While there is a small risk of transmission during oral intercourse, it is not as common as through vaginal or anal intercourse. HIV 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.
During anal sex, the skin lining the rectum can tear easily, providing an opening for the infection to enter.\textsuperscript{50} The inside of the vagina is lined with mucous membranes that allow the virus to enter the body.\textsuperscript{46} During penetration, the lining of the vagina can tear, providing additional locations for the virus to enter the body.\textsuperscript{44} 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.\textsuperscript{44}

\textit{Injecting drugs}
Along with sexual intercourse, sharing needles is the most common method of HIV transmission.\textsuperscript{46} 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.\textsuperscript{51} HIV 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.\textsuperscript{46}

\textit{Mother to child}
HIV 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.\textsuperscript{46} Additionally, the virus can be transmitted to the child during breastfeeding as breast milk also contains trace amounts of HIV.\textsuperscript{52} 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.\textsuperscript{52}

Transmission from mother to child is less common than transmission during sexual intercourse or from sharing needles.\textsuperscript{46} However, the risk is still present. With no medical interventions, the risk of transmission from mother to child is approximately 25\%.\textsuperscript{52}

\textit{Blood transfusions, blood products and organ/tissue donation}

HIV 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.\textsuperscript{53} However, 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.\textsuperscript{46}

\textbf{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.\textsuperscript{54} Most cases of HIV are transmitted through direct sexual intercourse or sharing needles.\textsuperscript{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.\textsuperscript{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>

CDC. HIV and the Law: HIV Transmission Risk.\(^5^6\)

**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.\(^4^6\) Additional education and
prevention measures are necessary to help these populations avoid becoming infected with HIV.

Co-Infection with Other STD’s
Individuals who engage in the type of risky behaviors that can transmit HIV are often co-infected with other STD’s and infections. Individuals who are already infected with other STD’s are at an increased risk of developing HIV because their immune systems are already compromised. Some STD’s 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 STD’s 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**

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.⁶⁵
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. 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.
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.\(^5\) 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.\(^6\)

Needle exchange

The most effective method of preventing the spread of HIV among injection drug users is through needle exchange programs.\(^6\) 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.\(^6\)

Mother to Child

HIV infected mothers are at risk of passing the infection on to their children during pregnancy, delivery and through breastfeeding if appropriate preventative measures are not taken.\(^4,5\) With proper prevention strategies, the risk of transmission from mother to child is lower than five percent.\(^5\)
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 HIV 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. HIV testing is also done on all organ and tissue donations to ensure that HIV is not transmitted during the donation process.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.

\textit{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.\textsuperscript{62} 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.\textsuperscript{71} 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.71

**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.72

**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.71,72

**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.73 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.\textsuperscript{74} In some cases, a 28-day course of antiretrovirals is prescribed to prevent HIV from spreading throughout the body.\textsuperscript{75} Post-exposure prophylaxis is standard protocol for healthcare workers who have come into contact with blood or other bodily fluids.\textsuperscript{71} 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.\textsuperscript{76}

**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.\textsuperscript{16} 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.\textsuperscript{24}

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.\textsuperscript{77} 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.\textsuperscript{78} In 2011, after further research and development, a vaccine was approved to begin trials on humans.\textsuperscript{79} While no vaccine currently exists, there is the potential that one will be developed in the near future.
Diagnosis

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. 80 Once the disease progresses, treatment is less successful and further complications can develop. 81

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. 82 Once the virus progresses, an individual can remain symptom free for ten or more years, which can make it difficult to diagnose the disease. 82 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. 55

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. 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. 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:

- diarrhea
- unexplained weight loss
- persistent fever
- persistent cough
- persistent vaginal candidiasis (women)
- thrush/oral candidiasis
- enlarged lymph nodes or other swollen glands

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. HIV testing should be recommended as part of this process.

Once an individual transitions 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 immune system of an AIDS patient has been destroyed by HIV, which results in more pronounced illness.

**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. 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.\textsuperscript{83}

Any individual who engages in behaviors that can transmit the infection should regularly be tested for HIV. There are two different testing options:

\textit{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.\textsuperscript{85}

\textit{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.\textsuperscript{85}

\textit{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.\textsuperscript{85}

\textit{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 posttest counseling without being denied the right to test.\textsuperscript{84}

\textit{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.\textsuperscript{86}

\textit{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.\textsuperscript{84} Individuals who test positive will require more in-depth counseling. In most instances, the testing provider will provide the post-test counseling.\textsuperscript{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.\textsuperscript{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.\textsuperscript{84} Counseling should also include discussions of prevention and treatment strategies, as well as strategies for notifying friends and family members.\textsuperscript{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.\(^{40}\)

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.\(^{87}\) However, screening tests are also less reliable than confirmatory tests, so a positive test result should always be verified using a confirmatory test.\(^{40}\) 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.\(^{40}\) 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). 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
HIV antibodies are present in the urine of infected patients. New screening tests are now available that can detect these antibodies using a standard urine sample 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. 

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. 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.⁸⁸

*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.⁸⁹ Home test kits provide another option for individuals, but they do not ensure appropriate pre- and post-test counseling.⁴⁰

**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 needlestick 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.\textsuperscript{40} 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 needlestick and need to determine status immediately following the exposure so that appropriate treatment can begin.\textsuperscript{90}

**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.\textsuperscript{82}

*Window period*

When an individual is infected with HIV, there is a window period during which no antibodies are present.\textsuperscript{40} Since screening tests measure the antibodies present in the individual, test results may come back negative even though the individual is infected.\textsuperscript{82} Some people may produce enough antibodies within a few weeks of becoming infected, but others can take up to twelve weeks.\textsuperscript{38} Therefore, the window period is defined as three months to ensure antibodies have time to develop.\textsuperscript{36} 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.\textsuperscript{40}

*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.\textsuperscript{94}

\textit{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.\textsuperscript{95} Prior to 2008, various methods were used for data collection and reporting, which negatively impacted the effectiveness of surveillance reports.\textsuperscript{87}

\textit{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.\textsuperscript{96} Post-test counseling provides information regarding partner notification. Patients can notify their partners themselves, or they can use a partner notification service.\textsuperscript{86} 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.\textsuperscript{96} 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.\textsuperscript{86}

Early diagnosis and treatment is imperative in helping prevent the spread of the infection to other individuals.\textsuperscript{83} 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. 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. The virus is able to quickly and efficiently replicate using the attributes of its own genetic makeup combined with those of the host cell. The human immune system is the ideal breeding ground for HIV and the viral load rapidly increases within the first few weeks of infection. Meanwhile, the healthy immune system becomes depleted as CD4 cells are destroyed during the replication process.
The Biology of HIV

HIV 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. There are proteins embedded within the viral envelope that came from the host cell, along with approximately 72 copies of a complex HIV protein. The HIV protein, which is called 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. The inside of the nucleoid contains Viral Genomic RNA and the associate enzyme called reverse transcriptase (RT). 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.

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**

HIV 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. The converted DNA is transported to the cell’s nucleus. From there, it is converted to human DNA by the HIV enzyme integrase. Once the integration is complete, the converted DNA becomes a provirus.

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. Once the cell is activated, it treats
the HIV genes as if they are human genes. The first stage of replication involves using human enzymes to convert the HIV genes into messenger RNA, which are removed from the nucleus. The messenger RNA is then used as a blueprint for the production of HIV proteins and enzymes.

The strands of messenger RNA contain complete copies of HIV genetic material. 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”. 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.

The mature viral cores are the result of a complete HIV lifecycle and are ready to begin the process with new CD4 cells. 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.

The National Institute of Health (NIH) Allergy and Infectious Diseases provides the following image of HIV viral replication, on page 54.
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. 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. 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.

**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.\(^9_8\)

**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.\(^8_2\) 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.\(^1_0_7\) However, since the body is still responding to the virus, antibodies might not yet be present.\(^4_0\)

**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.\(^8_2\) 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.\(^1_0_8\) Individuals who have not been tested for HIV will not be aware of their positive status while they are in this stage of infection.\(^4_0\) 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.\textsuperscript{55}

\textit{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.\textsuperscript{108} At this point in the illness, HIV has destroyed the immune system to a point that it is unable to fight off other infections.\textsuperscript{40} Patients in the symptomatic stage of infection will often present the following symptoms:\textsuperscript{36}

- 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.\textsuperscript{109} Patients can live for ten or more years with the virus without experiencing any symptoms.\textsuperscript{108} If a patient is not tested for HIV during the asymptomatic stage of infection, he or she will have no indication of the illness.\textsuperscript{40} 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.\textsuperscript{109} 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.\textsuperscript{109} HIV is managed well with antiretroviral treatment and patient care.\textsuperscript{37} This is difficult in patients that are unaware of their status.
AIDS

AIDS 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.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.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.36

Patients who receive adequate care during this stage have an increased likelihood of living longer than those that do not receive adequate care.113 The typical life expectancy of an individual with AIDS is 10 – 12 months.112 However, some patients can live four or more years with AIDS if the disease is managed properly.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.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.114 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
In later stages of infection, the CDC does incorporate documentation of AIDS-defining conditions as additional criteria. 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.

**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:¹¹⁶

**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 chelitis
- 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, bacteraemia)
- Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis
- Unexplained anemia (<8 g/dl), neutropaenia (<0.5 x 10^9 /L) and or chronic thrombocytopenia
- (<50 X 10^9 /L3)

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 septicaemia (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

Treatment

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. In recent years, advanced treatment options have made HIV easier to manage and have helped slow the progression of infection to a point that allows patients to remain symptom free for 10 – 20 years.

Although HIV is now a manageable disease that can remain symptom free for extended periods of time, the number of individuals who
remain untreated is concerning. Proper management of HIV is essential to preventing transmission and progression. Therefore, providers must work closely with patients to ensure proper diagnosis and treatment of the infection. Currently, only 69% of HIV positive individuals in the United States have used antiretroviral therapy to manage the infection. Of those who have used antiretroviral therapy, approximately 41% have discontinued use of their drug therapy. Only approximately 28% of patients have been able to reduce viral load and suppress the virus almost completely because of compliance with treatment plans and continuation of regular disease monitoring. It is apparent that more must be done to encourage patients to undergo regular testing and to consider antiretroviral therapy as part of their treatment plan. Appropriate clinical care and antiretroviral therapy are successful in slowing the progression of the infection, and the absence of such care can have significant consequences on the patient.

Unfortunately, due to a variety of factors, many patients are unlikely to undergo regular treatment and disease monitoring. With the development of a series of guidelines specific to HIV care and management, the onus is on the provider to encourage patients to start, and continue, appropriate treatment for HIV. Providers must be aware of the special considerations and factors that may prevent patients from undergoing regular care so that they can find ways to encourage patient participation.

Providers must work with patients to develop a treatment plan that works for the individual patient. During initial meetings with the patient, the provider must assess the patient’s specific needs and
develop a plan that will slow the progression of the infection and enable the patient to remain comfortable. Treatment options and interventions will depend on the stage of infection, the patient’s status and willingness to adhere to treatment, the presence of other conditions, and any factors that will impact treatment. Proper screening of the patient will help determine these factors and will enable the provider to develop an appropriate treatment plan.

Treatment of HIV patients is often administered by the patient’s primary care provider; however, a range of services must be made available to the patient to ensure proper care. Treatment plans typically include four distinct components of medical care, psychological care, social service needs and legal assistance, as discussed below:

**Medical care**
Patients require regular medical care to ensure that the disease is properly managed. Typical medical care includes regular monitoring of viral load and CD4 cell count, antiretroviral therapy, and symptom management.

**Psychological care**
HIV positive patients often require assistance coping with the psychological effects of being HIV positive. Therefore, psychological services are often a necessary component of a treatment plan. In addition, many HIV positive individuals have substance abuse issues or other mental health conditions. Part of the treatment plan should focus on these issues.
Social service needs
HIV care and management must be administered in conjunction with any necessary social service programs. These can include housing services, public assistance, and domestic violence services.¹²²

Legal assistance
HIV positive patients may require assistance navigating the legal system if faced with discriminatory practices due to the patient’s positive status. Assistance with legal issues may be required as part of the patient’s plan.¹²¹

New Patient Screening
HIV is diagnosed at various stages of disease progression. Providers must be familiar with the different stages of HIV infection to adequately diagnose, evaluate and treat patients at all stages. Proper management and treatment of the disease relies on the provider’s ability to assess the patients condition at the time of diagnosis and thereafter.¹²⁰ Through an initial assessment, a comprehensive baseline is developed for the patient, which will be used to monitor disease progress at subsequent visits.¹²⁴

The initial assessment is used to determine the stage of infection and to inform decisions regarding treatment. Patient education is also part of the new patient screening process.¹²¹ Providers can use this period to establish a relationship with the patient and help with the transition process.

As mentioned earlier, the early detection and diagnosis of HIV is imperative to the development of a safe and appropriate treatment
plan. Once a patient is diagnosed, a plan can be developed and treatment can begin immediately. When a patient is unaware of his or her status, treatment is not provided and the disease will progress quickly.

Once an individual is diagnosed with HIV, thorough screening can help determine the level of infection and the progression of the illness. This information can be used to develop a treatment plan that will minimize the impact of the illness and slow progression. The primary consideration is maintaining the integrity of the immune system so that it is not destroyed by the infection. A strong immune system will not eliminate HIV, but it will prevent the disease from progressing and will reduce the chances of the patient developing opportunistic infections.

Patients may be resistant to providing the information necessary to establish a comprehensive history and baseline. It is necessary for the provider to stress the importance of such information in the development of a patient treatment plan. Patients should be reassured that the information is confidential and that the provider is working alongside the patient to properly manage the disease. Issues with language barriers must be addressed and appropriate services should be utilized to ensure proper communication. It may take a few visits to gather all of the information necessary to develop a comprehensive patient history and establish a baseline. During visits, providers should encourage patients to be involved in the process and should provide opportunities for patients to express concerns about the process. Once a patient begins to feel comfortable with a provider, he or she will often be more receptive to the process.
Providers should refrain from using language that implies judgment about the patient’s past or current activities and lifestyle choices. Many of the topics surrounding the patient’s history are considered sensitive, and patients who feel as though their choices are unacceptable will not be willing to discuss them.\textsuperscript{25} It is important to obtain information about sexual activities and drug use early in the assessment process, and patients will be more comfortable discussing these topics with a provider if judgmental language is not used.\textsuperscript{120}

Proper communication between the provider and the patient is essential to establishing a patient-provider relationship. Due to the need for constant monitoring and changing treatment plans, patients need to feel confident in their provider.\textsuperscript{37} Often, the provider will make recommendations for the patient that go against the patient’s desires. If a solid relation has been established, the patient will be more receptive to the provider’s recommendations. This will make adherence to treatment more likely.\textsuperscript{25}

According to the New York State Department of Health guidelines for primary care of HIV infected individuals, the initial assessment of a newly diagnosed HIV patient should include the following components:\textsuperscript{125}

1. General history
   - Past hospitalizations, past and current illnesses
   - Current prescription and non-prescription medicines
   - Vaccination history
   - Reproductive history
   - Partner information for disclosure of human immunodeficiency virus (HIV) status
• Occupational history
• Allergies
• HIV treatment and staging including:
  – HIV exposure history
  – Most recent viral load and CD4 count
  – Current and previous antiretroviral (ARV) regimens
  – Previous adverse ARV drug reactions
• Opportunistic infections
2. Mental health and substance use history
3. Sexual history
4. Psychosocial history
5. Review of systems
6. Comprehensive physical examination:
  • Vital signs and pain assessment
  • Ophthalmologic assessment and referral
  • Head, ears, nose, and throat examination
  • Oral examination
  • Dermatologic examination
  • Lymph node examination
  • Endocrinologic examination
  • Pulmonary and cardiac examination
  • Abdominal examination
  • Genital examination
  • Rectal examination
  • Musculoskeletal examination
  • Neuropsychological examination
7. Laboratory assessment and diagnostic testing:
  • Immunologic assessment
  • Virologic assessment
• Tuberculosis evaluation
• Screening for sexually transmitted infections
• Cytologic screening
• Hematologic assessment
• Renal and hepatic assessment
• Metabolic assessment

8. Management/Counseling

9. Behavioral health counseling and health promotion:
   • Safer sex education
   • Substance use assessment and counseling
   • Smoking cessation education
   • Reproductive counseling
   • Domestic violence screening
   • Psychosocial assessment
   • Diet and exercise counseling

10. Coordination of care using case management

11. Appropriate use of acute and chronic care services

12. Prevention

13. Standard health maintenance interventions, such as
   mammogram, prostate specific antigen (PSA), colorectal cancer screen

14. Opportunistic infection prophylaxis
   (trimethoprim/sulfamethoxazole, azithromycin, clarithromycin)

15. Immunizations

Initial assessment is used to establish a baseline and to inform decisions regarding patient care and immediate treatment needs. Providers should conduct assessments every four months to monitor
the progress of the disease and make determinations regarding treatment.\textsuperscript{124}

During the initial assessment, a series of laboratory tests will be administered to establish a baseline for the patient. These tests will need to be repeated on an ongoing basis to monitor patient progress.\textsuperscript{124} The following table, provided by the U.S. Department of Health and Human Services (revised 10/2008), provides information regarding the different tests and the schedule a provider should follow:

<table>
<thead>
<tr>
<th>Laboratory Testing in HIV Primary Care</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test</td>
</tr>
<tr>
<td>Confirmed Positive HIV Status</td>
</tr>
<tr>
<td>Standard HIV serologic test</td>
</tr>
<tr>
<td>HIV Staging</td>
</tr>
<tr>
<td>CBC</td>
</tr>
<tr>
<td>CD4 count</td>
</tr>
<tr>
<td>HIV viral load</td>
</tr>
<tr>
<td>Health Status Evaluation</td>
</tr>
<tr>
<td>Chemistry panel</td>
</tr>
<tr>
<td>Pap smear</td>
</tr>
<tr>
<td>PPD</td>
</tr>
</tbody>
</table>
### Hepatitis screen

<table>
<thead>
<tr>
<th>Test</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>HAV</td>
<td>Optional</td>
</tr>
<tr>
<td>HBsAg</td>
<td>Test if abnormal liver function tests</td>
</tr>
<tr>
<td>anti-HBc or anti-HBs</td>
<td>Yes</td>
</tr>
<tr>
<td>HCV</td>
<td>Yes</td>
</tr>
</tbody>
</table>

### STDs

<table>
<thead>
<tr>
<th>Test</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>VDRL or RPR</td>
<td>Yes</td>
</tr>
<tr>
<td>Urine nucleic acid amplification test (NAAT) for N. gonorrhoeae and C. trachomatis</td>
<td>Consider for sexually active patients</td>
</tr>
<tr>
<td></td>
<td>Consider annual testing or more frequently if at high risk</td>
</tr>
<tr>
<td></td>
<td>First-catch urine or urethral (male)/cervical (female) specimen</td>
</tr>
<tr>
<td>Chest x-ray</td>
<td>Optional</td>
</tr>
<tr>
<td>Toxoplasma gondii IgG</td>
<td>Yes</td>
</tr>
</tbody>
</table>

### Baseline for HAART

<table>
<thead>
<tr>
<th>Test</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting glucose</td>
<td>Yes</td>
</tr>
<tr>
<td>Fasting lipids</td>
<td>Yes</td>
</tr>
</tbody>
</table>

---

**U.S. Department of Health and Human Services**

During the initial assessment, providers will utilize data regarding CD4 count and viral load to make determinations regarding antiretroviral therapy. Providers who are not familiar with antiretroviral therapy recommendations are advised to consult a colleague who can inform the decision.

When a patient transitions from one provider to another, the new provider should attempt to obtain all health records from the previous provider. These records will provide accurate information regarding HIV treatment history and past patient care. If no records are
available, the provider will have conduct a new patient assessment using the guidelines listed above.\textsuperscript{124}

**Patient Education**

A key component of patient care involves education. Informed patients often make better choices about treatment and disease management.\textsuperscript{124} In addition, proper education provides opportunities to reduce the spread of HIV to others.\textsuperscript{48} Providers should incorporate brief education sessions into each appointment. Since patients need a broad understanding of the scope and impact of the illness, ongoing education is imperative.\textsuperscript{25} The Health Resources and Services Administration provides the following topical guidelines for patient education:

- What is HIV?
- How is HIV transmitted?
- Progression of HIV; prognosis
- Interpretation of laboratory results
- Treatment information
  - Indications for treatment, goals of treatment
  - General information regarding the benefits of treatment
  - General information regarding potential side effects and risks of treatment
  - Access to medication
  - Insurance information
- Treatment options
- Prevention for positives
- Support services and support groups available to the patient

U.S. Health Resources and Services Administration.  
*Guide to Primary Care of People with HIV/AIDS*\textsuperscript{126}
The above topics are discussed during the initial assessment of a patient. However, more in-depth information should be given at subsequent appointments. Some clinics choose to appoint a patient educator who will work alongside the provider to provide ongoing education to the patient. However, in many instances, the education is provided directly by the provider. This can further enhance and strengthen the patient-provider relationship. It is imperative that the education be tailored to the specific needs of the patient and delivered in a format that is easily understandable by the patient. As patients are typically unfamiliar with technical medical language, it is best to deliver the information using words that are easily understood by the general population. In addition to information that is delivered during the visit, providers can recommend various online educational resources to their patients. This will encourage patients to take further responsibility for their own care and education. Patients should be encouraged to ask questions freely and request additional information on any of the topics covered during the education sessions.

**Long Term Care**

Patients will often participate in an initial appointment with a provider, but will fail to attend further sessions. Although the initial assessment is important, continual care and monitoring is crucial to the management of the infection. Providers must establish a system to ensure proper follow up with patients and encourage attendance at all appointments. Patients must be engaged in their care or they will be less likely to continue with treatment.

Long-term care consists of regular medical visits, ongoing laboratory testing to monitor disease progression, patient education and support,
referral services, and treatment of secondary infections. Typically, long-term care is managed by a variety of providers and may be coordinated by a case manager. Proper disease management is critical to slowing the progression of the virus and reducing complications and must include the components mentioned above.

The World Health Organization recommends the following treatment schedule, which follows the new definitions of clinical HIV established in 2007:

**Clinical Stage Management**

Stage 1:
- Patients are followed up every 3-6 months
- Check for clinical signs of progression
- Informed of the clinical signs of progression that would alert them to go back to their medical doctor:
  - enlargement of lymph glands
  - fever lasting more than 2 weeks
  - weight loss
  - diarrhea for more than 2 weeks
  - cough lasting more than 3 weeks or shortness of breath
  - persistent headache
- Total lymphocyte count or CD4 cell count if available
- Diagnosis and treatment of sexually transmitted infections STIs
- Counsel on safer sexual practices and contraception

Stage 2:
- Patients are followed up every 3-6 months
• Check for any symptom of disease progression (stage III symptoms)
  – fever lasting more than 2 weeks
  – weight loss >10% of body weight
  – diarrhea lasting of more than 2 weeks
  – oral thrush
  – persistent headache
  – persistent cough
  – mucocutaneous manifestations (seborrheic dermatitis, prurigo, recurrent oral ulceration)

• Symptom directed laboratory evaluation (if available)
  – Full blood count
  – ALT
  – Sputum smear for TB when productive cough
  – Total lymphocyte count or CD4 cell count

• Follow up STI management counseling as for stage 1 patients

• Cotrimoxazole prophylaxis
  – Start prophylaxis in all patients with WHO stage 2, 3 and 4 disease

• If CD4 testing is available, start cotrimoxazole prophylaxis in patients with:
  – Any WHO clinical stage and CD4 < 200 cells/mm3 where the aim of cotrimoxazole prophylaxis is the prevention of PCP and toxoplasmosis.
  – Any WHO clinical stage CD4< 350 cells/mm3 where the aim of cotrimoxazole prophylaxis is the reduction of morbidity and mortality associated with malaria, bacterial diarrheal disease and bacterial pneumonias in addition to the prevention of PCP and toxoplasmosis
Dose - One double strength cotrimoxazole tablet or two single strength tablets once daily; Total daily dose is 960 mg (800 mg SMZ + 160 mg TMP)

Stage III and IV:

- Frequency of follow up depends on the patient’s individual condition.
- Frequent visits are recommended at initiation of ART (1-2 weekly) then 1-3 monthly once the patient is stable on ART. The main objectives of examinations are to detect signs and symptoms of Immune Inflammatory
- Reconstitution Syndrome (IRIS) and OIs including pulmonary or extra pulmonary tuberculosis.
- Symptom directed laboratory evaluation (if available)
  - Full blood count
  - ALT
  - Sputum smear for TB when productive cough
  - Total lymphocyte count or CD4 cell count
- Start opportunistic infections (OI) prophylaxis
- Start cotrimoxazole (sulfamethoxazole 800 mg and trimethoprim 160 mg) P0 daily if symptom of stage III or stage IV

**Immunizations**

As part of a patients long-term care plan, regular immunizations against other infections are necessary. Since HIV damages the immune system, these immunizations help prevent the patients from becoming infected with a secondary infection, which could impact progression of the disease. The following immunizations are recommended by the U.S. Department of Health and Human Services,
Guide to Primary Care of People with HIV/AIDS, for HIV positive adults and adolescents:\textsuperscript{126}

Pneumococcal (polysaccharide):
- Recommended for all; consider revaccination 5 years after initial vaccination; some experts recommend vaccination every 5 years.
- If CD4 count is <200 cells/µL, may be less effective; consider revaccination when CD4 count increases in response to ART.

Hepatitis A Virus (HAV):
- Recommended, for persons with chronic liver disease, injection drug users, men who have sex with men, international travelers, and hemophiliacs. Consider for all, unless there is serologic evidence of previous disease.
- Serologic response (HAV IgG Ab) should be checked 1 month after completion of series, and nonresponders should be revaccinated.
- Two doses (0, 6-12 months).

Hepatitis B Virus (HBV):
- Recommended for all, unless there is evidence of immunity (HBV surface Ab+) or active HBV infection (HBV surface Ag+, or HBV core Ab+ and evidence of HBV activity).
- Many experts recommend giving a high dose of HBV vaccine (40 mcg), as is standard for hemodialysis patients; this may improve immunologic response in HIV-infected patients.
• Most HIV-infected patients with isolated HBV core Ab+ (without HBV viremia) are not immune and should receive a complete series of HBV vaccine.

• Anti-HBV surface Ab titers should be checked 1 month after completion of vaccine series. Patients whose titer level is ≤10 IU/mL should be revaccinated.

• Standard dosing schedule is three doses (0, 1, and 6 months). If 40 mcg is given, the recommended schedule is three doses of Recombivax HB at 0, 1, and 6 months or four doses of Engerix-B at 0, 1, 2, and 6 months.

Influenza (inactivated vaccine):

• Recommended (yearly).

• Vaccination is most effective among persons with CD4 counts of >100 cells/µL and HIV RNA of <30,000 copies/mL.

• In patients with advanced disease and low CD4 cell counts, inactivated vaccine may not produce protective antibodies. A second dose of vaccine does not improve response in these patients.

• Live, attenuated cold-adapted vaccine (LAIV, FluMist) is contraindicated for use in patients with HIV infection.

• Close contacts of severely immunocompromised persons (including household members and health care personnel) should not receive live, attenuated influenza vaccine.

H1N1 Influenza (inactivated vaccine):

• Recommended (inactivated vaccine), though not thoroughly studied in HIV-infected persons (see Centers for Disease Control
and Prevention (CDC) guidelines for up-to-date recommendations).

- The live, attenuated nasal vaccine is not recommended.

Tetanus, Diphtheria (Td), Tetanus, Diphtheria, Pertussis (Tdap):
- Recommended (booster is recommended every 10 years in adults; or, if potential exposure [wound], after 5 years).
- To protect against pertussis, substitute single dose of Tdap for Td booster in all patients aged 19-65 who have not received Tdap previously.

Measles, Mumps, Rubella (MMR):
- Live vaccine is contraindicated for use in patients with severe immunosuppression (CD4 count of <200 cells/µL).
- Recommended for all nonimmune persons with CD4 counts ≥200 cells/µL.

Varicella-Zoster (VZV):
- Live vaccine is contraindicated for use in patients with severe immunosuppression (CD4 count of <200 cells/µL).
- Consider for HIV-infected, VZV-seronegative persons with CD4 counts ≥200 cells/µL.
- If vaccination results in infection with attenuated virus, treat with acyclovir.
- Susceptible household contacts of susceptible HIV-infected individuals should be vaccinated.
- Avoid exposure to VZV, if possible. If someone without immunity to VZV is exposed to VZV, administer varicella-zoster immune globulin (VZIG) as soon as possible (but within 96 hours).
• Two doses (0, 3 months).

Human Papillomavirus (HPV):
• Two vaccines:
  – Gardisil includes HPV strains 16 and 18 (oncogenic) and 6 and 11 (wart causing)
  – Cervarix: includes HPV strains 16 and 18
• Recommended for females aged 9-26.
• Gardasil vaccine approved for males aged 9-26.
• Not contraindicated for use in HIV-infected individuals, though no data are available regarding use in this group.
• No data on efficacy in preventing anal dysplasia.

Meningococcal:
• Recommended if risk factor is present (i.e., college freshmen living in dormitory, military recruits, asplenia, complement component deficiency, travel to or residence in endemic area, occupational exposure).

Vaccinations rely on humoral response to work effectively. In patients who have a CD4 cell count below 200, the humoral response rate may be negatively impacted. Therefore, HRSA recommends all vaccinations be given prior to the CD4 cell count dropping below 200. In individuals with a CD4 count below 200, there is a chance that the vaccine will not work properly.

**Antiretroviral Therapy**
Early antiretroviral therapy (ART) focused on the use of a singular drug to treat the virus. Patients were prescribed a specific antiretroviral
drug, most commonly zidovudine or azidothymidine (AZT), and it was used as the only treatment.119 While AZT was successful at suppressing the virus initially, patients developed resistance over time and the drug was unable to maintain initial levels of suppression.128 Eventually, treatment evolved to incorporate the use of dual drugs to combat infection.120 The goal was to prevent HIV from developing resistance by attacking the virus with more than one drug.120

Early dual combination therapy proved more effective in virus suppression as it utilized a combination of two different types of antiretroviral, each of which targeted a different part of the virus.129 As the virus progressed, patients developed higher resistance to even the dual-drug therapy and a stronger approach was necessary.130 To address the issue of drug resistance, antiretroviral therapy evolved to include treatment with numerous antiretrovirals at once. Highly active antiretroviral treatment (HAART), also known as “cocktail” therapy, relies on a multi-drug approach to viral suppression.131 The combination of specific antiretrovirals from different categories enables practitioners to create a highly effective treatment plan for patients that attacks the virus quickly and maintains suppression for a longer duration.132

HAART has been proven to reduce HIV-associated morbidity and prolong survival, restore immune function, suppress HIV viral load, and prevent HIV transmission.129 Patients have shown improvements in immune function and a reduction of viral load within 12 – 24 weeks of starting HAART.133 Patient adherence is critical to the success of HAART. The success rate of therapy is significantly reduced when patients take less than 95% of their doses.129 Approximately 55% of
patients who take less than 95% of their doses will see no impact on viral load suppression. Incomplete adherence to HAART can result in drug resistance among patients as the virus mutates. While previous HAART required patients to take multiple pills at numerous times throughout the day, current combinations and increased potency of the drugs now allow for once-daily dosing, which makes adherence easier for the patient.

HAART is defined by treatment with minimum of three different antiretrovirals at the same time. However, current recommendations favor the use of more than three agents. HAART uses drugs from at least two classes. Typical combinations include two nucleoside or nucleotide reverse transcriptase inhibitors (NRTIs/NtRTIs) plus either a non-nucleoside reverse transcriptase inhibitor (NNRTI) or a boosted protease inhibitor. In special cases, different combinations will be used, especially if the patient requires a more potent combination. In some circumstances, a patient may require a less potent combination, which could also result in the use of a different combination. The provider must assess the patient’s situation and needs individually and develop a treatment plan that will work best for the patient’s specific needs.

Antiretroviral therapy (ART) is extremely effective in the management of HIV and is recommended for all patients to minimize disease progression. Once ART began to be utilized, as treatment against HIV, there was 60%-80% decrease in mortality, AIDS rates, and hospitalizations for HIV-associated complications. Therefore, the CDC recommends that all patients begin ART as soon as they test positive for HIV. Without antiretroviral therapy patients are at risk
of increased disease progression and early onset of opportunistic infections. The primary goal of ART is to suppress viral load so that it does not further destroy the immune system, thereby reducing the probability of HIV-associated morbidity and mortality. Viral load suppression also helps prevent the spread of infection to others as high viral load increases the chance of transmitting HIV to others.

Previously, antiretroviral therapy was recommended for patients with low CD4 cell counts. In patients with high CD4 counts and minimal symptoms, antiretroviral therapy was postponed. However, in recent years, recommendations have changed to include all patients who present with a positive status. The goal of these new recommendations is to prevent the progression of HIV to the symptomatic stage and to minimize further complications in the patient. Research shows that patients who do not begin antiretroviral therapy during one of the early stages of infection are at increased risk to develop non-AIDS related infections. Patients who do not receive therapy have a higher prevalence of kidney disease, cardiovascular disease (CVD), neurologic complications, liver disease, and malignancies.

While ART is recommended in all patients, it is something that should be discussed and decided on an individual basis. Some patients may not be receptive to ART and may fear reliance on multi-drug therapy. Providers should work with patients to allay fears and provide thorough education regarding ART. Patients should be encouraged to conduct their own research and work with the provider to develop a treatment plan that is comfortable for the patient.
However, providers should encourage patients to begin ART as soon as they are comfortable to minimize disease progression.\textsuperscript{136}

Antiretroviral therapy is recommended for all patients, but it is still crucial for some patients depending on HIV stage and clinical condition. ART is a priority for the following populations:\textsuperscript{137}

- patients with the lowest CD4 counts
- patients with the following clinical conditions: pregnancy, CD4 count <200 cells/mm\textsuperscript{3}, or history of an AIDS-defining illness, including HIV-associated dementia, HIV-associated nephropathy (HIVAN), hepatitis B virus (HBV), and acute HIV infection

When making determinations regarding whether a patient should receive ART, providers should use CD4 cell count as a primary guideline. Patients with low CD4 counts are at risk of developing opportunistic infections and other complications.\textsuperscript{127} Therefore, ART is highly recommended to slow progression.

The U.S. Department of Health and Human Services, \textit{Guide to Primary Care of People with HIV/AIDS}, provides the following guidelines for the initiation of antiretroviral therapy:\textsuperscript{126}

\textbf{Recommendation (Strength of Recommendation)}

ART is recommended for all HIV-infected individuals. The strength of this recommendation varies on the basis of pre-treatment CD4 cell count:

- CD4 count <350 cells/mm\textsuperscript{3} (AI)
- CD4 count 350 to 500 cells/mm\textsuperscript{3} (AII)
- CD4 count >500 cells/mm\textsuperscript{3} (BIII)
Regardless of CD4 count, initiation of ART is strongly recommended for individuals with the following conditions:

- Pregnancy (AI)
- History of an AIDS-defining illness (AI)
- HIV-associated nephropathy (AII)
- HIV/hepatitis B virus coinfection (AII)

Effective ART also has been shown to prevent transmission of HIV from an infected individual to a sexual partner; therefore, ART should be offered to patients who are at risk of transmitting HIV to sexual partners (AI [heterosexuals] or AIII [other transmission risk groups]).

*Rating of Recommendations: A = strong; B = moderate; C = optional.*

*Rating of Evidence: I = data from randomized controlled trials; II = data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = expert opinion.*

An initial CD4 cell count is used to establish a baseline before beginning ART, and should be tested every three to six months once ART has begun to determine success of treatment. Viral load testing is the most common form of assessment used to measure effectiveness of ART.

There are three types of viral load testing available, and these are the:

- viral RNA quantification by the polymerase chain reaction (PCR)
- branched-chain DNA assays
- nucleic acid sequence–based amplification
Currently, the RNA PCR assay is the most widely used viral load test for monitoring the effectiveness of ART. However, it is not used for initial viral load screenings during diagnosis unless the patient is suspected of having acute HIV, as viral load is often not significant enough to detect during the early stages of infection.\textsuperscript{126}

**Types of Antiretroviral Therapy**

In 1986, the first drug to treat HIV was developed and tested.\textsuperscript{16} This drug, zidovudine (AZT), is a nucleoside that has proven to be effective against the infection.\textsuperscript{16} AZT suppresses HIV replication in patients by preventing the reverse transcriptase enzyme from functioning. Reverse transcriptase creates viral DNA strands that integrate themselves into host cells, thereby enabling HIV transcription of viral RNA.\textsuperscript{8} By 1996, two new types of antiretroviral drugs, protease inhibitors (PIs) and non-nucleoside reverse transcriptase inhibitors (NNRTIs), were developed and approved for use.\textsuperscript{16} The development of antiretroviral therapy enabled providers to effectively treat patients with HIV and slow the progression of the illness.\textsuperscript{113} As antiretroviral therapy has evolved, new classes have been added and various combinations have been used to manage infection in patients.

Antiretrovirals suppress HIV in two ways. They either prevent the virus from fusing with the cell, or they block enzymes that are responsible for the reproduction of HIV.\textsuperscript{119} Antiretroviral are organized into four main classifications based on how they work within the immune system. The four types of antiretrovirals are:\textsuperscript{127}

1. Nucleoside and nucleotide reverse transcriptase inhibitors (NRTIs/NtRTIs), also called nucleoside or nucleotide analogues
2. Non-nucleoside reverse transcriptase inhibitors (NNRTIs)
3. Protease inhibitors (PIs)
4. Integrase inhibitors

Recently, two new classes of antiretroviral drugs have been added. However, the number of available drugs in each of these classes is relatively low due to the fact that they were recently introduced. Treatment with these drugs is still being assessed.\textsuperscript{137} Despite regulatory approval in 2009, the newest classes of drugs are not yet recommended for first-line therapy.\textsuperscript{127} The two new classifications of antiretroviral therapy are:\textsuperscript{137}

1. Chemokine receptor antagonist (CCR5 antagonist)
2. Fusion inhibitor (FI)

An understanding of each category of antiretrovirals and how they work within the immune system is necessary to properly develop a treatment plan for an HIV positive patient. The patient’s CD4 count, presence of secondary infections, and individual status must be taken into consideration when identifying appropriate antiretrovirals and the combination that should be used for treatment.\textsuperscript{127}

\textbf{Nucleoside and nucleotide reverse transcriptase inhibitors (NRTIs/NtRTIs)}

Nucleoside reverse transcriptase inhibitors (NRTIs) and nucleotide reverse transcriptase inhibitors (NtRTIs) work so similarly within the body that they are grouped into one antiretroviral category.\textsuperscript{137} Once HIV enters a T-cell, it uses the reverse transcriptase enzyme to help convert the viral RNA into a complementary piece of DNA. Using a process called reverse transcription the virus releases its genetic material into the cell and begins the process of conversion.\textsuperscript{101}
Reverse transcriptase inhibitors work with each of the nucleoside building blocks that make up the viral RNA individually to prevent the virus from converting the RNA into DNA.\(^8\) Reverse transcriptase inhibitors use the nucleoside building blocks as templates to develop a complementary DNA chain. The chain uses nucleotide building blocks present in the cell. Reverse transcriptase inhibitors manipulate the chain by mimicking the nucleotides that are used to form the DNA. The reverse transcriptase inhibitor is then placed in the growing chain and halts growth.\(^{128}\)

**Non-nucleoside reverse transcriptase inhibitors (NNRTIs)**

Non-nucleoside Reverse Transcriptase Inhibitors (NNRTIs) prevent reverse transcription by directly interfering with the function of the reverse transcriptase enzyme.\(^{128}\) This is accomplished when NNRTI’s attach directly to the enzyme and block RNA-dependent and DNA-dependent DNA polymerase activities.\(^{132}\) This interference prevents enzymatic conversion of RNA into DNA. When conversion is prevented, HIV is unable to insert its genetic material into the cell, thereby stopping reproduction of the virus.\(^8\)

**Protease inhibitors (PIs)**

During the replication process, HIV relies on its own protease to cut up the HIV proteins that were created by the manipulated CD4 cell during the initial stage of replication.\(^{98}\) These pieces of HIV protein become new HIV cells.\(^{105}\) Protease inhibitors block the enzyme and prevent it from cutting up the long protein strands into new viral cells.\(^{136}\) Protease inhibitors are rarely used on their own as they work best in combination with another class of antiretroviral.\(^{127}\) This ensures a multi-faceted attack against HIV.
**Integrase inhibitors**

These newer antiretrovirals were approved for use in 2007 and only comprise a small percentage of the antiretroviral options available. Integrase inhibitors block the enzyme integrase during the replication process. Integrase is the viral enzyme that is responsible for inserting the viral genome into the DNA of the host cell. Integrase inhibitors interact with the viral enzyme, thereby preventing it from completing the insertion process. Integrase inhibitors work well in conjunction with other antiretrovirals and are often used to treat patients who have developed resistance to other antiretrovirals.

**Chemokine receptor antagonist (CCR5 antagonist)**

The first CCR5 antagonist was approved by the FDA in 2007 and is used as a new line of defense against viral replication. Chemokine receptors CCR5 and CXCR4 function as co-receptors during the cellular entry phase of HIV replication. Specifically, CCR5 serves an entry cofactor for the R5-isolates of HIV-1. Its role in this process is essential to the prolific spread of the infection. Chemokine receptor antagonists inhibit the ability of the HIV-1 envelope protein to latch onto the CCR5 receptor. This process prevents cellular fusion between the virus and the host cell.

**Fusion inhibitor (FI)**

Fusion inhibitors are relatively new antiretroviral agents that were introduced in 2003. There is currently only one fusion inhibitor approved for use in the treatment of HIV. Fusion inhibitors prevent the virus from fusing with the outer cell membrane of the healthy host cell. Once the virus is prevented from fusing with the cell membrane, it is unable to activate penetration and begin the
replication process. In essence, fusion inhibitors stop the process before it begins. Therefore, fusion inhibitors work well with other classes of antiretrovirals and are recommended for use in combination therapy.

**Treatment Recommendations and Guidelines**

Providers must work with patients individually to assess their needs and develop a treatment plan. The assessment must include a review of the patient’s medical history, laboratory results, co-factors and treatment goals. A thorough assessment is crucial in determining how and when to treat the patient with ART.

The U.S. Department of Health and Human Services provides the following “SOAP” guidelines for providers to follow when determining whether to use antiretroviral therapy:

**S: Subjective**

Obtain the patient's history and review of systems, including:

- CD4 cell count history, including nadir
- HIV RNA (viral load) history, including pretreatment values if the patient is currently taking ARVs
- History of HIV-related conditions
- Previous and current ARV regimens, including start and stop dates, regimen efficacy, toxicity, resistance
- Current medications, including herbal preparations, supplements, and over-the-counter medications
- Medication allergies, intolerances, or prominent adverse effects
- Comorbid conditions (e.g., HBV, HCV, depression)
- Current and previous substance use, including alcohol and recreational drugs
Self-assessment of adherence to previous regimens  
Desire to start or continue an ARV regimen  
Commitment to adherence (see chapter Adherence)  
Occupation and daily schedule  
Willingness and indicators of ability to adhere to various types of regimens (i.e., once daily, twice daily, with or without food) given current life situation  
For women of childbearing potential: last menstrual period, current method of birth control (if any), current pregnancy status, thoughts on whether or when to have children

**O: Objective**
Perform the following objective tests:
- Complete physical examination  
- Current CD4 count and HIV viral load: preferably two or more separate results approximately 1 month apart.  
- Drug resistance test, as appropriate; to look for transmitted ARV resistance mutations, a genotype should be performed for all patients before initiating ART; this should be done as early in the course of infection as possible, because mutations may revert to wild-type. Review the results of previous resistance testing or obtain a baseline resistance test, if this was not done earlier; if a test was done in the past, consider retesting before ART is begun (see chapter Resistance Testing). Patients with detectable viral loads on ART also should undergo resistance testing.  
- Complete blood count (CBC) and platelet count, liver function tests (LFTs), renal function tests, fasting lipid panel, fasting glucose, rapid plasma reagin (RPR), tuberculin skin test, hepatitis serologies, Toxoplasma IgG, urinalysis, (see chapter Initial and Interim Laboratory and Other Tests).

**A: Assessment**
Make the following basic decisions:
- The patient is or is not likely to benefit from ART at this time (i.e., do potential benefits outweigh the risks?).
• The patient is or is not willing to start ARVs at this time (the choice to accept or decline therapy ultimately lies with the patient). If not, work with the patient on readiness issues, with more urgency if the CD4 count is low or the patient has symptoms or comorbidities that suggest treatment is needed.

• The patient is or is not likely to adhere to an ARV regimen (an adherence counselor, with or without a mental health clinician, may be able to assist with this assessment and should be called upon if available). No patient should be automatically excluded from consideration for ART; the likelihood of adherence must be discussed and determined individually.

P: Plan

After educating the patient about the purpose and logistics of the proposed regimen and assessing the patient’s potential for adherence, ART can be initiated, changed, or postponed accordingly.

The reduction of HIV-related morbidity and mortality is the primary goal of antiretroviral therapy.6 This is achieved through viral suppression and improved immune function. Once the virus is suppressed, the focus moves to improving the patient’s quality of life and reducing the risk of viral transmission.126

The following Antiretroviral Therapy table provides dosing information for all approved antiretroviral drugs.138 Providers should use the following guidelines; and, guidelines should be followed in consultation with patients to develop an appropriate ART treatment plan.
<table>
<thead>
<tr>
<th>Name</th>
<th>Dosage Form(s)</th>
<th>Adult Dose</th>
<th>Adverse Events</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Nucleoside reverse transcriptase inhibitors (NRTIs)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abacavir (Ziagen)</td>
<td>300-mg tablet; 20-mg/mL oral solution</td>
<td>600 mg PO qd or 300 mg PO bid</td>
<td>Hypersensitivity reaction (may include fever, rash, nausea, vomiting, diarrhea, malaise, shortness of breath, cough, pharyngitis); patients positive for HLA-B*5701 are at highest risk for hypersensitivity (perform HLA screening before initiating)</td>
</tr>
<tr>
<td>Didanosine (Videx)</td>
<td>125-mg, 200-mg, 250-mg, 400-mg enteric-coated capsule; 10-mg/mL suspension</td>
<td>&gt;60 kg: 400 mg PO qd &lt; 60 kg: 250 mg PO qd Take 30 min ac or 2 hr pc Oral solution: Divide daily dose bid</td>
<td>Peripheral neuropathy, pancreatitis, nausea, lactic acidosis</td>
</tr>
<tr>
<td>Emtricitabine (Emtriva)</td>
<td>200-mg capsule; 10-mg/mL oral solution</td>
<td>200 mg PO qd or 240 mg (24 mL) oral solution PO qd</td>
<td>Minimal toxicity, hyperpigmentation</td>
</tr>
<tr>
<td>Lamivudine (Epivir)</td>
<td>150-mg, 300-mg tablet; 10-mg/mL oral solution</td>
<td>300 mg PO qd or 150 mg PO bid</td>
<td>Minimal toxicity, severe acute exacerbation of hepatitis may occur with HBV-coinfection upon discontinuation</td>
</tr>
<tr>
<td>Stavudine (Zerit)</td>
<td>15-mg, 20-mg, 30-mg, 40-mg capsule; 1-mg/mL oral solution</td>
<td>&gt;60 kg: 40 mg PO bid &lt; 60 kg: 30 mg PO bid</td>
<td>Peripheral neuropathy, pancreatitis, lactic acidosis, lipoatrophy, hyperlipidemia</td>
</tr>
<tr>
<td>Tenofovir (Viread)</td>
<td>300-mg tablet</td>
<td>300 mg PO qd</td>
<td>Nausea, vomiting, diarrhea, headache, asthenia, renal insufficiency</td>
</tr>
<tr>
<td>Drug</td>
<td>Formulations</td>
<td>Dosage</td>
<td>Side Effects</td>
</tr>
<tr>
<td>-------------------------------------------</td>
<td>------------------------------------------------------------------------------</td>
<td>----------------------------------------------------------------------</td>
<td>-------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Zalcitabine (Hivid)</td>
<td>0.375-mg, 0.75-mg table</td>
<td>0.75 mg PO tid</td>
<td>Peripheral neuropathy, pancreatitis, lactic acidosis, stomatitis</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zidovudine (Retrovir)</td>
<td>300-mg tablet; 100-mg capsule; 10-mg/mL oral solution; 10-mg/mL intravenous solution</td>
<td>300 mg PO bid or 200 mg PO tid</td>
<td>Nausea, vomiting, headache, asthenia, anemia, neutropenia</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Nonnucleoside reverse transcriptase inhibitors (NNRTIs)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Delavirdine (Rescriptor)</td>
<td>100-mg, 200-mg tablets</td>
<td>400 mg PO tid</td>
<td>Rash, headache</td>
</tr>
<tr>
<td>Efavirenz (Sustiva)</td>
<td>600-mg tablet; 50-mg, 200-mg capsule</td>
<td>600 mg PO qd</td>
<td>Rash, CNS (eg, somnolence, vivid dreams, confusion, visual hallucinations), hyperlipidemia</td>
</tr>
<tr>
<td>Etravirine (Intelence)</td>
<td>100-mg, 200-mg tablets</td>
<td>200 mg PO bid</td>
<td>Rash, nausea</td>
</tr>
<tr>
<td>Nevirapine (Viramune, Viramune XR)</td>
<td>200-mg tablet; 400 mg XR tablet; 10-mg/mL suspension</td>
<td>200 mg PO bid(^{a})</td>
<td>Rash, hepatitis</td>
</tr>
<tr>
<td>Rilpivirine (Edurant)</td>
<td>25-mg tablet</td>
<td>25 mg PO qd with a meal</td>
<td>Depressive disorders, insomnia, headache, rash</td>
</tr>
<tr>
<td><strong>Protease inhibitors (PIs)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atazanavir (Reyataz)</td>
<td>100-mg, 150-mg, 200-mg, 300-mg capsules</td>
<td>400 mg PO qd or 300 mg + ritonavir 100 mg PO qd</td>
<td>Indirect hyperbilirubinemia, prolonged PR interval, hyperglycemia, skin rash (20%), hyperlipidemia</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Darunavir (Prezista)</td>
<td>75-mg, 150-mg, 300-mg, 400-mg, 600-mg tablets</td>
<td>800 mg qd + ritonavir 100 mg PO qd(^{b}) or 600 mg bid + ritonavir 100 mg PO bid</td>
<td>Rash, nausea, diarrhea, hyperlipidemia, hyperglycemia</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fosamprenavir</td>
<td>700-mg tablet; 700 mg bid + ritonavir 100 mg PO</td>
<td></td>
<td>Rash, nausea, vomiting, diarrhea, hyperlipidemia,</td>
</tr>
<tr>
<td>Drug Name</td>
<td>Description</td>
<td>Dosage</td>
<td>Administration</td>
</tr>
<tr>
<td>-----------</td>
<td>-------------</td>
<td>--------</td>
<td>----------------</td>
</tr>
<tr>
<td>(Lexiva)</td>
<td>50-mg/mL oral suspension</td>
<td>bid or 1400 mg PO bid or 1400 mg + ritonavir 100-200 mg PO qd&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Suspension: Take without food Boosted with RTV: Take with food</td>
</tr>
<tr>
<td>Indinavir (Crixivan)</td>
<td>100-mg, 200-mg, 400-mg capsules</td>
<td>800 mg PO q8h 800 mg PO bid + ritonavir 100-200 mg PO bid</td>
<td>Take 1 h ac or 2 h pc; may take with skim milk or low-fat meal</td>
</tr>
<tr>
<td>Lopinavir/ritonavir (Kaletra)</td>
<td>100-mg/25-mg, 200-mg/50-mg tablets; 80-mg/20-mg per mL oral solution</td>
<td>400 mg/100 mg PO bid or 800 mg/200 mg PO qd&lt;sup&gt;b&lt;/sup&gt; Oral solution: Take with meals</td>
<td></td>
</tr>
<tr>
<td>Nelfinavir (Viracept)</td>
<td>250-mg, 625-mg tablets, 50 mg/g oral powder</td>
<td>1250 mg PO bid or 750 mg PO tid (Nelfinavir cannot be boosted) Take with food</td>
<td></td>
</tr>
<tr>
<td>Ritonavir (Norvir)</td>
<td>100-mg tablet; 100-mg soft gelatin capsule; 80-mg/mL oral solution</td>
<td>Boosting dose for other protease inhibitors: 100-400 mg/d (refer to other protease inhibitors for specific dose) Nonboosting dose (Ritonavir used as sole protease inhibitor): 600 mg bid</td>
<td></td>
</tr>
<tr>
<td>Drug Name</td>
<td>Formulation</td>
<td>Dosing Information</td>
<td>Adverse Effects</td>
</tr>
<tr>
<td>---------------------------</td>
<td>--------------------------------------</td>
<td>----------------------------------------------------------</td>
<td>---------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Saquinavir (Invirase)</td>
<td>500-mg tablet; 200-mg hard gelatin capsule</td>
<td>1000 mg + ritonavir 100 mg PO bid</td>
<td>Nausea, diarrhea, headache, hyperlipidemia, hyperglycemia, PR and QT interval prolongation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unboosted saquinavir is not recommended</td>
<td>Take with food, or within 2 h pc</td>
</tr>
<tr>
<td>Tipranavir (Aptivus)(d)</td>
<td>250-mg soft gelatin capsule 100-mg/mL oral solution</td>
<td>500 mg + ritonavir 200 mg PO bid</td>
<td>Hepatotoxicity, rash, hyperlipidemia, hyperglycemia, intracranial hemorrhage (rare cases reported)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unboosted tipranavir is not recommended</td>
<td></td>
</tr>
<tr>
<td>Raltegravir (Isentress)</td>
<td>400-mg tablet</td>
<td>400 mg PO bid</td>
<td>Nausea, diarrhea, headache, CK elevations, myopathy/rhabdomyolysis (rare)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>With rifampin: 800 mg PO bid</td>
<td></td>
</tr>
<tr>
<td>Maraviroc (Selzentry)</td>
<td>150-mg, 300-mg tablets</td>
<td>300 mg PO bid</td>
<td>Constipation, dizziness, infection, rash</td>
</tr>
<tr>
<td></td>
<td></td>
<td>150 mg PO bid (CYP3A4 inhibitors ± inducers)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>600 mg PO bid (CYP3A4 inducers)</td>
<td></td>
</tr>
<tr>
<td>Enfuvirtide (Fuzeon)(d)</td>
<td>90-mg/mL powder for injection</td>
<td>90 mg SC bid</td>
<td>Injection-site reactions (eg, pain, erythema, induration, nodules)</td>
</tr>
<tr>
<td>Integrase inhibitor (II)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chemokine receptor antagonist (CCR5 antagonist)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trizivir</td>
<td>Abacavir (300 mg) + lamivudine (150 mg) + zidovudine (300 mg) bid</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atripla</td>
<td>Tenofovir (300 mg) + emtricitabine (200 mg) + efavirenz (600 mg) qd</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complera</td>
<td>Tenofovir (300 mg) + emtricitabine (200 mg) + rilpivirine (25 mg) qd</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Combivir - Zidovudine (300 mg) + lamivudine (150 mg) bid

* Dosing guides assume an absence of drug-drug interactions (except ritonavir) and normal renal and hepatic function:
  - Administer 200 mg qd for 2 weeks, then increase to 200 mg bid.
  - Approved only for antiretroviral treatment–naïve patients (or with darunavir, treatment-experienced patients without darunavir-resistant mutations).
  - Titrate dose over 14 days, beginning with 300 mg bid on days 1-2, 400 mg bid on days 3-5, and 500 mg bid on days 6-13.
  - Approved only for antiretroviral treatment–experienced patients with drug resistance.
  - CYP3A4 inhibitor; enhances the systemic exposure of CYP3A substrates, such as elvitegravir, where bioavailability is limited and half-life is shortened by CYP3A-dependent metabolism.

Combined therapy recommendations
Choosing the appropriate combination therapy for patients requires a complete assessment of the patient’s needs, including secondary conditions and other health factors. Providers must work with each patient individually to determine what combination of drugs will work best for the patient’s specific needs. While combination therapy typically includes drugs from at least three different classes, it is up to the provider to determine which drugs and which classes. Familiarity with the different drugs and their potential adverse affects is crucial for providers to adequately address the medical needs of their patients. Since antiretrovirals interact differently with each other, it is important to understand the ways in which specific combinations of drugs will work within the patient’s system. It is also important to understand the potential adverse affects that can occur from specific combinations of antiretrovirals.

There are numerous antiretrovirals within each class, with the exception of CCR5 antagonists, protease inhibitors and fusion
inhibitors. Therefore, providers have options for combination therapies. Regular monitoring of the patient and viral load is necessary to ensure drug effectiveness and compliance. If a specific combination does not prove effective, the provider can prescribe a new combination in an attempt to adequately treat the patient.

During the treatment selection phase, providers take the following factors into consideration when making a decision as to how to treat the patient:

- The stage of HIV infection
- Laboratory results from recommended tests, including drug-resistance testing
- How the medications will interact with other medications the patient is taking
- Potential adverse affects of the antiretrovirals
- The patient’s ability to adhere to the regimen
  - Convenience of the regimen – how often and how many pills the patient must take each day
  - Underlying issues that may make adherence difficult – depression, alcohol and substance abuse, other mental health issues, living situation, etc.

In addition to assessing the factors above, providers should look at the potential side effects of the specific combinations being considered, as well as the efficacy of each combination. Some combinations are more effective against viral replication and are specifically recommended for use in patients who have progressed to the symptomatic stage of infection. Other combinations provide better defense in the early stages of disease progression and help reduce the
replication rate to a level that almost completely suppresses the virus. As patients progress through the stages of infection, their specific treatment needs will change and providers must work to develop new antiretroviral strategies that will be effective in slowing and suppressing viral progression.

In patients who have not previously taken antiretrovirals, the WHO recommends the following combinations:

- Zidovudine (INN) or azidothymidine + lamivudine or epivir + Efavirenz
- Zidovudine (INN) or azidothymidine + lamivudine or epivir + nevirapine
- Tenofovir Disoproxil Fumarate + lamivudine or epivir OR Emtricitabine + Efavirenz
- Tenofovir Disoproxil Fumarate + lamivudine or epivir OR emtricitabine + nevirapine

The above combinations are recommended for standard patients who have not taken any other antiretrovirals. However, special considerations must be made for patients with specific conditions, including pregnant women, individuals with hepatitis B, individuals with tuberculosis, and individuals who have already developed a resistance to some antiretrovirals. The WHO makes specific treatment recommendations for each group. These recommendations were developed through careful analysis of the available treatments and their effects on the virus.

Antiretroviral therapy is important in managing the spread of HIV in pregnant women and preventing the mother from passing the infection.
to her unborn child. The following are the antiretroviral recommendations for pregnant women:\textsuperscript{127}

- Zidovudine (INN) or azidothymidine + lamivudine or epivir + Efavirenz
- Zidovudine (INN) or azidothymidine + lamivudine or epivir + nevirapine
- Tenofovir Disoproxil Fumarate + lamivudine or epivir OR Emtricitabine + Efavirenz
- Tenofovir Disoproxil Fumarate + lamivudine or epivir OR emtricitabine + nevirapine

(Do not start efavirenz during the first-trimester of pregnancy)

For patients with hepatitis B and tuberculosis, special consideration must be made regarding the potential effects the treatment will have on these other conditions. The recommended treatment plan for individuals with tuberculosis is as follows:\textsuperscript{127}

- Start ART in all HIV-infected individuals with active tuberculosis (TB) irrespective of CD4 cell count.
- Start TB treatment first, followed by ART as soon as possible after starting TB treatment.
- Use efavirenz (EFV) as the preferred non-nucleoside reverse transcriptase inhibitor (NNRTI) in patients starting ART while on TB treatment.

Treatment recommendations for patients with Hepatitis B include:\textsuperscript{127}

- Start ART in all HIV/HBV co-infected individuals who require treatment for their HBV infection, irrespective of CD4 cell count or clinical stage.
- Start Tenofovir Disoproxil Fumarate and lamivudine or epivir or emtricitabine containing antiretroviral regimens in all HIV/HBV co-infected individuals needing treatment.

Specific recommendations for antiretroviral combinations make it easier for providers to select the appropriate treatment plan for each patient. However providers should still assess patients on a case-by-case basis. Each patient has differing needs and special considerations that make it necessary to individualize the treatment plan for increased efficacy and viral suppression.\textsuperscript{136}

**Monitoring Treatment**

Once a patient begins antiretroviral therapy, the provider should regularly monitor the patient’s status through regular appointments and frequent blood work.\textsuperscript{127} Regular viral load testing, as well as drug resistance testing, is necessary to ensure that the combination therapy is working properly.\textsuperscript{121} An increase in viral load is indicative of decreased efficacy of the prescribed treatment and requires a modification in treatment.\textsuperscript{124} Patient adherence is important during the course of treatment, as missed doses can result in increased drug resistance and the development of complications.\textsuperscript{136} Providers should stress the importance of adherence to the treatment, as well as participation in regular monitoring visits to ensure continued response to treatment.\textsuperscript{127}

*Virologic failure*

When antiretroviral therapy is administered, the goal is to reduce the viral load to undetectable levels. In new patients, the goal is a reduction by \(1 \log_{10} \text{c/mL}\) within 1-4 weeks, a viral load of \(<500 \text{ c/mL}\)
at 16-24 weeks, and a viral load of <50 c/mL after 24 weeks. Providers are recommended to conduct viral load testing every three to six months to monitor the effectiveness of the treatment. During this period, viral load measurements are expected to remain at <50 c/mL. Occasionally, a patient may experience a temporary increase above this level, which is acceptable. However, virologic failure is defined as 2 consecutive viral load counts of >500 c/mL.

Virologic failure is caused by two factors:

1) Failure of the drug to reach the virus: This can occur as the result of a variety of factors, including but not limited to lack of adequate adherence (the most common cause), drug interactions, or drug malabsorption.

2) Resistance: When a virologic failure is a result of resistance, it is because the specific strain of HIV is resistant to one or more of the drugs in the regimen.

When virologic failure is confirmed, the provider must quickly determine the cause so that a new treatment plan can be developed. The first step is to determine if virologic failure is a result of failure of the drug to reach the virus. Lack of adherence to the regimen is the most common cause of failure and should be ruled out before attempting to change the treatment plan. Lack of adherence is often a result of a variety of factors, including intolerance of the side effects, mental or emotional issues that affect the patient’s ability to commit to treatment, a lack of access to ongoing care, and the stigma associated with HIV. Providers must address these issues and work with the patient to develop an appropriate treatment plan.
that he or she will be able to follow. As each patient’s situation is unique, the onus is on the provider to determine why the patient is unable to adhere to the regimen and encourage future adherence.\textsuperscript{124}

If failure is not a result of lack of adherence, it is often caused by drug interactions or drug malabsorption.\textsuperscript{137} These complications require the provider to assess exactly what is causing the failure and address it. In cases where failure is a result of drug interactions, the provider must identify other treatment options, either for the antiretroviral therapy or the other drugs that the patient is taking.\textsuperscript{125} If malabsorption is the cause, the provider will have to identify what conditions are causing malabsorption and correct them.\textsuperscript{125}

In some cases, the patient requires an intensification of treatment. This is the addition of another drug to the regimen with the goal of enhancing antiretroviral activity in a patient who is showing some response to therapy, but not at the level needed for viral suppression.\textsuperscript{137} Intensification is typically initiated when a patient still has a viral load below 5,000 c/mL, as anything above this level typically requires an entirely new regimen.\textsuperscript{127} The most common antiretrovirals for use in intensification are tenofovir (TDF), abacavir (ABC), or ritonavir (RTV).\textsuperscript{137}

Once failure of the drug to reach the virus has been ruled out as a cause, the provider will attempt to determine if drug resistance is causing virologic failure.\textsuperscript{124} Drug resistance is tested in two ways: genotypic and phenotypic.\textsuperscript{137} Genotypic testing measures gene mutations that are the target of antiretroviral drugs.\textsuperscript{137} Gene mutations are an indicator of resistance.\textsuperscript{126} Phenotypic testing uses
untreated virus strains to measure the activity of the drug against the patient’s virus and compare the results to the activity of the untreated virus. Genotypic testing is used more frequently due to its efficiency and lower cost. However, there is some question as to the merit and validity of either test as they require a great deal of precision and expertise in administering the test and interpreting the results. The tests only assess the impact of the drugs that the patient is currently taking and cannot evaluate the activity of drugs that were discontinued more than 2 weeks prior to the test.

If drug resistance is determined, the provider will need to begin treatment with a second line of antiretroviral therapy. To avoid further drug resistance, specific combinations are recommended for second line ART. The WHO provides the following recommendations for second line antiretroviral therapy, ART:  

- A boosted protease inhibitor (PI/r) plus two nucleoside analogues (NRTIs) are recommended for second-line ART.
- Atazanavir/Ritonavir and Lopinavir/Ritonavir are the preferred boosted protease inhibitors for second line ART.
- Simplification of second NRTI options is recommended.
  - If d4T (stavudine) or AZT (zidovudine) has been used in first-line, use tenofovir disoproxil fumarate + lamivudine or emtricitabine as the NRTI backbone in second-line.
  - If tenofovir disoproxil fumarate has been used in first-line, use AZT + lamivudine as the NRTI backbone in second-line.

Typically, further treatment after initial combination therapy can be effective in minimizing the effects of the virus on the immune system.
and may prevent the illness from progressing to the next stage. However, in cases where HIV is advanced and the virus has developed drug resistance, second line therapy may only work for a short period of time. At this point, the virus has most likely progressed to the symptomatic stage, or has transitioned to AIDS, and further treatment will need to be prescribed with the goal of slowing progress. To reduce the impact of the virus on the patient’s immune system providers will often resort to a third line regimen for treating the virus.

Due to the progression of the virus and the likelihood of drug resistance, providers must assess the situation carefully and consult the recommendations for third line therapy. To assist providers, the WHO provides the following recommendations when considering third line antiretroviral therapy:

- Third-line regimens should include new drugs likely to have anti-HIV activity such as integrase inhibitors and second generation NNRTIs and PIs.
- Patients on a failing second-line regimen with no new ARV options, should continue with a tolerated regimen.

**Adverse Affects**

Antiretroviral therapy can cause a number of adverse affects in patients, ranging from mild to severe. Regular monitoring of the patient can ensure that the adverse affects do not cause long-term problems or other complications in the patient. Many drugs will cause mild side effects such as nausea, fatigue and headaches. While these side effects are not dangerous, they do impact the patient’s adherence rate, which is problematic. Providers must work
with patients to minimize side effects whenever possible, and also provide education regarding the importance of adherence during drug therapy.\textsuperscript{25}

When adverse affects impact adherence, the provider can make modifications to the treatment plan to accommodate the patient's needs.\textsuperscript{118} In some instances, it will only require the provider to substitute one drug for another. However, in other instances, it can require a complete modification of the treatment plan.\textsuperscript{139}

Other side effects are more severe and can cause various medical complications, some of which can be lethal.\textsuperscript{136} These adverse affects are typically specific to the drug that the patient is taking.\textsuperscript{125} For example, didanosine can cause pancreatitis, while abacavir is known to cause hypersensitivity.\textsuperscript{128} In some instances, the adverse affects can be linked to an entire class of antiretrovirals. NNRTIs are known to cause Stevens-Johnson syndrome, nevirapine-associated hepatic necrosis, and lactic acidosis.\textsuperscript{139} In some cases, these conditions are only uncomfortable for the patient, but in other cases they can be very dangerous.\textsuperscript{125}

While specific, unrelated adverse affects are often associated with antiretroviral therapy, metabolic complications are the most common adverse affects associated with long-term use of antiretroviral therapy.\textsuperscript{137} Typical metabolic complications include the following:

\textit{Lipid abnormalities}
Patients using protease inhibitors have the highest risk of experiencing complications with triglycerides, total cholesterol, and low-density
lipoprotein (LDL) cholesterol. Nucleoside reverse transcriptase inhibitors (NRTIs) and non-nucleoside reverse transcriptase inhibitors do not appear to have an impact on lipids. Abnormal lipid levels in HIV positive patients appear to have the same affect on patient cardiovascular health as they do on non-positive patients, especially when other lifestyle factors such as smoking or obesity are present. As a result, patients who are taking protease inhibitors should undergo regular laboratory testing to monitor lipid abnormalities and cardiovascular health. If the results show damage, the clinician should consider switching to a different class of antiretroviral, or addressing lifestyle issues with the patient. In some cases, the use of a lipid-lowering agent can be effective.

Lipodystrophy
Lipodystrophy is generally defined as significant change in body morphology that does not result from either weight gain or weight loss and includes 3 subsets of morphologic changes: generalized fat accumulation, focal fat accumulation, and fat atrophy. While the use of protease inhibitors is often linked with the onset of lipodystrophy, the most significant risk factors include a history of severe immune suppression (nadir CD4 count <100 cells/mm3), older age, prolonged use of antiretroviral drugs, and highly active antiretroviral therapy.

Patients who experience lipodystrophy often have high insulin levels and show signs of insulin resistance. Therefore, lipodystrophy is considered by some to be a result of insulin resistance, but there is no data available to back that claim. Regular monitoring of fat and insulin levels is necessary during antiretroviral treatment.
Lactic acidosis
Patients undergoing antiretroviral treatment are at risk of developing hyperlactatemia. In patients, cases can range from asymptomatic to symptomatic hyperlactatemia. In patients with symptomatic hyperlactatemia, the symptoms can range from mild acidosis, to fulminant lactic acidosis, liver failure, and death. Some patients may also develop hepatic steatosis. Hyperlactatemia and lactic acidosis are associated with abnormal mitochondrial toxicity caused by NRTIs that inhibit the critical enzyme mitochondrial DNA polymerase gamma. In addition to the use of NRTI’s, other risk factors increase a patient’s likelihood of developing hyperlactemia and lactic acidosis. These include pregnancy, female gender, obesity, or concurrent treatment with ribavirin, hydroxyurea, or metformin. As with other abnormalities, regular monitoring of the patient is necessary to prevent the development of hyperlactemia and lactic acidosis.

Hyperglycemia
Protease inhibitors have been shown to have a direct impact on glucose metabolism, specifically by increasing insulin resistance. Therefore, patient’s using protease inhibitors may have a greater risk of developing diabetes mellitus. It is necessary to routinely monitor a patient for hyperglycemia if he or she is taking a protease inhibitor. If testing shows hyperglycemia and insulin resistance, the provider should switch from a protease inhibitor to a different antiretroviral. Past studies have shown a significant improvement in hyperglycemia and insulin resistance in patients who stop taking protease inhibitors.
Decreased bone mineral density
Some studies have linked the use of antiretroviral therapy with decreased bone mineral density and avascular necrosis. However, these connections are controversial and still require further testing to confirm. If a patient complains of focal bone pain, avascular necrosis should be considered and either confirmed or ruled out through the use of a CT scan or MRI. Once the condition develops, the provider must work with the patient to determine an appropriate course of action. Modification of antiretroviral therapy is not effective in eliminating avascular necrosis and is not recommended. Avascular necrosis does not respond to medical therapy and often requires surgical intervention. Patients should be monitored for metabolic complications so that providers can treat the conditions properly and prevent further complications. The following table provides guidelines for assessment and monitoring of metabolic complications in HIV patients.

| Recommendations for Assessment and Monitoring of Metabolic Complications of Antiretroviral Therapy for HIV Infection |
|---|---|
| **Glucose and lipid abnormalities** | The following assessments are recommended before initiation of potent ART, at the time of a switch of therapy, 3 to 6 months after starting or switching therapy, and at least annually during stable therapy:  
Fasting glucose (if therapy includes a PI)  
Fasting lipid panel (total cholesterol, HDL, and LDL cholesterol [calculated or direct], and triglyceride levels)  
A blood glucose level after oral administration of 75 g of glucose may be used to identify impaired glucose tolerance in patients with risk factors for type 2 diabetes mellitus or those with severe body fat changes. |
| **Body fat distribution abnormalities** | • No specific technique can be recommended at the present time for routine assessment and monitoring of body fat distribution changes. |
In addition to regular monitoring for metabolic complications, providers should follow specific guidelines when treating metabolic abnormalities in HIV positive patients. The following guidelines have been established for treating metabolic conditions in HIV patients; obtained from international recommendations on the management of metabolic complications associated with antiretroviral therapy.\textsuperscript{140}

| Lactic academia | • Routine measurement of lactic acid levels is not recommended.  
• Lactic acid levels should be monitored in those receiving NRTIs who have clinical signs or symptoms of lactic acidemia, and in pregnant women receiving NRTIs.  
• If alternative NRTIs are resumed in those who have interrupted antiretroviral therapy for lactic acidemia, lactate levels should be monitored every 4 weeks for at least 3 months. |
|-----------------|---------------------------------------------------------------------------------------------------------------|
| Osteopenia, osteoporosis, and osteonecrosis | • Routine screening for osteoporosis or osteonecrosis is not recommended.  
• Radiographic examination of involved bone is recommended for those with symptoms of bone or joint pain; the contralateral joint should also be assessed. |

DEXA = dual-energy x-ray absorptiometry  
HDL = high-density lipoprotein  
LDL = low-density lipoprotein  
NCEP = National Cholesterol Education Program  
NNRTI = non-nucleoside reverse transcriptase inhibitor  
NRTI = nucleoside reverse transcriptase inhibitor

### Recommendations for Treatment of Metabolic Complications of Antiretroviral Therapy for HIV Infection

| Glucose intolerance and diabetes mellitus | • Weight loss for overweight subjects is recommended.  
• Follow established guidelines for treating diabetes in the general population, with preference given to insulin sensitizing agents such as metformin (except for those with renal disease or history of lactic acidemia) or thiazolidinediones (except for those with preexisting liver disease).  
• Avoid use of a PI as initial therapy in patients with preexisting glucose intolerance or diabetes mellitus. |
### Lipid and lipoprotein abnormalities

- Follow NCEP III guidelines for assessment of risk factors for cardiovascular disease, and dietary and lifestyle alterations for lowering cholesterol and triglyceride levels.
- Avoid use of PIs, if possible, in those with preexisting cardiovascular risk factors, family history of hyperlipidemia, or elevated lipid levels.
- Follow NCEP guideline thresholds for lipid-lowering therapy.
- Fibrates are recommended as initial therapy for those with isolated fasting hypertriglyceridemia.
- Pravastatin or atorvastatin are preferred statin agents for those with isolated fasting hypercholesterolemia requiring treatment in the setting of PI or other CYP 3A4 inhibitor therapy.
- If combination therapy for hypercholesterolemia and hypertriglyceridemia is indicated, therapy should begin with a statin, followed by the addition of a fibrate if there is insufficient response after 3 to 4 months of treatment.

### Body fat distribution abnormalities

- No therapies for fat distribution abnormalities in the absence of other metabolic complications can be routinely recommended.

### Lactic acidemia

- ART should be withheld for all patients with confirmed lactate levels >10 mmol/L (90 mg/dL) or those with confirmed lactate levels >5 mmol/L (45 mg/dL) who are symptomatic.
- No intervention apart from NRTI cessation is recommended.
- Restart combination NNRTI and PI therapy after lactate levels return to normal and symptoms resolve.

### Osteopenia, osteoporosis, and osteonecrosis

- Surgical resection of involved bone is the only effective therapy for symptomatic osteonecrosis.
- If radiography or regional DEXA scanning demonstrates osteoporosis, or if a pathological fracture occurs in the setting of osteoporosis, therapy with a bisphosphonate should be considered.

---

**DEXA** = dual-energy x-ray absorptiometry  
**HDL** = high-density lipoprotein  
**LDL** = low-density lipoprotein  
**NCEP** = National Cholesterol Education Program  
**NNRTI** = non-nucleoside reverse transcriptase inhibitor  
**NRTI** = nucleoside reverse transcriptase inhibitor

---

Antiretroviral therapy is highly effective in the treatment of HIV. When used in conjunction with other treatments, it can drastically reduce the spread of the virus and slow progression of the disease. However, antiretroviral therapy requires constant monitoring and proper adherence by the patient. Providers should encourage patients to be...
involved in the process, as it will increase the likelihood that therapy will work.

**Case Management**

The care of an HIV positive patient requires a variety of services that will address the medical, emotional, and social service needs of the patient. While a medical provider can provide the medical care that a patient needs, it can be difficult for the patient’s primary care provider to coordinate the other services that the patient needs to live with the virus. Providers can provide referrals to other services, but often the patient requires a more coordinated effort. Therefore, many HIV positive individuals work with a case manager. The case manager serves as the patient’s care coordinator and, occasionally, their advocate. Case managers work directly with patients to assist them with the various services they need to manage their disease. HIV positive individuals often have issues that extend beyond their positive status, and case managers coordinate care for the patient that assists with all the individual’s needs.

The relationship between a patient and the case manager is a partnership. The case manager works with the patient to coordinate treatment and provide guidance as the patient seeks appropriate services. Specifically, a case manager will help the patient by providing the following services:

- Works with the patient to apply for and obtain health insurance and/or apply for Medicaid to pay for the necessary medical services
- Assists the patient with finding appropriate medical
- Helps coordinate medical tests and appointments
• Encourages patient adherence to treatment plan and works with patient to ensure attendance at all scheduled medical appointments
• Assists patient with the application process for various social service programs such as Supplemental Security Income (SSI) or Temporary Assistance to Needy Families (TANF)
• Assist with paperwork completion for various services
• Help patients secure appropriate housing
• Provide patients with information and support to assist with substance abuse problems
• Provide educational programming to reduce the transmission of HIV to others
• Locate and secure counseling services for the patient

Case management is an ongoing relationship between the patient and the provider. Patients meet regularly with their case managers and rely on them for assistance with their various care needs.144 When a patient establishes a relationship with a case manager, it begins with an initial intake and assessment meeting. During this meeting, the case manager will assess the patient’s health and evaluate the patient’s overall situation to determine the specific medical and social service needs of the patient.145 The case manager will also gather information about the patient’s living situation and specific lifestyle choices of the patient.143 Typically, the case manager will schedule a home visit to assess the patient’s living conditions.145 During the intake and assessment period, the case manager will address any immediate needs of the patient and attempt to resolve any emergency issues.143
Once the initial intake is over, the case manager will use the information obtained to write a service plan with the patient. This plan identifies and outlines the specific service needs of the patient and prioritizes what needs are to be addressed first. In some instances, the case manager develops a long-term plan while other patients need a short-term plan to address immediate issues. The type of plan needed is determined during the assessment period. In addition to the patient, the service plan can include specific services that will benefit family members who reside in the home with the patient, such as spouses and children. The case manager works with the patient to ensure that the service plan is followed and provides encouragement. As part of the process, the case manager works with other agencies to coordinate services and serves as a liaison between the patient and these agencies.

As the patient completes steps in the service plan, the case manager reviews and modifies the plan to ensure it is relevant to the patient’s situation and specific needs. The case manager also works with the patient to help him or her understand the treatment options available and provides any necessary education. As emergencies arise, the case manager works with the patient to develop solutions and obtain the appropriate assistance. Case managers are valuable assets to patients as they work to obtain the care they need to successfully manage their infection.

**Complications**

HIV positive individuals are susceptible to a host of coinfections and other conditions as a result of their weakened immune systems.
Proper care of an HIV positive individual requires an understanding of these conditions and the impact they have on the patient’s care.\textsuperscript{143}

\textit{Coinfections:}
HIV positive individuals are often infected with other diseases that are transmitted by the same behaviors that transmit HIV.\textsuperscript{37} Common coinfections are hepatitis B, hepatitis C and tuberculosis.\textsuperscript{146,147} These conditions are not a result of HIV, which is why they are considered coinfections. Individuals would have these conditions regardless of their HIV status.\textsuperscript{126} Providers should treat coinfections separately from HIV treatment.\textsuperscript{126} However, it is important for the provider to be aware of any complications that may arise when a patient receives treatment.\textsuperscript{25} In addition, providers should be familiar with any complications that may arise when a patient is coinfected with HIV and another illness. For example, patients who have hepatitis B are at a higher risk of liver failure.\textsuperscript{146}

Hepatitis affects the liver directly, and the use of antiretroviral drugs in a patient with a compromised liver can pose a risk for the patient.\textsuperscript{146} Therefore, the provider must use caution when developing an HIV treatment plan for an individual who is also infected with hepatitis B. Since a coinfection can be any illness that the individual may have that is not associated with HIV infection, it is crucial for the provider to assess the patient on an individual basis.\textsuperscript{126} Coinfections should be taken into consideration when developing a treatment plan and should be monitored as part of the patient’s regular care.\textsuperscript{25} By minimizing the impact of the coinfection, the provider is better able to treat the patient’s HIV and reduce the impact on the patient’s immune system and organs.
Complications
Many HIV patients experience complications during the course of the illness. These complications are typically a result of a weakened immune system, and not a direct result of HIV infection.\textsuperscript{148} HIV complications differ from opportunistic infections, which are directly related to AIDS.\textsuperscript{126} Unlike opportunistic infections, HIV complications can occur at any stage of the virus.\textsuperscript{148} However, there is an increased likelihood of complications once a patient progresses to the symptomatic stage of infection.\textsuperscript{25} It should be noted, however, that these complications are not symptoms of HIV infection and should not be used to diagnose the illness.\textsuperscript{149} HIV complications also differ from the adverse affects associated with antiretroviral therapy.\textsuperscript{150} It is important to differentiate between complications and the aforementioned conditions, as treatment will differ for each condition.\textsuperscript{126}

Human immunodeficiency virus complications are conditions that the patient typically would not experience in the absence of HIV, but they are not specific to HIV infection.\textsuperscript{149} Other illnesses can cause similar complications, as they are a result of a weakened immune system, not the illness itself.\textsuperscript{150} Therefore, providers must treat the complications separate from the infection, without impacting the treatment plan and antiretroviral regimen that the patient is following.\textsuperscript{149} HIV complications can further affect a patient’s immune system, thereby allowing the disease to progress more rapidly.\textsuperscript{150} It is imperative that complications be managed effectively to minimize further complications. In unmanaged patients, complications can often result in death, not from the virus, but from the complication itself.\textsuperscript{148}
The most common HIV-related complications are listed as follows:

- Heart disease
- Stroke
- Liver disease
- Kidney disease
- Nerve damage
- Eye disease
- Cancer

The complications listed above can affect those who are HIV negative, but they pose a significant problem for HIV positive individuals, as those living with the virus are susceptible to additional complications. Heart disease and stroke can have devastating affects on any patient. For HIV positive individuals who are already compromised, the affects are often fatal. Antiretroviral therapy helps minimize the spread of HIV, but it can also impact the individual’s body. The liver is especially impacted by treatment as antiretroviral therapy taxes the liver more than other medications. Therefore, liver complications are significant in HIV positive patients. Other complications are also concerning as they further tax the patient’s already compromised immune system. Providers must work with each patient to address any complications that may arise from either the infection of the treatment.

**Care for AIDS Patients**

AIDS is the end stage of HIV infection, and it is always fatal. Once a patient progresses to AIDS, he or she permanently retains that status. The prognosis for patients who have transitioned to AIDS is not positive. However, while patient mortality is always associated
with AIDS, the patient can maintain some quality of life during this final stage of infection.\textsuperscript{145} Proper treatment and monitoring can prolong a patient’s life and management of opportunistic infections can reduce patient discomfort.\textsuperscript{153}

Patients who receive adequate care during this stage have an increased likelihood of living longer than those that do not receive adequate care.\textsuperscript{154} The typical life expectancy of an individual with AIDS is 10 – 12 months.\textsuperscript{155} However, some patients can live four or more years with AIDS if the disease is managed properly.\textsuperscript{154}

Patient mortality is not a direct result of HIV. It is the result of complications from HIV, typically as the result of opportunistic infections.\textsuperscript{156} Once a patient develops AIDS, the primary concern is managing opportunistic infections and providing palliative care.\textsuperscript{145}

\textit{Opportunistic infections}

When an individual’s immune system is functioning properly, it is able to fight off most viruses, bacteria and parasites.\textsuperscript{103} However, in HIV positive individuals, the virus destroys the immune system, thereby rendering it unable to fight off these other infections. During all stages of infection, an HIV positive individual has the potential to become infected with a secondary infection due to the individual’s weakened system.\textsuperscript{154} However, the CDC has identified more than twenty specific illnesses that are considered opportunistic infections, meaning they take advantage of the individual’s suppressed immune system and cause numerous complications.\textsuperscript{111} These infections differ from other complications that an HIV positive individual might experience; they are a specific set of illnesses that are indicative of a fully weakened
immune system. In fact, opportunistic infections are the most common cause of death in individuals with HIV/AIDS.

Opportunistic infections produce a variety of symptoms and can have a significant effect on the patient. They can be localized or systemic and differ in impact and severity. Due to the nature of these opportunistic infections, and the direct correlation between the patient’s weakened immune system and the onset of these specific illnesses, opportunistic infections are considered one of the indicators of AIDS. Opportunistic infections typically present when an individual’s CD4 count is below 200. However, some can appear when the CD4 count is higher. Therefore, once a person presents with one or more opportunistic infection, he or she is automatically diagnosed with AIDS, regardless of the CD4 cell count.

The CDC identified opportunistic infections, which are:

- 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

Treatment of opportunistic infections
Opportunistic infections range in severity and some are easier to treat than others. Ultimately, appropriate and affective treatment is dependent upon the provider’s ability to select, obtain and administer the appropriate drugs to treat the illness. In addition, the provider must work with the patient to monitor his or her status and assess treatment response. In some instances, minor opportunistic infections such as candidiasis of the mouth, throat or vagina (thrush), herpes
Zoster (shingles) and herpes simplex can be treated using basic home-based care. Initial diagnosis is made through an observation of the patient’s symptoms, and the patient is responsible for treating the condition at home.

In other instances, the diagnosis and treatment may require additional interventions and treatment. In instances of pulmonary tuberculosis and cryptococcal meningitis, the provider may require further observation and the use of a microscope to diagnosis the illness, but treatment will often require minimal care outside of the patient’s home. For more severe opportunistic infections such as extrapulmonary tuberculosis, cryptosporidiosis, isopsoriasis, PCP and Kaposi’s sarcoma, the provider will need to utilize additional diagnostic and treatment options, such as X-ray equipment and culture facilities. More complex opportunistic infections such as toxoplasmosis, Mycobacterium Avium Complex MAC, and cytomegalovirus (CMV) infection require advanced diagnostic and treatment services and are difficult to treat when access to hospital care and laboratory technology is limited.

The use of antiretroviral therapy, along with treatment specific to the infection, is recommended to treat patients with acute opportunistic infections. Typically, ART will improve the patient’s immune function and reduce the impact of the opportunistic infection. ART is especially effective against opportunistic infections that do not have their own treatment option, most specifically cryptosporidiosis, microsporidiosis, and progressive multifocal leukoencephalopathy (PML). In patients with Kaposi’s sarcoma, ART has been shown to reduce lesions and minimize the impact of the illness. ART is also
necessary to prevent the patient from acquiring a second opportunistic infection.\(^{156}\)

Often, a patient will develop an opportunistic infection (OI) after initiating ART.\(^ {113}\) The Center for Disease Control categorizes these infections as follows:\(^ {122}\)

**Group 1:**
The first group includes OIs that occur shortly after initiating ART (within 12 weeks). These cases might be subclinical infections that have been unmasked by early immune reconstitution or simply OIs that occurred because of advanced immunosuppression and are not considered to represent early failure of ART. Many of these cases represent IRIS.

**Group 2:**
The second group includes OIs that occur >12 weeks after initiation of ART among patients with suppressed HIV ribonucleic acid (RNA) levels and sustained CD4+ counts >200 cells/µL. Determining whether these represent a form of IRIS rather than incomplete immunity with the occurrence of a new OI is difficult.

**Group 3:**
The third group includes OIs that occur among patients who are experiencing virologic and immunologic failure while on ART. These represent clinical failure of ART.\(^ {122}\)
If a patient is already using ART when an opportunistic infection develops, he or she should continue treatment with ART and also begin treatment for the opportunistic infection.\textsuperscript{163} However, if a patient is experiencing virologic failure at the onset of an opportunistic infection, treatment should be assessed and modified.\textsuperscript{126} In this instance, the patient should immediately begin treatment for the opportunistic infection, and antiretroviral resistance testing should be conducted.\textsuperscript{163} After the completion of testing, the treatment regimen should be modified with the goal of improved virologic control.\textsuperscript{122}

\textit{Palliative care}

Due to the availability of advanced HIV treatment and care, the mortality rate for HIV infected individuals has decreased.\textsuperscript{6} With the use of antiretroviral treatment, patients can manage the disease and prevent progression. In fact, patients can expect to live a number of years without experiencing symptoms.\textsuperscript{125}

Although the disease can remain a manageable, chronic infection for a number of years, the mortality rate is still significant. Approximately 14,000 individuals in the United States die each year from complications from the illness.\textsuperscript{164} Once a patient transitions to AIDS the treatment becomes focused on preventing opportunistic infections and providing palliative care. Palliative care provides patients with care and comfort during the final stage of infection.\textsuperscript{165}

The focus during palliative care is on the patient and the patient’s family.\textsuperscript{111} The goal is maintaining quality of life while treating the symptoms that cause suffering in the patient. Typically, palliative care is a team approach between the physician, case manager, hospital and
nursing staff, and hospice. Palliative care is a multi-faceted approach that addresses the physical, emotional, social, and spiritual needs of the patient and the patient’s family. The focus is on providing support and education to help minimize suffering and maintain quality of life.

The focus during palliative care is not curative. Instead, care provided during this time is meant to support the patient. Typically, palliative care has four main goals:

- Management of symptoms (i.e., fatigue, pain)
- Treatment of adverse effects (i.e., nausea, vomiting)
- Psychosocial support (i.e., depression, advance care planning)
- End-of-life care

Palliative care includes the continuation of treatment, including antiretroviral therapy with HIV positive patients. However, treatment also incorporates measures to address symptoms and conditions associated with opportunistic infections. Treatment includes strategies to minimize symptoms that are caused by such infections, while also striving to prevent further opportunistic infections. Care also includes case management services focused on obtaining or maintaining social services and non-HIV specific needs.

Providers should assess and monitor patient symptoms and infections and provide appropriate care to minimize the suffering associated with such conditions. The following table, provides guidelines for providers to identify and assess common symptoms in patients with AIDS and determine disease-specific and palliative interventions:
<table>
<thead>
<tr>
<th>Constitutional</th>
<th>Possible Causes</th>
<th>Disease Specific Rx</th>
<th>Palliative Rx</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue, weakness</td>
<td>AIDS, Opportunistic Infections, Anemia</td>
<td>HAART, treat specific infections, erythropoietin, transfusion</td>
<td>Corticosteroids (prednisone, dexamethasone), Psychostimulants (methylphenidate, pemoline, dextroamphetamine, modafinil)</td>
</tr>
<tr>
<td>Weight loss/anorexia</td>
<td>HIV, Malignancy</td>
<td>HAART, chemotherapy, nutritional support, enteral feedings</td>
<td>Corticosteroids, Testosterone/androgens, Oxandrolone, Megestrol acetate, Dronabinol, Recombinant growth hormone</td>
</tr>
<tr>
<td>Fevers/Sweats</td>
<td>DMAC, CMV, HIV, Lymphoma, malignancy</td>
<td>Azithromycin, ethambutol, ganciclovir, foscarnet, HAART, chemotherapy</td>
<td>NSAIDS (ibuprofen, indomethacin, cox-2 inhibitors), Corticosteroids, Anti-cholinergics (hyoscine, thioridazine), H2-antagonists (cimetidine)</td>
</tr>
<tr>
<td>Pain</td>
<td>Opportunistic infections, HIV-related malignancies, non-specific, HIV-related peripheral neuropathy, CMV, VZV, Didoxynucleosides (didanosine, zalcitabine, stavudine)</td>
<td>treat specific disease entities, HAART, ganciclovir, foscarnet, acyclovir, famiciclovir, change antiretroviral or other regimen</td>
<td>NSAIDS, Opioids, Corticosteroids, NSAIDS, Opioids (esp. methadone) and adjuvants, - tricyclic antidepressants (amitriptyline, imipramine), - benzodiazepines (clonazepam), - anti-convulsants (gabapentin), Corticosteroids</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>Nausea/Vomiting</td>
<td>Fluconazole, amphotericin-B, ganciclovir, foscarnet, change antiretroviral regimen</td>
<td>Dopamine antagonists (haloperidol, prochlorperazine), Prokinetic agents (metoclopramide), Antihistamines (diphenhydramine, promethazine), Anticholinergics (hyoscine, scopolamine), Serotonin antagonists (granisetron, ondansetron, dolasetron), H2- blockers (cimetidine), Proton pump inhibitors (omeprazole), Somatostatin analogues (octreotide), Benzodiazepines (lorazepam), Corticosteroids</td>
</tr>
<tr>
<td>------------------</td>
<td>-----------------</td>
<td>--------------------------------------------------------------------------------</td>
<td>----------------------------------------------------------------------------------</td>
</tr>
</tbody>
</table>

(isoniazid) | Acupuncture |
<table>
<thead>
<tr>
<th>Diarrhea</th>
<th>MAI, Cryptosporidiosis, CMV, microsporidiosis, Other intestinal parasites, Bacterial gastroenteritis, Malabsorption</th>
<th>azithromycin, ethambutol, paraomomycin, ganciclovir, foscarinet, albendazole, other anti-parasitic agents, other antibiotics</th>
<th>Bismuth, methylcellulose, kaolin, diphenoxylate + atropine, loperamide, octreotide, tincture of opium</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constipation</td>
<td>dehydration, malignancy, anticholinergics, opioids</td>
<td>hydration, radiation/chemotherapy, medication adjustment</td>
<td>Activity/diet, Prophylaxis on opioids, Softening agents, surfactant laxatives (docusate), bulk-forming agents (bran, methylcellulose), osmotic laxatives (lactulose, sorbitol), saline laxatives (magnesium hydroxide), Peristalsis-stimulating agents, anthracenes (senna), polyphenolics (bisacodyl)</td>
</tr>
<tr>
<td>Respiratory</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dyspnea</td>
<td>PCP, bacterial pneumonia, anemia, pleural effusion/mass/obstruction, decreased respiratory muscle function</td>
<td>trimethoprim/sulfamethoxazole, pentamidine, atovaquone etc. other antibiotics, erythropoietin, transfusion, drainage/radiation/surgery</td>
<td>Use of fan, open windows, oxygen, opioids, bronchodilators, methyl xanthines, benzodiazepines (lorazepam)</td>
</tr>
<tr>
<td>Cough</td>
<td>PCP, bacterial pneumonia, TB</td>
<td>anti-infective therapy (as above) anti-tuberculous chemotherapy</td>
<td>Cough suppressants (dextromethorphan, codeine, other opioids), Decongestants, expectorants (various)</td>
</tr>
</tbody>
</table>


<table>
<thead>
<tr>
<th>Increased secretions (&quot;death rattle&quot;)</th>
<th>Fluid shifts, ineffective cough, sepsis, pneumonia</th>
<th>Antibiotics as indicated</th>
<th>Atropine, hyoscine, transdermal scopolamine, glycopyrrolate, fluid restriction, discontinue intravenous fluids</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th><strong>Dermatologic</strong></th>
<th><strong>Pruritis</strong></th>
<th><strong>Decubiti/Pressure Sores</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Dry skin</td>
<td>Dehydration</td>
<td>Poor nutrition, decreased mobility, prolonged bed rest</td>
</tr>
<tr>
<td>End-stage renal disease</td>
<td>End-stage liver disease</td>
<td>Nutrition</td>
</tr>
<tr>
<td>Malnutrition</td>
<td>Dehydration</td>
<td>Increase mobility</td>
</tr>
<tr>
<td>Eosinophilic folliculitis</td>
<td>Antifungals</td>
<td>Prevention</td>
</tr>
<tr>
<td>Dialysis</td>
<td>Hydration</td>
<td>Nutrition, mobility, skin integrity</td>
</tr>
<tr>
<td>Nutritional support</td>
<td>Steroids, antifungals</td>
<td>Wound protection</td>
</tr>
<tr>
<td>Emollients +/- salicylates</td>
<td>Topical agents</td>
<td>(menthol, phenol, calamine, doxepin, capsaicin)</td>
</tr>
<tr>
<td>Lubricating ointments</td>
<td>Anti-histamines</td>
<td>(diphenhydramine)</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>Serotonin antagonists</td>
<td>(ondansetron)</td>
</tr>
<tr>
<td>Thalidomide</td>
<td>Opioid antagonists</td>
<td>(naloxone, naltrexone)</td>
</tr>
<tr>
<td>Topical agents</td>
<td>Anti-depressants</td>
<td>Antidepressants</td>
</tr>
<tr>
<td>Anxiolytics</td>
<td>Neuroleptics</td>
<td>Anxiolytics</td>
</tr>
<tr>
<td>Neuroleptics</td>
<td>Thalidomide</td>
<td>Neuroleptics</td>
</tr>
</tbody>
</table>

Prevention (nutrition, mobility, skin integrity) Wound protection (semi-permeable film/hydrocolloid dressing) Debridement (normal saline, enzymatic agents, alginates)
<table>
<thead>
<tr>
<th>Neuropsychiatric</th>
<th>electrolyte imbalances dehydration toxoplasmosis cryptococcal meningitis sepsis</th>
<th>correct imbalances hydration sulfadiazine/pyrimethamine antifungals antibiotics</th>
<th>Neuroleptics (haloperidol, risperidone, chlorpromazine) Benzodiazepines (lorazepam, midazolam)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delirium/agitation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dementia</td>
<td>AIDS-related dementia</td>
<td>HAART</td>
<td>Psychostimulants (methylphenidate) Low dose neuroleptics (haloperidol)</td>
</tr>
<tr>
<td>Depression</td>
<td>Chronic illness, reactive Depression, major depression</td>
<td>antidepressants (tricyclics, SSRI’s MAO inhibitors, other)</td>
<td>Psychostimulants (methylphenidate, pemoline, dextroamphetamine, modafinil) Corticosteroids (prednisone, dexamethasone)</td>
</tr>
</tbody>
</table>

Palliative care also provides education and counseling services to address patient concerns regarding end of life issues. During this stage, patients should be encouraged to engage in advance care planning. Specifically, patients should be encouraged to develop an advance directive and a health care proxy. Patient education should include information regarding end of life planning and care. Family members should be included in this discussion and should be encouraged to ask questions and be engaged in the planning process. Patient fears should be identified and addressed and the various care options should be presented and discussed.
Special Populations

HIV affects individuals differently. Providers must understand the implications of the virus on these populations and address the specific needs of the patients. Pregnant women and children require special treatment plans and additional monitoring to ensure the disease does not progress more rapidly than it does in patients with no special considerations.

Pregnant women

Comprehensive care is essential for pregnant women as the disease must be managed in a way that will help maintain the woman’s health, while providing appropriate antiretroviral treatment. The goal of prenatal HIV care is to ensure that the virus is suppressed in a way that allows the patient to remain healthy and decreases the chance of perinatal transmission. The U.S. Department of Health and Human Services recommends that all HIV positive women begin antiretroviral treatment immediately after testing positive for pregnancy as ART is essential for disease management and transmission prevention.

In many instances, women become aware of their positive HIV status during pregnancy as routine HIV testing is a component of early pregnancy screening. For these patients, it is necessary to begin the new patient screening that is part of initial HIV intake and assessment while also beginning standard prenatal care. Providers can recommend appropriate counseling services and HIV specialists to help the patient obtain the appropriate treatment. In women who are already aware of their HIV positive status prior to becoming pregnant, initial services will be different. Patients who are already aware of a positive status will not require initial intake and assessment services,
but will require education and counseling specific to pregnancy and HIV.¹⁷⁴

Ideally, an HIV positive woman will consult with her provider prior to becoming pregnant so the appropriate services can be initiated. When an HIV positive woman is considering pregnancy, she should be counseled about the potential implications of HIV and pregnancy.¹⁷⁵ The patient should be given the tools to make an informed reproductive decision. Initial discussions with the patient should include information about the risk or perinatal transmission of HIV; initiation, continuation or modification of antiretroviral therapy; potential complications of both pregnancy and HIV infection; as well as the services available to maintain patient health and ensure positive outcomes for both the mother and child.¹⁷⁶

In some instances, an HIV positive woman will become pregnant accidentally. In these cases, the woman should be educated about the recommended treatment options and encouraged to establish a treatment plan immediately.¹⁷³ If the woman is not already being treated with antiretrovirals, she should be encouraged to start immediately.¹⁷² She should also receive information about the potential complications and outcomes associated with the lack of appropriate maternal care.¹⁷³

Regardless of whether the patient knew of her status prior to pregnancy, all HIV positive pregnant women require a multi-faceted approach to treatment. In addition to treatment for HIV, pregnant women require all of the traditional prenatal services provided to women who are not HIV positive.¹⁷² Therefore, the provider must work
with the patient to ensure all maternal and HIV-related care issues are being addressed. In addition to maternal and HIV-related services, pregnant patients may also require additional social services and mental health assistance.\textsuperscript{173} The patient may need assistance obtaining other services as well, including social services, substance abuse treatment services, domestic violence counseling, and housing assistance.\textsuperscript{173} The patient should be referred to a case manager to ensure a coordinated effort in obtaining the appropriate services.

Ideally, pregnant patients will have access to an HIV-experienced obstetrician and HIV specialist during the duration of care.\textsuperscript{171} This will increase the chances of a successful pregnancy and reduce the risks of diminished maternal health and fetal transmission. Throughout the pregnancy, patients should be educated about the risks of perinatal transmission and should be provided with strategies to reduce the risks.\textsuperscript{173} In addition, patients should receive information about the potential risks associated with HIV infection and treatment during pregnancy.

The U.S. Department of Health and Human Services provides the following recommendations and guidelines for prenatal evaluation and counseling of HIV positive patients:\textsuperscript{126}

- Therapy-associated adverse effects, including hyperglycemia, anemia, and hepatic toxicity, may have a negative effect on maternal and fetal health outcomes. Pregnant women should be advised about possible ARV-related adverse effects and should be monitored regularly for these events.
- HIV-infected women should receive evaluation and appropriate prophylaxis for opportunistic infections (OIs), as well as the vaccinations indicated for persons with HIV infection (see below).
- Some medications, both ARVs and other drugs, may cause fetal anomalies or toxicity when taken during pregnancy. These should be avoided in pregnant women, unless the anticipated benefit outweighs the risk. Consult with an HIV or obstetric specialist, a pharmacist, or the drug labeling information before prescribing medications for pregnant women.
- Options for mode of delivery should be discussed early. The benefits and risks of vaginal vs. cesarean delivery are outlined in the perinatal guidelines. If the HIV viral load is >1,000 copies/mL at 36 weeks of pregnancy, a scheduled cesarean delivery at 38 weeks' gestation is recommended to further reduce the risk of transmission.

Other evaluation and support measures for pregnant women should include the following:\textsuperscript{126}
- Screening for other potential maternal health problems, such as diabetes and hypertension
- Maternal nutritional evaluation and support, including initiation of a prenatal multivitamin containing folate (0.4-0.8 mg PO once daily) to reduce the risk of fetal neural tube defects; for women receiving trimethoprim-sulfamethoxazole, some experts recommend a folate dose of 4 mg daily
- Screening for psychiatric and neurologic disease
- Counseling about the risks of tobacco smoking; smoking cessation support as indicated
• Counseling about the risks of alcohol or drug use and support for discontinuation of these activities as needed
• Intimate partner violence screening
• Review of medications, including over-the-counter and nutritional agents, and discontinuation of medications with the potential for fetal harm
• Immunizations (i.e., influenza, hepatitis B) as indicated
• Institution of the standard measures for evaluation and management (i.e., assessment of reproductive and familial genetic history, screening for infectious diseases or sexually transmitted infections [STIs])
• Planning for maternal-fetal medicine consultation, if desired or indicated
• Selection of effective and appropriate postpartum contraceptive methods, if desired.

Antiretroviral therapy is crucial in the management of HIV in pregnant women. When possible, treatment should begin prior to pregnancy to ensure suppression of the virus through a reduction in viral load. \(^ {177}\)

However, some antiretrovirals can cause complications in pregnancy or potential birth defects. Providers must take these factors into consideration when prescribing ART to patients considering pregnancy.

The following antiretrovirals should be avoided as they have an increased risk of causing teratogenicity (i.e., efavirenz), hepatotoxicity (i.e., nevirapine), or metabolic complications such as lactic acidosis (i.e., didanosine and stavudine). \(^ {178}\)
In addition to antiretroviral treatment, HIV women should receive immunizations during pregnancy to reduce the risk of developing other infections that may cause complications.\textsuperscript{173}

\textit{Children}

Human immunodeficiency virus in children requires special consideration as the effects and treatment options differ from those for adults. The primary cause of HIV in children is perinatal transmission.\textsuperscript{64} Therefore, HIV management typically begins at birth.\textsuperscript{179} As the result of advanced prenatal care for HIV positive mothers, the rate of HIV in children has decreased significantly.\textsuperscript{173} In 2008, there were only 182 new infections in children under the age of thirteen and 41 new diagnoses of AIDS in the U.S.\textsuperscript{180} In instances where the mother does not know she is infected, children are often not diagnosed until they present symptoms.\textsuperscript{173} HIV symptoms in children differ from those in adolescents and adults. Typical childhood symptoms include the following:\textsuperscript{181}

- Failure to thrive
- Failure to reach developmental milestones
- Brain or nervous system problems, such as seizures, difficulty with walking, or poor performance in school
- Frequent illnesses such as ear infections, colds, upset stomach, and diarrhea

HIV progression is rapid in children and the onset of AIDS can occur suddenly.\textsuperscript{182} Children typically develop opportunistic infections more easily as HIV quickly destroys their developing immune systems.\textsuperscript{181} Children typically have higher CD4 cell counts and viral load counts than adults.\textsuperscript{179} Children also respond differently to antiretrovirals.\textsuperscript{179}
They typically recover faster and see greater increases in CD4 cell counts. With appropriate ART, children often recover more of their immune response than adults.\textsuperscript{179}

The National Institute for Health provides current clinical guidelines for the use of antiretrovirals in children, as outlined below:\textsuperscript{183}

\textit{When to Start Antiretroviral Therapy}

- CD4 T lymphocyte (CD4 cell) count and CD4 percentage thresholds for initiation of treatment are now offered for children aged \(>12\) months, but in the case of discordance between CD4 cell counts and percentages, decisions should be based on the lower value.
- Although CD4 percentage had been preferentially used to monitor immunologic status in children aged \(<5\) years, recent analyses show that CD4 cell counts provide greater prognostic value than CD4 percentage for short-term disease progression in children aged \(<5\) years as well as in older children.
- CD4 thresholds for treatment have been further subdivided into age groups \(1\) to \(<3\), \(3\) to \(<5\), and \(\geq 5\) years to more precisely link them to age-related changes in absolute CD4 cell count.
- The Panel continues to recommend treatment of all HIV-infected infants aged \(<12\) months, regardless of clinical status, CD4 percentage, or viral load (AI for infants aged \(<12\) weeks and AII for infants aged \(\geq 12\) weeks to 12 months).
- The Panel discusses current adult antiretroviral (ARV) guidelines and similarities and differences between children and adults. Adult guidelines have been modified to recommend treatment for
all HIV-infected individuals, with the strength of the recommendation based on the pre-treatment CD4 cell count.

- In addition to recommending treatment for all children with AIDS or significant HIV-related symptoms (AI*), the Panel also generally recommends treatment for all children aged ≥1 year with minimal or no symptoms (Clinical Categories N and A, or Clinical Category B disease due to a single episode of bacterial infection), with the strength of recommendation based on age and CD4 cell count/percentage. However, on a case-by-case basis, providers may elect to defer therapy based on clinical and/or psychosocial factors.

- ART should be initiated in HIV-infected children aged ≥1 year with minimal or no symptoms with the following CD4 values:
  - Aged 1 to <3 years:
    With CD4 cell count <1000 cells/mm3 or CD4 percentage <25% (AII)
  - Aged 3 to <5 years:
    With CD4 cell count <750 cells/mm3 or CD4 percentage <25% (AII)
  - Aged ≥5 years:
    With CD4 cell count ≤500 cells/mm3 (AI* for CD4 cell count <350 cells/mm3, BII* for CD4 cell count 350–500 cells/mm3)

- ART should be considered for HIV-infected children aged ≥1 year with minimal or no symptoms with the following CD4 values:
  - Aged 1 to <3 years:
    With CD4 cell count ≥1000 cells/mm3 or CD4 percentage ≥25% (BIII)
• Aged 3 to <5 years:
  With CD4 cell count ≥750 cells/mm3 or CD4
  percentage ≥25% (BIII)
• Aged ≥5 years:
  With CD4 cell count >500 cells/mm3 (BIII)

• In children with lower-strength (B level) recommendations for
treatment, plasma HIV RNA levels >100,000 copies/mL provide
stronger evidence for initiation of treatment (BII).

Specific recommendations for combination antiretroviral therapy for
pediatric HIV patients include the following:183

• Tenofovir disoproxil fumarate (tenofovir) has recently been FDA-
  approved for children as young as age 2 years. Tenofovir, in
  combination with lamivudine or emtricitabine, is part of a
  Recommended nucleoside reverse transcriptase inhibitor (NRTI)
  combination for adolescents who are Tanner stage 4 or 5 (AI*),
  an Alternative choice for those who are Tanner stage 3, and
  reserved for Special Circumstances for those aged ≥2 years and
  Tanner stage 1 or 2.

• Etravirine and rilpivirine are also FDA-approved but are not
  recommended as initial therapy at this time because of lack of
  experience and dosing information in children.

• Boosted fosamprenavir is now FDA-approved for infants as
  young as age 4 weeks, provided that they were born at ≥38
  weeks’ gestation. However, because of palatability and lower
  drug exposure in young infants, boosted fosamprenavir, when
used in combination with 2 NRTIs, is an Alternative option only in infants and children aged 6 months and older.

- Darunavir with low-dose ritonavir is now FDA-approved and, when used in combination with 2 NRTIs, an Alternative regimen in children aged ≥3 years. Once-daily dosing of boosted darunavir in children aged <12 years is not recommended.
- Raltegravir is now FDA-approved for children aged ≥2 years, but are not recommended for initial therapy at this time because of insufficient data. Elvitegravir, another integrase inhibitor, is only available as a fixed-dose combination tablet containing elvitegravir/cobicistat/emtricitabine/tenofovir, and is FDA-approved for HIV-1-infected ARV treatment-naive adults, but not children aged <18 years. Given the lack of data in individuals aged <18 years, it cannot be considered for use as initial therapy in children at this time.

Proper care of pediatric HIV patients is essential in the management and suppression of the virus. Therefore, pediatric patients should work with pediatricians who are familiar with HIV in children. Without appropriate treatment, the virus will spread quickly in pediatric patients and will result in an increase in patient morbidity and mortality.

**HIV and Other STD’s**

There is a direct link between HIV and sexually transmitted diseases in patients. Patients who test positive for sexually transmitted diseases have an increased risk of testing positive for HIV. Since the virus is transmitted through sexual intercourse, it is common for patients to
test positive for a number of sexually transmitted diseases. The presence of other STD’s also increases the risk of transmitting HIV.

The presence of STD’s increases susceptibility to HIV by two mechanisms. STDs such as syphilis and herpes cause genital ulcers, which result in breaks in the genital tract or lining of the mucous membrane. These breaks in the skin provide a route of entry for the virus. The presence of these STD’s also results in increased inflammation, which increases the concentration of cells in the genital secretions. These cells serve as targets for HIV. The presence of STD’s increases the likelihood of transmitting HIV as there is a higher concentration of HIV in the genital secretions of those infected with other STD’s. This results in an increase in the amount of virus that is transmitted during sexual intercourse.

Patients who are infected with both HIV and other STD’s require treatment for both to prevent further spread of HIV. Treatment of other STD’s will also improve the results of HIV treatment as other infections can impact the patient’s immune system and provide an opportunity for HIV to spread more rapidly. Providers should work with their patients to develop a treatment plan that works to eliminate any other STD’s while also managing the spread of HIV. Special consideration must be made to any potential drug interactions or complications that may result from the presence of other STD’s.

**Social and Cultural Issues**

HIV impacts the patient in a variety of ways, and there are a number of social and cultural factors that must be considered to fully understand the impact the virus has on individuals and society as a
whole. While the transmission and progression of HIV is easy to understand from a medical standpoint, the socioeconomic and cultural factors associated with the virus are more difficult to understand.\textsuperscript{185}

\textit{Race}

The rate of HIV and AIDS among African Americans and Hispanics is disproportionately higher than it is in Caucasian populations.\textsuperscript{27} Even though there is no biological explanation for the disparity, there is still solid evidence that the disparity exists.\textsuperscript{186} African American and Hispanic women account for 77\% of all reported AIDS cases, yet they comprise less than 25\% of the total US population.\textsuperscript{4} African Americans account for 37\% of the total AIDS cases in the United States, yet they are only 12\% of the total population.\textsuperscript{4} Meanwhile, Hispanics account for 20\% of the AIDS cases, even though they make up only 13\% of the population.\textsuperscript{4}

Researchers have no concrete explanation as to why these disparities exist, although there are some theories. Health disparities are often linked to socioeconomic conditions, which are often linked to racial issues.\textsuperscript{187} When individuals are coping with socioeconomic disparities, healthcare is often secondary to other concerns such as housing, food and employment.\textsuperscript{126} In some racial groups, distrust of the healthcare system is common. This often results in some racial groups refusing medical care, thereby causing HIV to progress.\textsuperscript{188} While income may not be a barrier in these groups, distrust of the system may prevent them from obtaining early intervention and treatment.\textsuperscript{188}

Cultural barriers are another factor among these groups. In some populations, language barriers prevent patients from fully
understanding the information available.\textsuperscript{64} In other instances, cultural beliefs regarding sex, gender roles and the healthcare system may impact a patient’s willingness or ability to obtain appropriate services.\textsuperscript{188} Due to the diversity within this group, it can be difficult to provide targeted information and educational programming.\textsuperscript{126}

Fear and stigmatization regarding HIV and AIDS is also a factor with racial groups, which can often result in denial about HIV risk.\textsuperscript{189} It is necessary to present prevention education in a manner that is culturally and linguistically appropriate so that individuals are receptive to the message.\textsuperscript{74} It is best to disseminate information through channels that are accepted by the group, such as religious institutions, peer educators, elders, or respected community members.\textsuperscript{190} Utilizing these channels is crucial for obtaining respect and trust from members of the group.\textsuperscript{190} This also provides an avenue for reducing the stigma associated with the virus, as well as the stigma associated with obtaining the appropriate care.\textsuperscript{189}

Successful HIV programs understand the importance of tailoring programs to best meet the needs of diverse communities. It is best to obtain input from members of the group affected and develop a program that will address the key concerns of the group.\textsuperscript{190}

\textit{Socioeconomic status}

One of the key factors in HIV prevalence is socioeconomic status.\textsuperscript{187} In fact, research shows that HIV affects those of a lower socioeconomic status at a disproportionately higher rate.\textsuperscript{191} Additionally, socioeconomic status has a direct impact on the quality of life individuals will experience after being diagnosed with HIV.\textsuperscript{192} Research
shows that individuals who lack socioeconomic resources have a higher incidence of engaging in risky health behaviors. These behaviors can result in the transmission of HIV. While ethnicity is a factor in the HIV/AIDS epidemic, socioeconomic status has a stronger impact. Women of lower socioeconomic status are more likely to engage in riskier sexual practices, especially at a young age, and are less likely to use condoms. Homeless individuals are more likely to engage in unsafe behaviors and have a higher risk of becoming infected with HIV.

Socioeconomic status has a direct impact on an individuals’ HIV status. However, HIV can also cause socioeconomic problems for individuals living with the disease. HIV often impacts an individual’s ability to maintain employment; thereby reducing the amount of income the individual can access. Current research estimates that approximately 45% of people who are HIV positive are also unemployed. HIV has a significant impact on the physical and mental well being of the patient, which impacts the individual’s ability to secure and maintain regular employment.

Socioeconomic status also has an impact on the treatment of HIV positive patients. An individual’s socioeconomic status can impact access to treatment, resulting in delayed treatment initiation and increased progression of the virus. Lack of access to HIV treatment increases a patient’s morbidity and mortality rate. In fact, research shows a direct correlation between an individual’s socioeconomic status and probability of death from HIV. Individuals who lack adequate health insurance and access to preventative services are more prone to complications from HIV infection.
Gender
The rate of transmission for women in the U.S. is steadily increasing, and women who are HIV positive are impacted differently than their male counterparts.\footnote{193} Due to a host of social issues, women have a higher chance of becoming infected with HIV against their will. For example, many women do not have control over when and how they engage in sexual intercourse as a result of domestic violence, social and cultural expectations, and sexual violence.\footnote{194,195} Socially and culturally, there are a number of barriers that prevent women from getting the appropriate services and treatment necessary to properly manage the infection.\footnote{196}

Stigma
Due to a variety of factors, there is a great stigma associated with HIV.\footnote{189} For some, the fear of contracting the virus causes them to be fearful of those who are infected.\footnote{197} Others associate the virus with the behaviors that transmit it, which are often considered deviant or immoral.\footnote{185} The impact of such stigmas on patients can be extremely detrimental. Some patients have been excluded from family or community activities and have suffered psychological trauma as a result.\footnote{198} Others minimize the illness and delay medical care because they are concerned about how they will be perceived by others.\footnote{144} This can be very detrimental to the patient’s health as the virus is not properly managed during this time and will most likely progress at a much faster rate. It is important for providers to work with patients to address these concerns and encourage them to participate fully in the treatment process.
**Discrimination**

HIV positive individuals often report of specific instances of discrimination as a result of their status. In some instances, individuals have been denied or lost employment after disclosing that they are HIV positive. Other individuals have reported that they encountered discrimination from the educational system, social services, and other healthcare providers. However, HIV positive individuals are protected by federal law under Title II of the Americans with Disability Act of 1990 (ADA) and Section 504 of the Federal Rehabilitation Act of 1973, as amended. Therefore, individuals who feel they have been discriminated against can file a complaint with the Office for Civil Rights (OCR) of the U.S. Department of Health and Human Services.

**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.

Human immunodeficiency virus is a worldwide pandemic that has affected individuals since it was first discovered as the cause of rare cancers and infections in otherwise healthy individuals in 1981. Since the epidemic began, approximately sixty million people worldwide have contracted the disease and over thirty-five million have died from complications related to the virus. During the first twenty years of the epidemic, the virus spread rapidly. However, 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.
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/hivaids/

Please take time to help the NURSECE4LESS.COM course planners evaluate nursing knowledge needs met following completion of this course by completing the self-assessment Knowledge Questions after reading the article. Correct Answers, page 154
1. The most common strain of HIV-1 infecting most patients today is believed to have been transmitted by:
   a. Humans in Africa
   b. Cameroon chimps to humans
   c. Insects to humans
   d. West African parrots

2. True or False. In both confidential and anonymous testing, the patient is required to give informed consent.
   a. True
   b. False

3. In 2011, there were __________children worldwide who tested positive for HIV.
   a. 1.5 million
   b. 2.5 million
   c. 3.3 million
   d. None of the above

4. Post-test counseling regarding partner notification allows patients to:
   a. notify their partners themselves
   b. use a free-standing partner notification service
   c. have their name and identifying information kept confidential
   d. all of the above

5. True or False. Latex and polyurethane condoms are an ineffective means of preventing the transmission of HIV when used correctly.
   a. True
   b. False
6. The CDC 2011 Surveillance Report showed about ________new HIV infections per year.
   a. 50,000
   b. 37,000
   c. 25,000
   d. 125,000

7. True or False. HIV 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.
   a. True
   b. False

8. The WHO Classification System lists stage 1 symptoms as:
   a. moderate unexplained weight loss
   b. persistent generalized lymphadenopathy
   c. herpes zoster
   d. recurrent oral ulceration

9. The primary form of HIV screening is the:
   a. Complete blood count
   b. Sputum test
   c. ELISA (enzyme-linked immunosorbent assay) test
   d. Chest X-Ray

10. The common confirmatory test for HIV is the:
    a. Elisa test
    b. Western blot
    c. Chest X-Ray
    d. none of the above
11. **The World Health Organization recommends Clinical Stage Management for Stage 1 to include:**
   a. patient follow up every 6 – 12 months
   b. check for clinical signs of progression
   c. total lymphocyte count or CD4 cell count if available
   d. answers a and b above

12. **Seroconversion is the period of time:**
   a. between initial infection and the development of adequate antibodies
   b. when individuals often test positive for HIV
   c. when symptoms are experienced
   d. None of the above

13. **True or False. In patients with a CD4 cell count below 200, an immunization vaccination will not work properly.**
   a. True
   b. False

14. **Early antiretroviral therapy (ART) commonly included:**
   a. the use of a singular drug to treat the virus
   b. use of antiretroviral drug zidovudine or azidothymidine
   c. dual drugs to combat infection
   d. answers a and b above

15. **True or False. The strength of ART recommendation varies on the basis of pre-treatment CD4 cell count.**
   a. True
   b. False
16. True or False. Patients who experience lipodystrophy often have low insulin levels.
   a. True
   b. False

17. The CCR5 antagonist:
   a. was first approved by the FDA in 2007
   b. is used as a new line of defense against viral replication
   c. helps prevent cellular fusion between the virus and host cell
   d. all of the above

18. Treatment for patients co-infected with HIV/HBV include:
   a. ART with ABV treatment irrespective of CD4 cell count
   b. ART with ABV treatment irrespective of clinical stage
   c. Tenofovir Disoproxil Fumarate and lamivudine, epivir or emtricitabine antiretroviral regimens
   d. All of the above

19. True or False. There is a direct link between HIV and sexually transmitted diseases.
   a. True
   b. False

20. True or False. HIV-infected women should receive evaluation and appropriate prophylaxis for opportunistic infections (OIs), however, vaccinations indicated for persons with HIV infection should be avoided until after childbirth.
   a. True
   b. False
Correct Answers:

<p>| | | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>b</td>
<td>11.</td>
<td>d</td>
<td></td>
</tr>
<tr>
<td>2.</td>
<td>a</td>
<td>12.</td>
<td>a</td>
<td></td>
</tr>
<tr>
<td>3.</td>
<td>c</td>
<td>13.</td>
<td>a</td>
<td></td>
</tr>
<tr>
<td>4.</td>
<td>d</td>
<td>14.</td>
<td>d</td>
<td></td>
</tr>
<tr>
<td>5.</td>
<td>b</td>
<td>15.</td>
<td>a</td>
<td></td>
</tr>
<tr>
<td>6.</td>
<td>a</td>
<td>16.</td>
<td>b</td>
<td></td>
</tr>
<tr>
<td>7.</td>
<td>a</td>
<td>17.</td>
<td>d</td>
<td></td>
</tr>
<tr>
<td>8.</td>
<td>b</td>
<td>18.</td>
<td>d</td>
<td></td>
</tr>
<tr>
<td>9.</td>
<td>c</td>
<td>19.</td>
<td>a</td>
<td></td>
</tr>
<tr>
<td>10.</td>
<td>b</td>
<td>20.</td>
<td>b</td>
<td></td>
</tr>
</tbody>
</table>

Footnotes:


31. Hamouda O. Global Epidemiology of HIV. Sexually Transmitted Infections and Sexually Transmitted Diseases 2011: 249-270.


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.


58. Fleming DT, Wasserheit JN. From epidemiological synergy to public health policy and practice: the contribution of other sexually transmitted diseases to sexual transmission of HIV infection. Sex Transm Infect 1999;75:3-17.


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.


164. Neuhaus J, Angus B, Kowalska JD, et al; INSIGHT SMART and ESPRIT study groups. Risk of all-cause mortality associated with nonfatal AIDS and serious


187. An Q, Prejean J, McDavid Harrison K, Fang X. Association between community socioeconomic position and HIV diagnosis rate among adults and adolescents


The information presented in this course is intended solely for the use of healthcare professionals taking this course, for credit, from NurseCe4Less.com. The information is designed to assist healthcare professionals, including nurses, in addressing issues associated with healthcare.

The information provided in this course is general in nature, and is not designed to address any specific situation. This publication in no way absolves facilities of their responsibility for the appropriate orientation of healthcare professionals. Hospitals or other organizations using this publication as a part of their own orientation processes should review the contents of this publication to ensure accuracy and compliance before using this publication.

Hospitals and facilities that use this publication agree to defend and indemnify, and shall hold NurseCe4Less.com, including its parent(s), subsidiaries, affiliates, officers/directors, and employees from liability resulting from the use of this publication.

The contents of this publication may not be reproduced without written permission from NurseCe4Less.com.