HIV as a Retrovirus

By Dr. Lita Kurle

When HIV invades the body, it looks for cells called CD4+ T lymphocytes, the targeted host cell. (See diagram). These CD4+ cells play a significant role in the body's immune system. What makes HIV infection serious and eventually fatal is that when the virus is replicated in enormous quantity, it gradually weakens the immune system. The clinical condition called AIDS is characterized by a significantly weakened immune system measured as a CD4+ count less than 200/ml of blood. The total collapse of the very protection that the body needs to fight off the infection and later other infections is the cause of death for people living with AIDS.

Here's how HIV affects the human immune system:

1. HIV first attaches to and penetrates its target cell.

2. HIV releases ribonucleic acid (RNA)**,** the genetic code of the virus, and an enzyme called reverse transcriptase into the cell. For the virus to replicate, its RNA must be converted into DNA using the viral RNA as a pattern. This reverses the pattern of human cells, which copy RNA from the pattern of human DNA (thus the term "retro" for "backward"). Reverse transcriptase performs this conversion from viral RNA to viral DNA. HIV mutates itself at this point, because reverse transcriptase is prone to errors during this conversion from viral RNA to viral DNA.

3. The viral DNA enters the cell's nucleus. Once inside, HIV finds the host cell DNA in the cell nucleus. HIV makes a copy of itself from the host cell DNA.

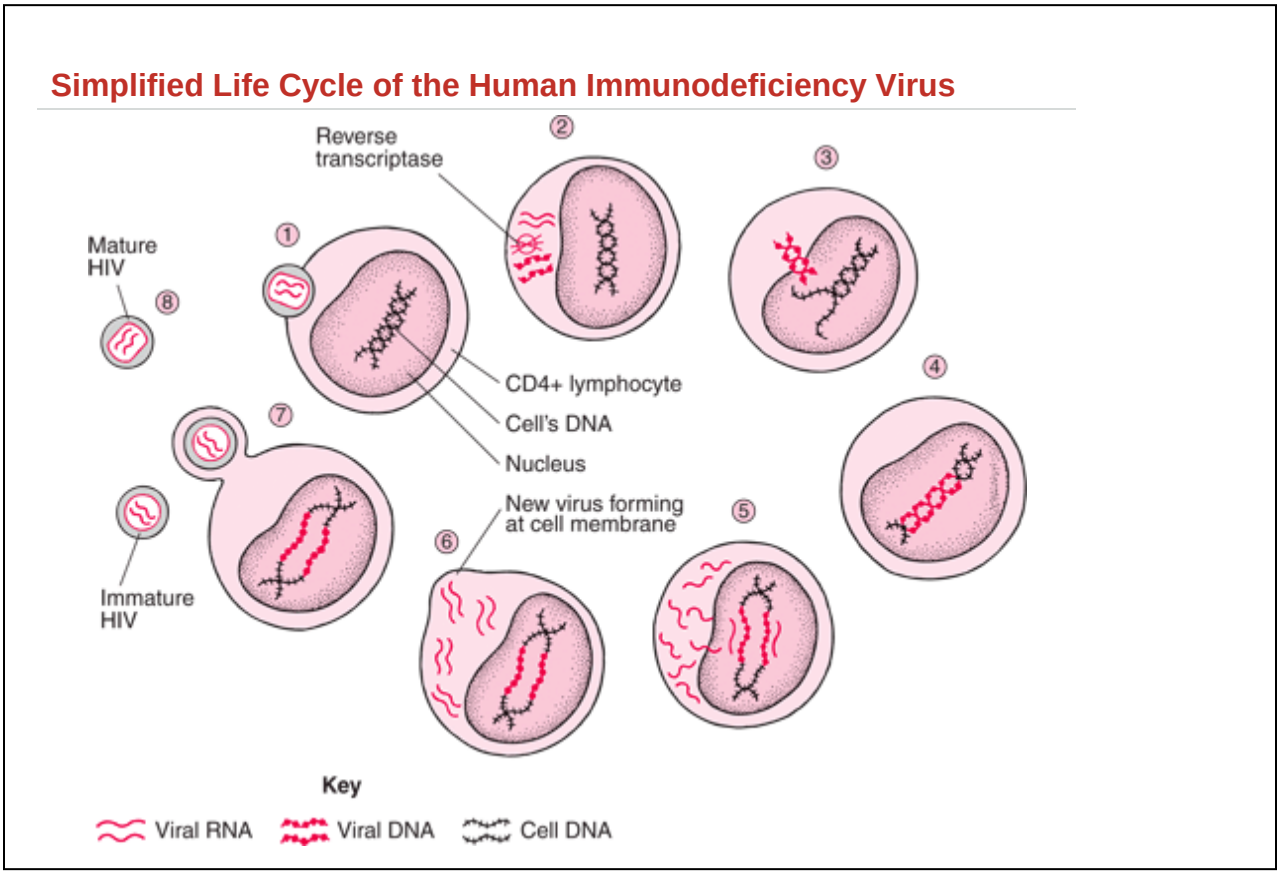
4. With the help of another enzyme called integrase, the viral DNA becomes integrated with the host cell's DNA. The viral DNA often hides itself in the cell's DNA. Under the microscope, the cell's DNA appears normal, even though it is now mixed with HIV DNA.

5. Once safely hidden in the cell's DNA, the HIV can do one of two things. It can stay quietly in the cell, or it can turn on the cell's DNA and use the cell's machinery to make copies of itself. If it begins reproducing, it can make millions of new HIV. Some scientists think the virus makes a billion copies of itself a day.

6. The HIV DNA now replicates and reproduces HIV RNA and proteins.
   A new virus is assembled from this RNA and short pieces of protein.

7. The virus buds through the membrane of the host cell, wrapping itself in a fragment of the cell membrane (envelope).

8. To be able to infect other cells, the budded virus must mature. Another viral enzyme called protease performs this process by cutting and rearranging the viral proteins. These new viruses leave the cell and enter other CD4+ cells and the process repeats itself.



There is more to know about HIV; How do we contract this fatal virus? What does it do to the immune system? Not everyone who has HIV has AIDS - What's the difference? The fool-proof way to avoid HIV/AIDS.

How a Person Gets Infected with HIV

HIV is a unique virus in that it is not spread through the air like most other viruses such as the common cold virus, the flu virus, measles, mumps and others. HIV is not spread by being in the same room with an infected person, touching, hugging, mosquito bites, etc. HIV is spread through the intermingling or exchange of body fluids that contain the virus. HIV can appear in nearly any body fluid, but transmission mainly comes from blood, semen, vaginal secretions, and breast milk. Transmission from tears, saliva, and urine is extremely rare.

The two basic ways for exchange of body fluids are: (*Life at the CrossRoads* Curriculum)

1. **Virus-to-blood contact.** The virus found in the blood may enter the bloodstream of another person through injection drug use (sharing contaminated needles and syringe) or transfusion of contaminated blood. Currently, HIV spread through blood transfusion is extremely uncommon because the blood supply is thoroughly screened. However more than 90% of people exposed to infected blood will become infected (Optimal Sexual Health:Scientific Dimension, Medical Institute for Sexual Health –slide 7)

2. **Virus-to-mucus membrane contact.** Mucus membrane is a special kind of tissue composed of cells that secrete mucus. It lines the mouth, vaginal area, anus and the tip of the penis providing moisture. HIV in an infected person is present in body fluids such as semen, vaginal secretions, blood, and breast milk. When sexual intercourse takes place between an HIV+ person and HIV- person, semen and vaginal fluids are exchanged (intermingled) and the virus comes in contact with the mucus membrane lining of the genital areas and enters CD4+ T cells, highly concentrated in the membrane. Most of the new cases of HIV have been spread through heterosexual intercourse.

Common Ways HIV Spreads:

1. Sexual activity

- *Heterosexual or Vaginal Intercourse.* Most new HIV infection has taken place through vaginal (heterosexual) intercourse. The virus can spread easily from male to female or female to male. The pre-ejaculatory fluid of an infected person contains HIV, so this means that withdrawal prior to ejaculation does not necessarily prevent infection. A study has shown that HIV hides in the testicles and can dodge powerful antiretroviral drugs (BBC news article – Feb 4, 2007). Heterosexual transmission has become the leading cause of the HIV epidemic in Sub-Saharan Africa, and the number one driving force is having **multiple concurrent partners**. (*Evidence that Demands Action* – Dr. Edward Green).
- *Men Having Sex with Men* (*MSM)* Unprotected receptive anal intercourse poses the highest risk in contracting HIV (Optimal Sexual Health: Scientific Dimension, Medical Institute for Sexual Health , slide 10). In other words, anal sex is the most certain way HIV can infect a person because of its violent, forceful nature. The thin lining of the rectum more easily tears than the thicker, more resilient vaginal lining. Any break in the rectal lining provides an easy entry into the bloodstream. MSM have the highest risk of getting a new infection. (MISH- slide 7)
- *Oral Sex* HIV contained in the sexual fluid can enter the bloodstream in the presence of abrasions, inflammation, or any kind of break in the mouth.
- *Presence of Other Sexually Transmitted Infections (STIs)* STIs enhance HIV transmission. Sores associated with STIs such as syphilis and herpes are easy portals for HIV. Pus in gonorrhea contains lymphocytes that may have been invaded by the virus. Studies have shown that treating other STIs reduces the risk of HIV infection.

2. **Injection Drug Use**
    - *Drug Abuse* – People who inject drugs directly into their veins (IV drug use) can contract HIV when they use a HIV contaminated syringe or needle.
    - *Injections with Contaminated Syringes* – This can happen in hospitals or clinics where they reuse contaminated syringes and needles. A patient must ask if needles and syringes used for injection medications are sterilized or new.
    - *Tattooing* – the same principle of reused contaminated needles applies. The best prevention is to avoid the risk all together by not getting a tattoo.

3. **Mother-to-Child Transmission (MTCT/Vertical Transmission)**
    - *During birth* – 2/3 of MTCT happens when the baby passes through the vaginal canal during birth because of blood contact especially when the baby's skin has cuts or abrasions.
    - *Breast feeding* – 1/3 of MTCT happens through the breast milk during nursing.. The risk to the baby increases as breast feeding continues. Antiretroviral drugs have dramatically reduced the MTCT risk to about 5%. Expectant mothers who might have been exposed to HIV should go for voluntary testing and counseling (VTC).

4. **Blood Transfusions**
    When HIV had not been identified in the blood, blood transfusion was highly risky. Now blood is so thoroughly screened for HIV that the risk of getting infected is uncommon. A sure way to prevent this mode of transmission is for a patient who might need blood during surgery or a medical procedure to donate his own blood before treatment or get trusted family to donate blood.

5. **Organ Transplant**
    This is another highly risky way to be infected with HIV. It is absolutely necessary to test donor tissues for HIV.

What Happens After a Person Gets Infected with HIV

HIV progressively destroys the immune system. It results in a wide range of conditions varying from asymptomatic (carrier) state to a severe, fatal condition called autoimmune deficiency syndrome or AIDS (Merck Manual, p.1312). AIDS is the full blown stage of the infection. It is a syndrome, meaning it constitutes a group of diseases that result when a person's immune system is damaged by HIV. Many factors including age, nutrition, immunity and medication determine the disease progression into AIDS.

When a person is exposed to HIV, the virus multiplies and spreads within 4-11 days (MISH, slide 8). It invades or attaches to special white cells called CD4+ lymphocytes, a vital part of the body's immune system.

The initial phase is also called the **primary or acute phase** of the infection, which occurs two to four weeks after exposure to the virus (Merck Source, Resource Library, p.1). "This acute phase can resemble the flu, infectious mononucleosis, or other viral infections. Typical symptoms include fever, headache, fatigue, and swollen nodes. People may also experience aching muscles and a rash that occurs on any part of the body and may change locations. These symptoms may last for a few days or weeks, and then subside" A new study has also revealed that the highest concentration of virus (viral load) has been found in the semen 3-4weeks of the primary infection and during the advanced stage. Research has shown that individuals recently infected with HIV probably do not know it and will even test negative. This is because the body has not yet produced sufficient antibodies to be detected by testing. These people are just as infectious as those with advanced HIV disease, but because they do not realize they are carrying the virus, they may continue infecting sexual partners.

The time frame during which a person is infected with HIV but tests negative may last up to six months and is called the <u>window period.</u>

After an infection with HIV, antibodies to the virus can be detected in the blood. This is called HIV **seroconversion** (converting from HIV negative to HIV positive), and it occurs within three months of exposure, but on rare occasions may occur up to a year of exposure.

"Following the acute infection, there may be no further evidence of illness for a decade. Acute HIV infection can, but does not always, progress to early symptomatic HIV infection and to advanced HIV disease (AIDS), but time has shown that the vast majority do." (Merck Resource Library, p.2)

How HIV Progresses to AIDS

"Immune" means safe and protected. The immune system is part of the body's defense against invasion of disease, especially infections caused by virus (the flu, HIV), bacteria (TB, typhoid fever), parasites (malaria, amebiasis) and fungi (oral thrush).

The immune system consists of several types of cells. The body is made of billions of tiny (microscopic) cells specialized to form different tissues, which in turn form organs such us the heart, the stomach, the brain, muscles, bones, blood, and the immune system.

Cells of the immune system, such as lymphocytes, like other cells in the body, have a center called the nucleus. The nucleus or the "headquarters" of the cell contains DNA (deoxyribonucleic acid). The sequences in the long spiral of DNA constitute genes. Genes determine what kinds of proteins need to be manufactured and also the traits that make a person unique.

The nucleus controls the cell's activities such as cell replication or the manufacture of substances (protein) needed by the body. For each person, the DNA found in all cells is

the same, though a particular cell uses a different section of the DNA to control its activities.

If the immune system is exposed to a virus or bacteria (from outside the body), it makes small (microscopic) particles made of protein called antibodies or immunoglobulins. The antibodies fight off the "invaders" by sticking to them and help the rest of the immune system find and destroy them. This immune response allows the body to avoid illness or to become well if already ill.

A special protein called CD4 marks the outside of some immune system cells (lymphocytes), making them different from other cells. The CD4 marking is like the stripes that make a zebra different from a horse. CD4 cells are also called helper T cells, because the body sends them to identify and defend against invaders like viruses and bacteria. What makes HIV different from other viruses is that it attacks, enters and eventually destroys CD4 marked cells, the very cells that seek to fight it off.

What makes HIV fatal is that when uncontrolled and allowed to multiply, the high concentration of the virus in the blood (viral load) will eventually destroy enough T helper cells (CD4+lympocytes) and therefore weaken the ability of the body to fight off infection. In other words the CD4+ lymphocyte level is so low that the body will easily succumb to other infections (hepatitis, tuberculosis) and other diseases like cancer (Kaposi's sarcoma, lymphoma) that will eventually cause death. These complications are called opportunistic infections or diseases. AIDS continues to be the primary cause of death for HIV infected people.

HIV Causes AIDS

AIDS (Acquired Immune Deficiency Syndrome) is the final and most serious stage of HIV infection, which progressively destroys the body's immune system – the system responsible to fight off infections and other diseases.

AIDS means **acquired immune deficiency syndrome**. "**Acquired**" means it is the result of HIV infection that a person **acquires** from contact with another person who is infected with HIV. **"Immune**" means HIV attacks and progressively destroys the body's immune system. "**Deficiency**" means the immune system is significantly damaged. "**Syndrome**" means a group of diseases or related symptoms that are associated with a particular clinical condition, in this case the full-blown stage of HIV. **However, not everybody who has HIV has AIDS.**

AIDS is a fatal condition resulting from HIV infection that has severely damaged the immune system causing the body to succumb (be vulnerable) to a variety of life-threatening diseases, called **opportunistic infections and cancers**. Common pathogens or disease causing organisms such as bacteria, yeast, parasites, and viruses ordinarily do not cause serious illness. However, when the immune system is extremely compromised these organisms can multiply causing infection that can lead to death.

Without antiretroviral drugs that inhibit its replication, HIV multiplies to a very high concentration (viral load) in the blood. A high viral load destroys the very cells that protect the body from disease caused by infection.

Most people with HIV feel or look healthy the first few years after acquiring the virus. However, most HIV+ individuals will progress to AIDS if not treated. Very few people with HIV develop AIDS slowly or never at all.

HIV, like other viruses, is not curable. Viruses are not eliminated by antibiotics that work against bacteria. **There is no known cure for HIV.**

However, health science has successfully developed treatment for HIV in the form of antiretroviral drugs (ARV's). These drugs function to inhibit the enzymes transcriptase and protease that are necessary to replicate HIV. They cannot eliminate the virus. They just slow down its replication and therefore deter symptoms associated AIDS. In developed countries such as the Unites States, HIV has been labeled as a chronic illness because antiretroviral drugs have made the disease manageable, and people are living longer.

The ABC of Prevention

The good news about HIV-AIDS is that it can be prevented. It is mainly a behavior driven pandemic. Ugandans invented what they called the **ABC** strategy and dramatically turned around the epidemic in their country. (**Abstinence** before marriage, **be faithful** in marriage, and **condoms** for high risk groups or couples where one partner is already infected.) The major focus was on the **A** and **B**, and research shows that condoms are 85% effective in preventing the transmission of HIV <u>if they are used consistently and correctly</u>.)

With strong evidential support, *CrossRoads* bases its approach on these foundational principles:

- The best way to curb the AIDS epidemic is to choose abstinence before marriage and fidelity within marriage.
- Abstinence and fidelity are behavioral choices.
- Healthy behavioral choices are outcomes of one's values and character.
- The best way to change one's character is through a relationship with Jesus Christ.

Thus, our approach uses the ABC strategy with an emphasis on the A and B elements.

References:

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Optimal Sexual Health: Scientific Dimension – Medical Institute for Sexual Health
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Merck Manual, 17th edition
Evidence that Demands Action – Dr. Edward Green

Preventive Strategies Against HIV

The best way to control or stop the spread of viruses like HIV is prevention, to keep a person from getting infected in the first place. For some viral diseases like measles, chickenpox and flu, prevention is best done through the use of vaccines. Since these viral diseases are spread by coughing and sneezing, vaccines are used to prevent infection.

HIV is different in that there has been no vaccine developed to prevent a person from being infected. Since it is primarily behavior driven, changing behavior is the most effective way to stop its spread.

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