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# Microbiology Team

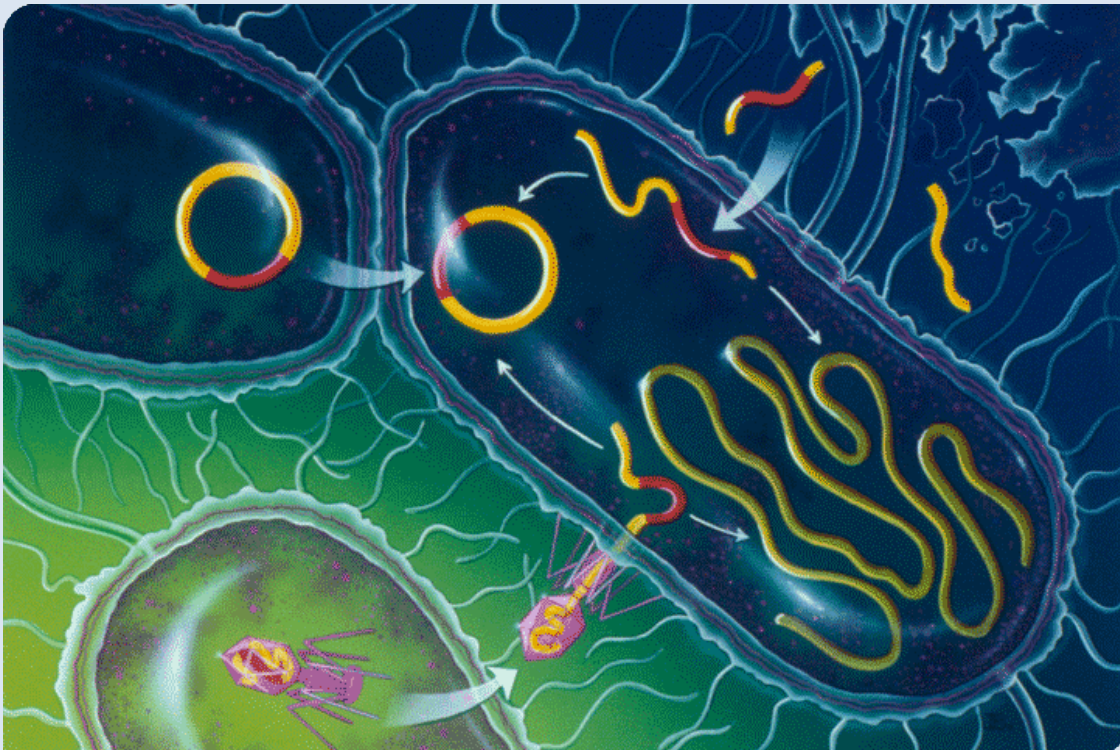
## HIV & AIDS

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Doctors notes = Green

Important notes = Red

Not important = Grey

## Introduction:

- When a patient is infected by HIV we say he is HIV positive, we only say AIDS when he reaches the end stage of the infection ( we will discuss it later )
- HIV is **H**uman **i**mmunodeficiency **v**irus, it infects and destroys **CD4 T helper cells** , which are responsible for immunity (CD4 has an effect on CD8 also) , this leads to very low immunity and multiple opportunistic infections , unusual cancer and death.
- HIV can also infect other cells that express the **CD4 receptor** which are the antigen presenting cells (macrophages and dendritic cells ) .

There are 2 types of HIV which can cause AIDS.

The overall sequence homology between HIV-1 & 2 is less than 50%.  
But they cause the same disease .

### HIV -1

Worldwide

Highly virulent

Highly susceptible to mutations so no vaccine is made for it

### HIV-2

Specific region, in Africa

Less virulent

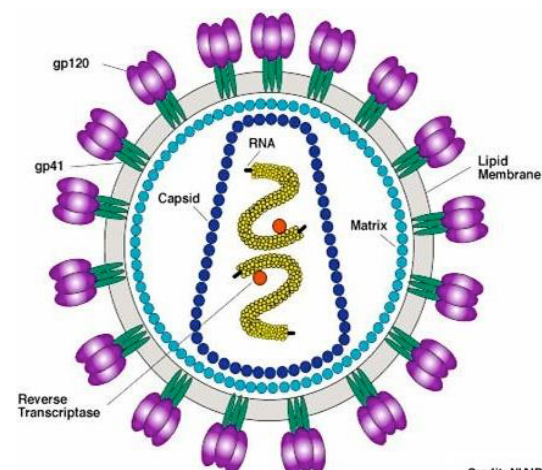
Less susceptible to mutations

Treated easier than HIV-1

## Characteristics of HIV

- Family of *Retroviridae*.
- Consists of **Glycoprotein Envelope** ( gp 120, gp41).
- Matrix layer ( P-17 ) , Capsid ( core , P24 ) .
- 2 copies of SS RNA.
- Important enzymes **reverse transcriptase**, **Integrase** and **Protease** in the nucleus.

Gp 120 attaches to the CD4 antigen receptor on the host cell.



**HIV genome :** The genome consists of 9 genes:

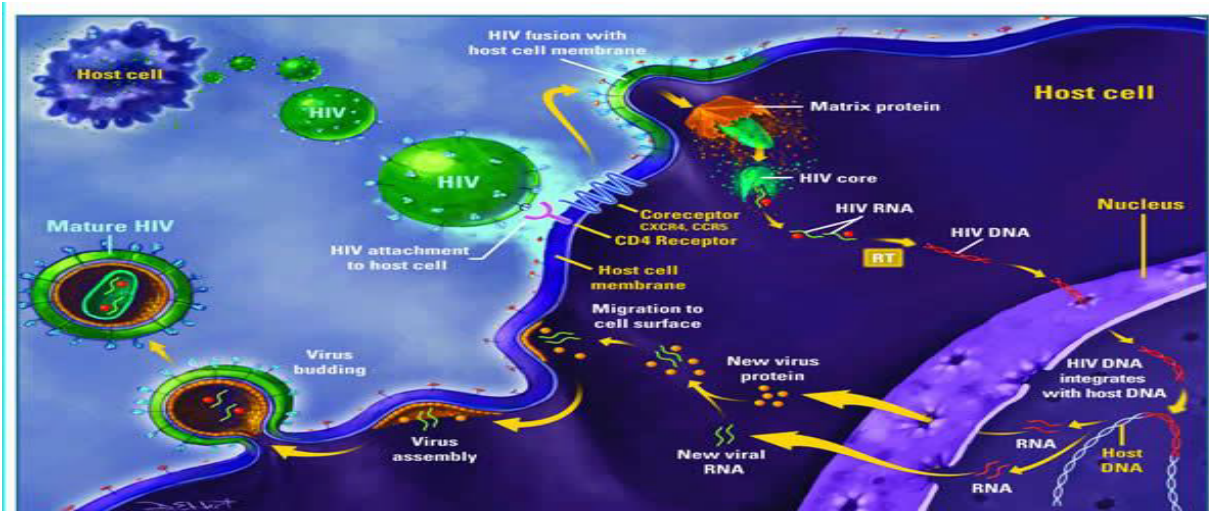
- 3 structural genes (gag (structure proteins), pol (enzymes), env (envelope)).
- 6 non-structural genes (tat, nef, rev, vif, vpr, vpu). (Essential for replication of the virus ) .

## Pathology of HIV

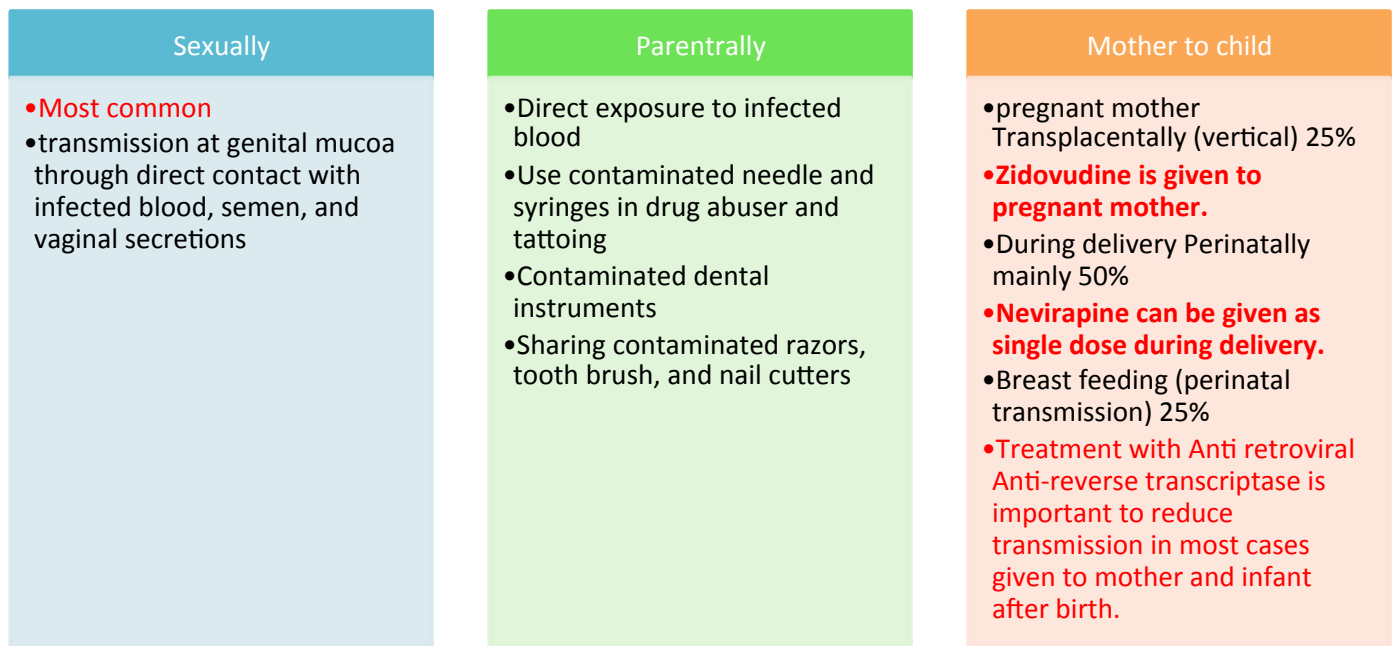
Don't worry, you are not asked to memorize this, however read it carefully and focus on the colored stuff. Understanding the pathology will make it easier to remember the function of the enzymes and the way the drugs work.

To establish infection HIV must first attach to the host cell. Attachment occurs by interacting between GP120 ( on the surface of the virus ) and the CD4 antigen receptor on the surface of the host cell. There must also be a co-receptor on the host cell ( CXCR-4 on T-lymphocytes , CCR-5 on macrophages ).After attachment , the envelope will fuse with the host cell membrane and the virus will enter the cell. RNA is then released in the cytoplasm of the host cell ,Reverse transcriptase then makes a DNA copy of the viral genome. Viral enzyme integrase then inserts the viral DNA into the host DNA. This DNA could be dormant (inactive) or it could be activated resulting in the production of new Messenger RNA and viral genome RNA. Some of the proteins are formed by cleavage of long polyprotein by the enzyme Protease. Finally the new virus is released by budding.

When the virus infects the antigen presenting cells , it will transport to the lymph nodes which could cause infections to the intestine , brain ( causes dementia ) etc ...



## Transmission of HIV

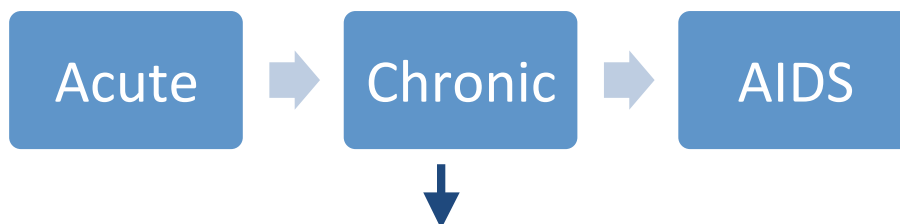


HIV is easily inactivated by treatment for 10 min at 37°C with any of the following:

- 10% House hold bleach, Sodium hypochlorite
- 50% Ethanol
- 35% Isopropanol
- 0.5% Paraformaldehyde
- 0.3% Hydrogen peroxide

**In Summary: it does not survive in the environment .**

**Course of HIV Infection ( 3 stages ) ( based on the CD4 cell count & the presence or absence of opportunistic infections )**



**1-PGL(Persistent Generalized Lymphadenopathy ) 2-ARC ( Aids Related Complex )**



## Acute

- IP: **1 month** (2- 4) weeks can last to 12 weeks
- Viral load: High, **rapid viral replication**
- CD4: gradual decrease in cell count
- No symptoms or **flu like symptoms** (fever, headache, fatigue, lymphadenopathy and skin rash) 25 to 65 %
- 20 % may develop aseptic meningitis
- **CD-4 T cell count is slightly decreased .**

## Chronic

- Lasts 10 years in adult, 5 years in children(**without treatment , it is usually prolonged with drugs )**
- Low viral load. **CD4- T cell count: >500/ ml**
- **Totally asymptomatic but the patients still contagious.**
- When it reaches to the end of chronic pahse (before AIDS), we should have :
  - **1- PGL ( persistant generalized lymphadenopathy) it is enlargement of lymph nodes must be in 1- two or more extra inguinal area 2- persists at least 3 months 3- no illness or medication that may cause PGL.**
  - **2- ARC (AIDS- related complex) group of clinical symptoms : fever of unknown origin >1month ,chronic diarrhea>1month , weight loss 10 % ( slim disease ),fatigue , night sweating ,neurological disease as myelopathies and peripheral neuropathy.**
- **Most cases of HIV are diagnosed within the chronic phase .**

## AIDS

Acquired  
ImmunoDeficiency  
Syndrome

- End stage of disease = **death**
- High viral load RNA
- very low CD4 T cell count < 200
- **Persistent multiple opportunistic infections: viruses,bacteria, protozoa and fungi**
- **Kaposi sarcoma** : unusual cancer, sarcoma of skin ( **caused by Human Herpes Virus 8 )**

These are some of the common infections in AIDS, Just read them and you can find the most important ones in the summary.

OPPORTUNIST INFECTIONS AND TUMORS IN AIDS	
viruses	disseminated CMV (including retina, brain, peripheral nervous system, gastrointestinal tract) HSV (lungs, gastrointestinal tract, CNS, skin) JC virus (brain – PML) EBV (hairy leukoplakia, primary cerebral lymphoma)
bacteria*	mycobacteria (e.g. <i>Mycoplasmavium</i> , <i>M. tuberculosis</i> – disseminated, extrapulmonary) <i>Salmonella</i> (recurrent, disseminated) septicemia
protozoa	<i>Toxoplasma gondii</i> (disseminated, including CNS) <i>Cryptosporidium</i> (chronic diarrhea) <i>Isospora</i> (with diarrhea, persisting more than one month)
fungi	<i>Pneumocystis jiroveci</i> (pneumonia) <i>Candida albicans</i> (esophagitis, lung infection) <i>Cryptococcus neoformans</i> (CNS) histoplasmosis (disseminated, extrapulmonary) <i>Coccidioides</i> (disseminated, extrapulmonary)
tumors	Kaposi's sarcoma** B cell lymphoma (e.g. in brain, some are EBV induced)
other	wasting disease (cause unknown) HIV encephalopathy

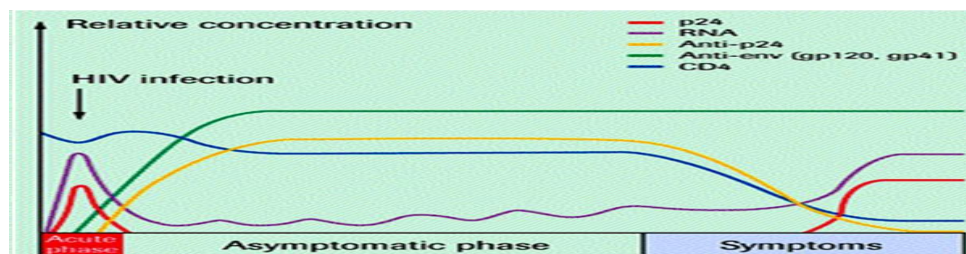
\*also pyogenic bacteria (e.g. *Haemophilus*, *Streptococcus*, *Pneumococcus*) causing septicemia, pneumonia, meningitis, osteomyelitis, arthritis, abscesses etc.; multiple or recurrent infections, especially in children  
\*\*associated with HHV8, an independently-transmitted agent; 300-times as frequent in AIDS as in other immunodeficiencies

## Serological Profile of HIV infection

**Acute stage:** First marker to appear in blood is the Viral RNA , followed by the P24 ( core antigen ). P24 is a marker for viral replication. Then the antibodies appear (Anti-envelope gp120 , gp41 & Anti core gp24 ). **The 1<sup>st</sup> marker for detection HIV in the acute phase is HIV RNA.**

**Chronic Stage:** in the beginning of this stage, the CD4 cells will increase due to activation of the immune system, and the Viral load ( RNA ) will decrease because it will be in the dormant stage. Then while the disease progresses, the CD4 cells will decrease and The RNA will start to increase. The antibodies are also positive, however the P24 is usually negative.

**AIDS stage:** All the markers are present in the blood and CD4 count very low less than 200.



## Diagnosis:

- 1- Patient history: may give hint if exposed to HIV or not.
- 2- **ELISA (Enzyme-linked immunosorbent assay)**: screening patient serum for both HIV Ag and HIV Ab. **If the result is positive repeat it twice.** If still positive do **confirmatory test: western blot, RIBA or PCR to confirm.**
- 3- PCR detect blood viral load RNA, we don't do it routinely because its expensive. **It is used to follow up response to treatment and important for HIV diagnosis in infant of infected mother.**

## Treatment

**HAART = highly active antiretroviral therapy.**

Composed of 2 reverse transcriptase inhibitors and 1 protease inhibitor.

**Does not clear (eradicate) the virus.**

**Even if patient is treated and viral load is not detected , the patient is still contagious, because the drugs do not reach all the body compartments (semen).**

Reverse transcriptase inhibitors:

**Zidovudine** (Nucleoside analog )

**Nevirapine** (Non-nucleoside , used only in HIV 1 )

Zalcitabine , Didanosine

Stavudine , Lamivudine

Protease Inhibitors:

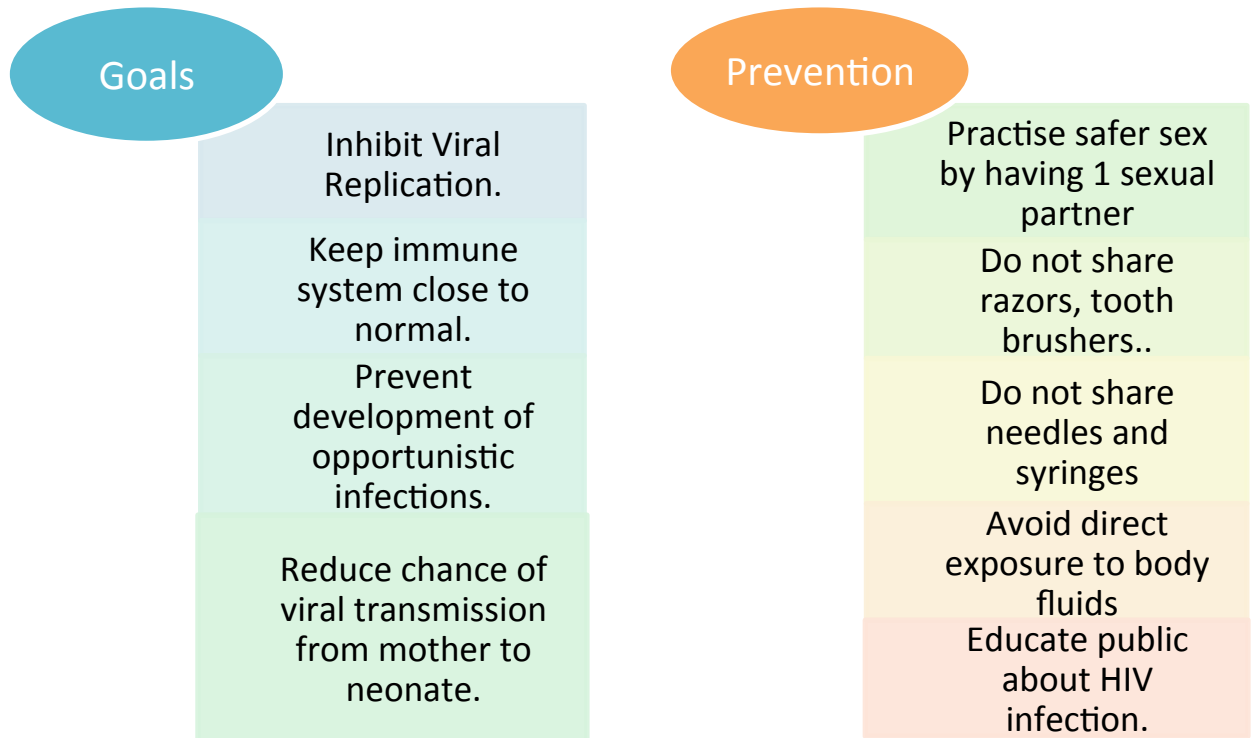
Saquinavir

Indinavir

Ritonavir

Nelfinavir

**The doctors only mentioned the drugs in red which are used in pregnancy as stated earlier.**



## SUMMARY

- HIV is the name of the virus that causes AIDS . The infection starts as an acute stage , then a chronic stage and finally AIDS.
- HIV infects T-helper cells mainly or any cell that has CD4 on its surface.
- HIV contains an envelope ( gp 120 , gp 41 ) which binds to the CD4 receptor & one of the Co-receptors CXCR-4 & CCR-5.If any of these receptors are absent , the person won't be infected .HIV also contains three important enzymes : Reverse transcriptase , integrase and protease .
- HIV is transmitted either : Sexually , Parentrally or from mother to child.
- The acute stage of HIV infection is characterized by : High Viral load ( RNA ) and slightly decreased CD4 –T cell count , and is positive for P24 , anti-envelope and anti-core antibodies. Accompanied by flu like symptoms.
- The chronic stage is asymptomatic in the beginning , and usually is negative for P24 and positive for the rest of the markers.CD4-T cell count is decreased but usually above 500/ml , it could be lower but always above 200/ml.
- The end of the chronic stage is when PGL & ARC appear .



- **AIDS** is the end stage of the disease and has a **CD4-T cell count of less than 200/ml**, and is positive for all markers.
- AIDS is accompanied by opportunistic infections like : **oral candidiasis** ,**Cryptococcus** , TB , salmonella , toxoplasma gondi , **Cytomegalovirus** , herpes virus , epstein barr virus , pneumocystis carinii .
- **AIDS is also accompanied by unusual cancers ( Kaposi sarcoma & b-cell lymphoma )**.
- To diagnose a patient with HIV infection : start with ELISA as screening test, if positive , repeat it twice .Then confirm by RIBA , PCR or western bolt.
- PCR is used for follow up response to treatment and HIV diagnosis in infants.
- Zidovudine is given to pregnant mother and Nevirapine can be given as single dose during delivery to prevent infecting the child.
- Patients who are treated for AIDS are still contagious .

**Question 1** : If you suspect a patient with HIV , and he is positive for HIV antigen & antibody by ELISA , what is your next step ?

- A- Confirm by PCR
- B- Confirm by Western bolt or RIBA
- C- Repeat ELISA in duplicate ( twice )

**Question 2** : The first marker to appear in a blood sample of a patient who is HIV + is :

- A- Anti-envelope antibody
- B- HIV RNA
- C- P24 ( Core antigen )

**Answers : C , B**