



Deep Study of HIV and Anti HIV agents

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Abstract:

5.9 million Were adults and 1.7 million were children (<15 years old). New HIV Infections—an estimated 1.5 million individuals worldwide acquired HIV in 2020, marking a 30% decline in new HIV infections since 2010. 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/mm³). 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.

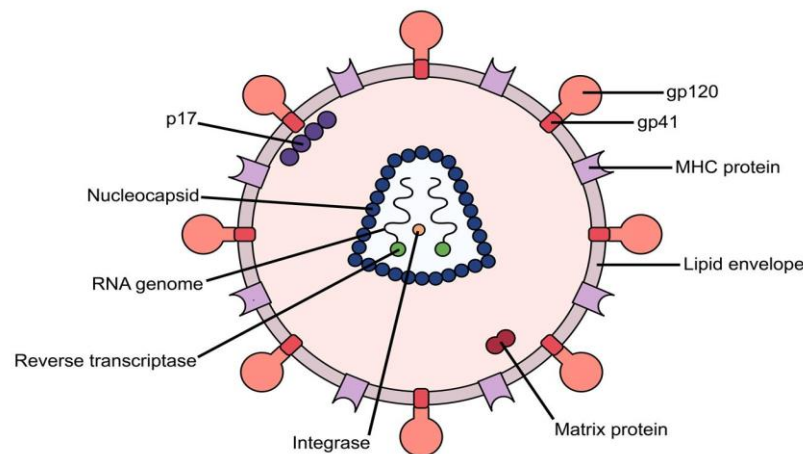
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Introduction:

HIV/AIDS a global pandemic. As of 2016 approximately 36.7 million people worldwide have HIV, the number of new infections that year being about 1.8 million. This is down from 3.1 million new infections in 2001. Slightly over half the infected population are women and 2.1 million are children. It resulted in about 1 million deaths in 2016, down from a peak of 1.9 million in 2005.

Sub-Saharan Africa is the region most affected. In 2010, an estimated 68% (22.9 million) of all HIV cases and 66% of all deaths (1.2 million) occurred in this region. This means that about 5% of the adult population is infected and it is believed to be the cause of 10% of all deaths in children. Here, in contrast to other regions, women comprise nearly 60% of cases. South Africa has the largest population of people with HIV of any country in the world at 5.9 million. Life expectancy has fallen in the worst-affected countries due to HIV/AIDS; for example, in 2006 it was estimated that it had dropped from 65 to 35 years in Botswana. Mother-to-child transmission in Botswana and South Africa, as of 2013, has decreased to less than 5%, with improvement in many other African nations due to improved access to antiretroviral therapy.

HIV Structure



South & South East Asia is the second most affected; in 2010 this region contained an estimated 4 million cases or 12% of all people living with HIV resulting in approximately 250,000 deaths. Approximately 2.4 million of these cases are in India.

During 2008 in the United States approximately 1.2 million people were living with HIV, resulting in about 17,500 deaths. The US Centers for Disease Control and Prevention estimated that in that year, 20% of infected Americans were unaware of their infection. As of 2016 about 675,000 people have died of HIV/AIDS in the US since the beginning of the HIV epidemic. In the United Kingdom as of 2015, there were approximately 101,200 cases which resulted in 594 deaths. In Canada as of 2008, there were about 65,000 cases causing 53 deaths. Between the first recognition of AIDS (in 1981) and 2009, it has led to nearly 30 million deaths. Rates of HIV are lowest in North Africa and the Middle East (0.1% or less), East Asia (0.1%), and Western and Central Europe (0.2%) The worst-affected European countries, in 2009 and 2012 estimates, are Russia, Ukraine, Latvia, Moldova, Portugal and Belarus, in decreasing order of prevalence.

Definitions

Definition of HIV:

Human immunodeficiency virus (HIV) is an infection that attacks the body's immune system, specifically the white blood cells called CD4 cells.

What Is HIV?

HIV (human immunodeficiency virus) is a virus that attacks cells that help the body fight infection, making a person more vulnerable to other infections and diseases. It is spread by contact with certain bodily fluids of a person with HIV, most commonly during unprotected sex (sex without a condom or HIV medicine to prevent or treat HIV), or through sharing injection drug equipment.

If left untreated, HIV can lead to the disease AIDS (acquired immunodeficiency syndrome).

The human body can't get rid of HIV and no effective HIV cure exists. So, once you have HIV, you have it for life.

However, by taking HIV medicine (called antiretroviral therapy or ART), people with HIV can live long and healthy lives and prevent transmitting HIV to their sexual partners. In addition, there are effective methods to prevent getting HIV through sex or drug use, including pre-exposure prophylaxis (PrEP) and post-exposure prophylaxis (PEP).

First identified in 1981, HIV is the cause of one of humanity's deadliest and most persistent epidemics.

What Is AIDS?

AIDS is the late stage of HIV infection that occurs when the body's immune system is badly damaged because of the virus.

Where did HIV come from?

History of HIV

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. To learn more about the history of HIV in the United States and CDC's response to the epidemic, see CDC's HIV and AIDS Timeline.

How do I know if I have HIV?

The only way to know for sure whether you have HIV is to get tested. Knowing your HIV status helps you make healthy decisions to prevent getting or transmitting HIV.

Are there symptoms?

Graphic listing symptoms of HIV: Fever, HIV Symptoms and Testing, Chills, Rash, Night sweats, Muscle aches, Sore throat, Fatigue, Swollen lymph nodes, and Mouth ulcers. Some people have flu-like symptoms within 2 to 4 weeks after infection (called acute HIV infection). These symptoms may last for a few days or several weeks. Possible symptoms include Fever, Chills, Rash, Night sweats, Muscle aches, Sore throat, Fatigue, Swollen lymph nodes, and Mouth ulcers.

But some people may not feel sick during acute HIV infection. These symptoms don't mean you have HIV. Other illnesses can cause these same symptoms.

See a health care provider if you have these symptoms and think you may have been exposed to HIV. Getting tested for HIV is the only way to know for sure.

What are the stages of HIV?

When people with HIV don't get treatment, they typically progress through three stages. But HIV medicine can slow or prevent progression of the disease. With the advancements in treatment, progression to Stage 3 is less common today than in the early days of HIV.

Stage 1: Acute HIV Infection

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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

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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)

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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

Anti HIV agents

Drug used in the treatment of human immunodeficiency virus are known as Anti HIV agents

Use of anti HIV agents:

- Control the growth of the virus.
- Improve how well your immune system works.
- Slow or stop symptoms.
- Prevent transmission of HIV to others.

Mechanism of Action of anti HIV agents:-

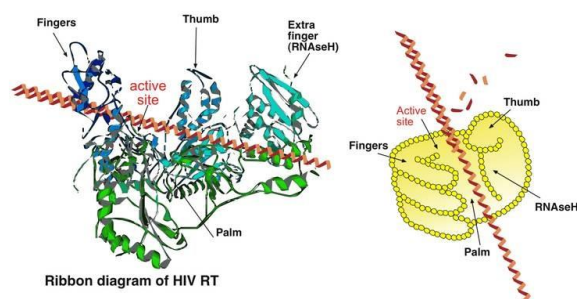
Mechanisms of HIV antiretroviral drug action and drug resistance

Nucleoside reverse transcriptase inhibitors (NRTI)

Mechanism of action-

The NRTI class of antiretroviral drugs are chemical compounds that are nucleotide base analogues. They function as chain-terminators during the extension of the DNA chain during the reverse transcription process which is carried out by HIV reverse transcriptase. The NRTI compounds permit correct base-pairing and incorporation into the DNA chain, however, an important hydroxyl group required for addition of the next nucleotide has been replaced by a non-reactive group.

Why a right-hand?



The three dimensional structure of HIV reverse transcriptase resembles a right-hand. It has a flat central part like a palm as well as upward directed domains resembling fingers and a thumb. The nucleic-acid template passes between the thumb and finger domains where the active site for DNA polymerisation is located. An "extra finger" represents the RNaseH domain that removes RNA from hybridised DNA:RNA molecules during reverse transcription.

With the exception of Tenofovir, the NRTI compounds that are taken up by the cell do not contain phosphate groups and require three phosphate groups to generate the triphosphate form of the base analogue before it can be used as a substrate by reverse transcriptase. Tenofovir contains a single phosphonate group to which only two phosphate groups need to be added to generate the active compound. The additional phosphorylation is carried out by host cellular enzymes.

Agents used for treatment of HIV:

1. Atripla (efavirenz + tenofovir + emtricitabine) combines an NNRTI and two NRTIs into one medication. The usual dose is once daily on an empty stomach—one hour before or two hours after a meal. Dizziness, diarrhea and tiredness are common side effects. Serious, life-threatening side effects are also possible, such as liver problems and a buildup of lactic acid in the blood.
2. Complera (rilpivirine + tenofovir + emtricitabine) combines an NNRTI and two NRTIs. The usual dose is once daily with a meal. Strange dreams, trouble sleeping, depressed mood, headache, and digestive problems are common. Serious liver problems and lactic acid buildup in the blood can occur.
3. Genvoya, Stribild (elvitegravir + cobicistat + tenofovir + emtricitabine) combines an INSTI, a pharmacokinetic booster, and two NRTIs. You usually take it once a day with food. Headache, nausea, and diarrhea are common side effects. Like Atripla and Complera, serious liver problems and lactic acid buildup in the blood are possible.
4. Isentress (raltegravir) is an INSTI you usually take twice a day. Nausea, headache, dizziness and fatigue are common side effects. Although rare, muscle breakdown leading to kidney failure may occur.
5. Norvir (ritonavir) is a PI you usually take twice daily with meals. Digestive side effects are common, as are headache and burning or tingling sensations. Norvir can also cause serious side effects and drug interactions. Tell your doctor and your pharmacist about all of your medications.

6. Prezista (darunavir) is a PI you usually take with ritonavir either once or twice a day. Ritonavir acts as a pharmacokinetic booster. Digestive problems, headache, and changes in body fat are common side effects. Severe skin reactions and liver problems are also possible.

7. Tivicay (dolutegravir) is an INSTI you take once or twice a day. Headache, fatigue, sleep problems, and changes in body fat are common side effects. Serious liver problems are also possible.

8. Triumeq (dolutegravir + abacavir + lamivudine) combines an INSTI and two NRTIs. The usual dose is once daily. Headache, fatigue, sleep problems, and changes in body fat are common side effects. It is also possible to have serious side effects, including a serious allergic reaction, liver problems, and a buildup of lactic acid in the blood.

9. Truvada (emtricitabine + tenofovir) combines two NRTIs. The usual dose is once daily. Abnormal dreams, trouble sleeping, depressed mood, headache, and dizziness are common side effects. Like other NRTI combinations, liver problems and lactic acidosis buildup in the blood is also possible.

10. Vemlidy, Viread (tenofovir) is an NRTI you usually take once a day. Digestive problems, fatigue, headache, depressed mood, sleep problems, and changes in body fat are common side effects. Like other NRTIs, serious side effects are possible, including liver problems and lactic acid buildup in the blood.

Side effects of retroviral drugs:

- Hypersensitivity or allergic reactions, with symptoms such as fever, nausea, and vomiting.
- Bleeding.
- Bone loss.
- Heart disease.
- High blood sugar and diabetes.
- Lactic acidosis (high lactic acid levels in the blood)
- Kidney, liver, or pancreas damage.

Prevention:

Prevention measures include:

- Knowing your HIV status as well as your partner's.
- Using latex condoms correctly during every sexual encounter.
- Limiting the number of sexual partners.

- Abstaining from injectable drug use and never sharing needles or syringes.
- Seeking treatment immediately after suspected HIV exposure, since newer medications known as post-exposure prophylaxis (PEP) may prevent infection if started early.
- Reducing the chance of becoming infected by obtaining pre-exposure prophylaxis (PrEP), which is a daily pill taken by people at high risk for HIV because of their sexual behavior or from injecting drugs.

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