

## HUMAN IMMUNODEFICIENCY VIRUS: A REVIEW

Anuru Sen\*, Arpita Biswas and Dr. Dhrubo Jyoti Sen

Department of Pharmaceutical Chemistry, School of Pharmacy, Techno India University, Salt-Lake City, Sector-V, EM-4, Kolkata-700091, West Bengal, India.

Received date: 20 March 2022

Revised date: 10 April 2022

Accepted date: 01 May 2022

\*Corresponding Author: Anuru Sen

Department of Pharmaceutical Chemistry, School of Pharmacy, Techno India University, Salt-Lake City, Sector-V, EM-4, Kolkata-700091, West Bengal, India.

### ABSTRACT

HIV (human immunodeficiency virus) is a virus that attacks the body's immune system. If HIV is not treated, it can lead to AIDS (acquired immunodeficiency syndrome). Learning the basics about HIV can keep you healthy and prevent HIV transmission. The human immunodeficiency virus (HIV) is a retrovirus – a virus built of RNA instead of more typical DNA. It attacks the very cells of the immune system that should be protecting the body against it – T lymphocytes and other white blood cells with CD4 receptors on their surfaces. The virus destroys a type of white blood cell in the immune system called a T-helper cell, and makes copies of itself inside these cells. T-helper cells are also referred to as CD4 cells. As HIV destroys more CD4 cells and makes more copies of itself, it gradually weakens a person's immune system. This means that someone who has HIV, and isn't taking antiretroviral treatment, will find it harder and harder to fight off infections and diseases. If HIV is left untreated, it may take up to 10 or 15 years for the immune system to be so severely damaged that it can no longer defend itself at all. Many of the clinical features of HIV/AIDS can be ascribed to the profound immune deficiency which develops in infected patients. The destruction of the immune system by the virus results in opportunistic infection, as well as an increased risk of autoimmune disease and malignancy. In addition, disease manifestations related to the virus itself may occur. For example, during the primary illness which occurs within weeks after first exposure to HIV, clinical symptoms occur in at least 50% of cases, typically as a mononucleosis syndrome. HIV-related complications are rarely encountered in patients with preserved immunity (i.e. CD4 T-cell counts greater than 500 cells/mm<sup>3</sup>). Recurrent mucocutaneous herpes simplex (HSV), herpes zoster (VZV), oral candidiasis and oral hairy leukoplakia occur with increasing frequency as the CD4 count drops below this level. Immune thrombocytopenia (ITP) occurs in association with HIV and often presents early in the clinical course. The risk of developing opportunistic infections and malignancies typical of AIDS increases progressively as CD4 counts fall below 200 cells/mm<sup>3</sup>.

**KEYWORDS:** AIDS, HIV, ITP, HSV, CD4, ART.



Figure-1: Red ribbon of AIDS.

### INTRODUCTION

The human immunodeficiency viruses (HIV) are two species of *Lentivirus* (a subgroup of retrovirus) that

infect humans. Over time, they cause acquired immunodeficiency syndrome (AIDS), a condition in which progressive failure of the immune system allows

life-threatening opportunistic infections and cancers to thrive. Without treatment, average survival time after infection with HIV is estimated to be 9 to 11 years, depending on the HIV subtype.<sup>[1]</sup> In most cases, HIV is a sexually transmitted infection and occurs by contact with or transfer of blood, pre-ejaculate, semen, and vaginal fluids. Research has shown (for both same-sex and opposite-sex couples) that HIV is untransmittable through condomless sexual intercourse if the HIV-positive partner has a consistently undetectable viral load. Non-sexual transmission can occur from an infected mother to her infant during pregnancy, during childbirth by exposure to her blood or vaginal fluid, and through breast milk. Within these bodily fluids, HIV is present as both free virus particles and virus within infected immune cells.<sup>[2]</sup>

HIV infects vital cells in the human immune system, such as helper T cells (specifically CD4<sup>+</sup> T cells), macrophages, and dendritic cells. HIV infection leads to low levels of CD4<sup>+</sup> T cells through a number of mechanisms, including pyroptosis of abortively infected T cells, apoptosis of uninfected bystander cells, direct viral killing of infected cells, and killing of infected CD4<sup>+</sup> T cells by CD8<sup>+</sup> cytotoxic lymphocytes that recognize infected cells. When CD4<sup>+</sup> T cell numbers decline below a critical level, cell-mediated immunity is lost, and the body becomes progressively more susceptible to opportunistic infections, leading to the development of AIDS.

**Why HIV-AIDS is a syndrome?** Acquired immunodeficiency syndrome (AIDS) is a chronic, potentially life-threatening condition caused by the human immunodeficiency virus (HIV). By damaging your immune system, HIV interferes with your body's ability to fight infection and disease.

**History of AIDS-HIV:** Infection in humans came from a type of chimpanzee in Central Africa.

The chimpanzee version of the virus (called simian immunodeficiency virus, or SIV) was probably passed to humans when humans hunted these chimpanzees for meat and came in contact with their infected blood.

- Studies show that HIV may have jumped from chimpanzees to humans as far back as the late 1800s.

- Over decades, HIV slowly spread across Africa and later into other parts of the world. We know that the virus has existed in the United States since at least the mid to late 1970s.<sup>[3]</sup>

**Stages of HIV:** Stage 1: Acute HIV Infection

- People have a large amount of HIV in their blood. They are very contagious.
- Some people have flu-like symptoms. This is the body's natural response to infection.
- But some people may not feel sick right away or at all.
- If you have flu-like symptoms and think you may have been exposed to HIV, seek medical care and ask for a test to diagnose acute infection.
- Only antigen/antibody tests or nucleic acid tests (NATs) can diagnose acute infection.

Stage 2: Chronic HIV Infection

- This stage is also called asymptomatic HIV infection or clinical latency.
- HIV is still active but reproduces at very low levels.
- People may not have any symptoms or get sick during this phase.
- Without taking HIV medicine, this period may last a decade or longer, but some may progress faster.
- People can transmit HIV in this phase.
- At the end of this phase, the amount of HIV in the blood (called *viral load*) goes up and the CD4 cell count goes down. The person may have symptoms as the virus levels increase in the body, and the person moves into Stage 3.
- People who take HIV medicine as prescribed may never move into Stage 3.

Stage 3: acquired immunodeficiency syndrome (AIDS)

- The most severe phase of HIV infection.
- People with AIDS have such badly damaged immune systems that they get an increasing number of severe illnesses, called opportunistic infections.
- People receive an AIDS diagnosis when their CD4 cell count drops below 200 cells/mm, or if they develop certain opportunistic infections.
- People with AIDS can have a high viral load and be very infectious.
- Without treatment, people with AIDS typically survive about three years.<sup>[4]</sup>

Species	Virulence	Infectivity	Prevalence	Inferred origin
HIV-1	High	High	Global	Common chimpanzee
HIV-2	Lower	Low	West Africa	Sooty mangabey

The human immunodeficiency virus (HIV) is grouped to the genus *Lentivirus* within the family of *Retroviridae*, subfamily *Orthoretrovirinae*. On the basis of genetic

characteristics and differences in the viral antigens, HIV is classified into the types 1 and 2 (HIV-1, HIV-2).

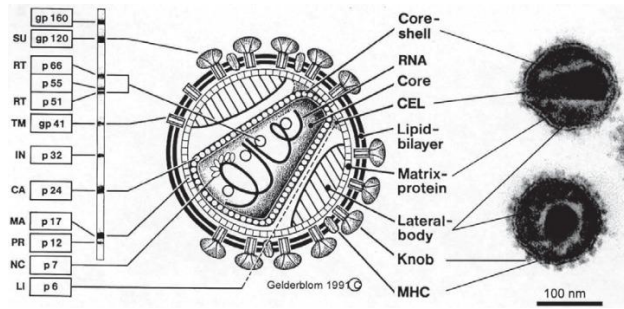


Figure-2: HIV genome.

**Difference between HIV-1 & HIV-2:** It is the most common type of HIV and accounts for 95% of all infections, whereas HIV-2 is relatively uncommon and less infectious. HIV-2 is mainly concentrated in West Africa and the surrounding countries. HIV-2 is less fatal and progresses more slowly than HIV-1.<sup>[5]</sup>

**Causes of HIV:** HIV infection is caused by the human immunodeficiency virus. You can get HIV from contact with infected blood, semen, or vaginal fluids.

- Most people get the virus by having unprotected sex with someone who has HIV.
- Another common way of getting it is by sharing drug needles with someone who is infected with HIV.
- The virus can also be passed from a mother to her baby during pregnancy, birth, or breastfeeding.

HIV doesn't survive well outside the body. So it can't be spread by casual contact like kissing or sharing drinking glasses with an infected person.

**Symptoms:** HIV may not cause symptoms early on. People who do have symptoms may mistake them for the flu or mono. Common early symptoms include:

- Fever.
- Sore throat.

- Headache.
- Muscle aches and joint pain.
- Swollen glands (swollen lymph nodes).
- Skin rash.

Symptoms may appear from a few days to several weeks after a person is first infected. The early symptoms usually go away within 2 to 3 weeks. Within a few weeks of HIV infection, flu-like symptoms such as fever, sore throat and fatigue can occur. Then the disease is usually asymptomatic until it progresses to AIDS. AIDS symptoms include weight loss, fever or night sweats, fatigue and recurrent infections. First main symptoms of HIV is Fever. Many people also experience other flu-like symptoms as the disease manifests itself two to four weeks after exposure. This early, acute phase of HIV can last up to several weeks.<sup>[6]</sup> After the early symptoms go away, an infected person may not have symptoms again for many years. After a certain point, symptoms reappear and then remain. These symptoms usually include:

- Swollen lymph nodes.
- Extreme tiredness.
- Weight loss.
- Fever.
- Night sweats.

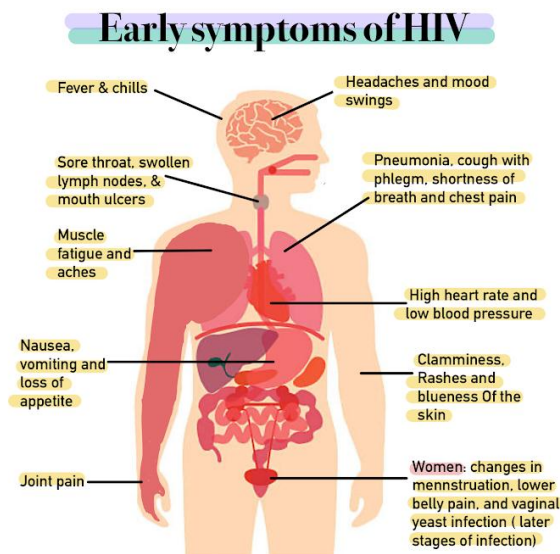


Figure-3: HIV diagnosis.

**Diagnosis of HIV:** Blood tests are the most common way to diagnose HIV. These tests look for antibodies to the virus that the body creates in an attempt to fight the virus. People exposed to the virus should get tested immediately, although it can take the body anywhere from six weeks to a year to develop antibodies to the virus.

- Antigen/antibody tests. These tests usually involve drawing blood from a vein. Antigens are substances on the HIV virus itself and are usually detectable — a positive test — in the blood within a few weeks after exposure to HIV. Antibodies are produced by your immune system when it's exposed to HIV. It can take weeks to months for antibodies to become detectable. The combination antigen/antibody tests can take two to six weeks after exposure to become positive.<sup>[7]</sup>
- Antibody tests. These tests look for antibodies to HIV in blood or saliva. Most rapid HIV tests, including self-tests done at home, are antibody tests. Antibody tests can take three to 12 weeks after you're exposed to become positive.
- Nucleic acid tests (NATs). These tests look for the actual virus in your blood (viral load). They also involve blood drawn from a vein. If you might have been exposed to HIV within the past few weeks, your doctor may recommend NAT. NAT will be the first test to become positive after exposure to HIV.

Tests to stage disease and treatment

- Determine whether you need additional testing
- Determine which HIV antiretroviral therapy (ART) will be best for you
- Monitor your progress and work with you to manage your health

Diagnosis of HIV/AIDS, several tests can help your doctor determine the stage of your disease and the best treatment, including:

- CD4 T cell count. CD4 T cells are white blood cells that are specifically targeted and destroyed by HIV.

Even if you have no symptoms, HIV infection progresses to AIDS when your CD4 T cell count dips below 200.

- Viral load (HIV RNA). This test measures the amount of virus in your blood. After starting HIV treatment the goal is to have an undetectable viral load. This significantly reduces your chances of opportunistic infection and other HIV-related complications.
- Drug resistance. Some strains of HIV are resistant to medications. This test helps your doctor determine if your specific form of the virus has resistance and guides treatment decisions.

**Treatment of HIV:** Currently, there's no cure for HIV/AIDS. Once you have the infection, your body can't get rid of it. However, there are many medications that can control HIV and prevent complications. These medications are called antiretroviral therapy (ART). Everyone diagnosed with HIV should be started on ART, regardless of their stage of infection or complications.<sup>[8]</sup>

ART is usually a combination of three or more medications from several different drug classes. This approach has the best chance of lowering the amount of HIV in the blood. There are many ART options that combine three HIV medications into one pill, taken once daily.

Each class of drugs blocks the virus in different ways. Treatment involves combinations of drugs from different classes to:

- Account for individual drug resistance (viral genotype)
- Avoid creating new drug-resistant strains of HIV
- Maximize suppression of virus in the blood

Two drugs from one class, plus a third drug from a second class, are typically used.



**Figure-4: HIV virus.**

The classes of anti-HIV drugs include:

- Non-nucleoside reverse transcriptase inhibitors (NNRTIs) turn off a protein needed by HIV to make copies of itself. Examples include efavirenz (Sustiva), rilpivirine (Edurant) and doravirine (Pifeltro).
- Nucleoside or nucleotide reverse transcriptase inhibitors (NRTIs) are faulty versions of the building blocks that HIV needs to make copies of

itself. Examples include abacavir (Ziagen), tenofovir (Viread), emtricitabine (Emtriva), lamivudine (Epivir) and zidovudine (Retrovir). Combination drugs also are available, such as emtricitabine/tenofovir (Truvada) and emtricitabine/tenofovir alafenamide (Descovy).

- Protease inhibitors (PIs) inactivate HIV protease, another protein that HIV needs to make copies of itself. Examples include atazanavir (Reyataz), darunavir (Prezista) and lopinavir/ritonavir (Kaletra).
- Integrase inhibitors work by disabling a protein called integrase, which HIV uses to insert its genetic material into CD4 T cells. Examples include bictegravir sodium/emtricitabine/tenofovir alafenamide fumar (Biktarvy), raltegravir (Isentress) and dolutegravir (Tivicay).
- Entry or fusion inhibitors block HIV's entry into CD4 T cells. Examples include enfuvirtide (Fuzeon) and maraviroc (Selzentry).
- Keep your immune system strong
- Reduce your chances of getting an infection
- Reduce your chances of developing treatment-resistant HIV

- Reduce your chances of transmitting HIV to other people

Staying on HIV therapy can be challenging. It's important to talk to your doctor about possible side effects, difficulty taking medications, and any mental health or substance use issues that may make it difficult for you to maintain ART.

Having regular follow-up appointments with your doctor to monitor your health and response to treatment is also important.<sup>[9]</sup> Let your doctor know right away if you're having problems with HIV therapy so that you can work together to find ways to address those challenges. Treatment side effect. Treatment side effects can include:

- Nausea, vomiting or diarrhea
- Heart disease
- Kidney and liver damage
- Weakened bones or bone loss
- Abnormal cholesterol levels
- Higher blood sugar
- Cognitive and emotional problems, as well as sleep problems

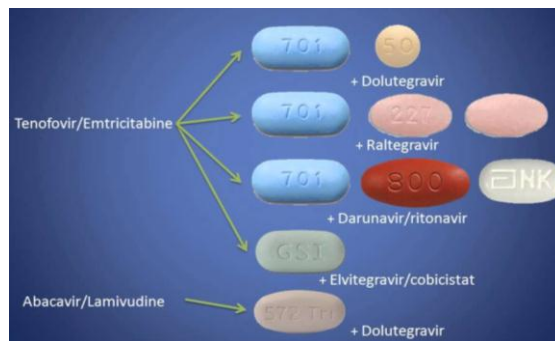


Figure-5: AIDS medicines.

**Medicines used in HIV:** U.S. Food and Drug Administration (FDA) has approved more than 30 HIV medicines to treat HIV infection. Some HIV medicines are available in combination (in other words, two or more different HIV medicines combined in one pill). HIV medicines are grouped into seven drug classes according to how they fight HIV.<sup>[10,11]</sup>

- Didanosine (Videx, dideoxyinosine, ddI)
- Emtricitabine (Emtriva, FTC)
- Lamivudine (Epivir, 3TC)
- Stavudine (Zerit, d4T)
- Tenofovir (Viread, TDF)
- Zalcitabine (Hivid, ddC)
- Zidovudine (Retrovir, ZDV or AZT)

Names of medicines are-

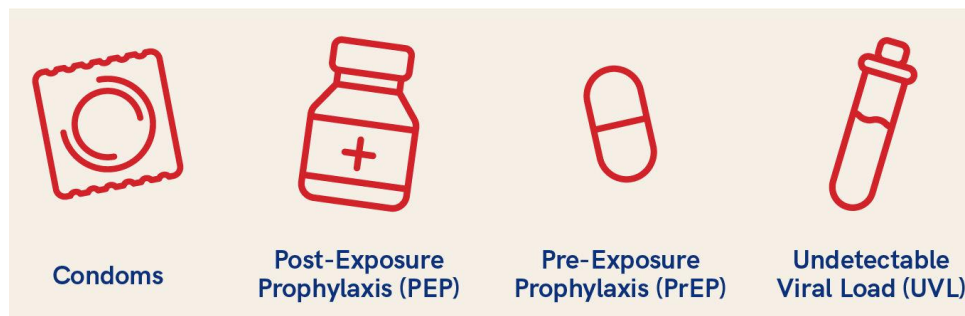
- Abacavir (Ziagen, ABC)



Figure-6: Medicine of AIDS.

**Prevention of HIV:** Practice safer sex. Use a condom every time you have sex (including oral sex) until you are sure that you and your partner aren't infected with HIV or other sexually transmitted infection (STI).<sup>[11]</sup>

- Don't have more than one sex partner at a time. The safest sex is with one partner who has sex only with you.
- Talk to your partner before you have sex the first time. Find out if he or she is at risk for HIV. Get tested together. Use condoms in the meantime.
- Don't drink a lot of alcohol or use illegal drugs before sex. You might let down your guard and not practice safer sex.
- Don't share personal items, such as toothbrushes or razors.
- Never share needles or syringes with anyone.
- People whose sexual practices put them at high risk for HIV infection, such as men who have sex with men and people who have many sex partners.
- People who inject illegal drugs, especially if they share needles.
- Adults who have a sex partner with HIV.



**Figure-7: Devices for safe sex.**

## CONCLUSION

HIV/AIDS is the deadliest epidemic of our time. Over 22 million people have already lost their lives, and more than 42 million are currently living with HIV/AIDS. Even if a vaccine for HIV were discovered today, over 40 million people would still die prematurely as a result of AIDS.

## REFERENCES

1. Blower SM, Bodine E, Kahn J, McFarland W. The antiretroviral rollout and drug-resistant HIV in Africa: insights from empirical data and theoretical models. *AIDS*, 2005; 19: 1–14.
2. Cohen MS, Gay C, Kashuba AD, Blower S, Paxton L. Narrative review: antiretroviral therapy to prevent the sexual transmission of HIV-1. *Ann Intern Med*, 2007; 146(8): 591–601.
3. Weiss RA. Special anniversary review: twenty-five years of human immunodeficiency virus research: successes and challenges. *Clin Exp Immunol*, 2008; 152(2): 201–10.
4. Children and AIDS Fifth stocktaking report. New York: United Nations Children's Fund, 2010.
5. WHO; UNICEF; UNAIDS. Global update on HIV treatment 2013: results, impact and opportunities. Geneva: World Health Organization; 2013.
6. Global report: UNAIDS report on the global AIDS epidemic 2013. Geneva: Joint United Nations Programme on HIV/AIDS; 2013.
7. Kasedde S, et al. Reducing HIV and AIDS in adolescents: opportunities and challenges. *Current HIV/AIDS Report*, 2013; 10: 159–168.
8. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Geneva: World Health Organization, 2013.
9. UNAIDS World AIDS Day report—Results. World AIDS Day Report. Geneva: Joint United Nations Programme on HIV and AIDS; 2012. <http://www.unaids.org/en/resources/publications/2012/name,76120,en.asp>.
10. Nachega JB, et al. Antiretroviral therapy adherence, virologic and immunologic outcomes in adolescents compared with adults in southern Africa. *Journal of Acquired Immune Deficiency Syndromes*, 2009; 51(1): 65–71.
11. Kushal Nandi, Pritam Bakshi, Sandip Sarkar, Subhanjana Guha, Shreya Sarkar, Maitri Sahoo, Souradip Mandal, Tanistha Mumtaz Chatterjee, Barnamoni Saha, Anirbita Ghosh, Dr. Dhruvo Jyoti Sen, Shaktijit Das, Dr. Partha Ranjan Bhattacharya and Dr. Beduin Mahanti; Analysis of the blueprint of HIV: *European Journal of Biomedical and Pharmaceutical Sciences*, 2020; 7(7): 306–318.