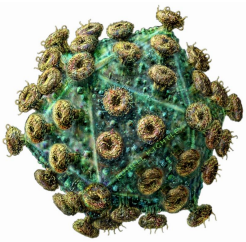
AIDS/HIV

by Dr. Fahad Al Majid



Done by: Nawaf Alfawzan

Revised by: Sarah Almubrik & Mohanad Alsuhaim

Objectives:

- **Not given yet**

Color Guideline:
Important- Red
Emphasis - Blue
Everything else- Black
Extra explanation - Grey

Optional:

Editing file

❖ Introduction

Human Immunodeficiency Virus (HIV) is an infection, which is chronic and without treatment usually fatal.
HIV is characterized by:
1) Progressive immunodeficiency
2) Long latency period
3) Opportunistic infection
HIV causes a disease called acquired immune deficiency syndrome (AIDS) by disrupting the immune system function as measured by CD4 cell depletion.
HIV is Retrovirus (a group of RNA viruses that insert a DNA copy of their genome into the host cell in order to replicate), falls under the genus lentivirus, which uses reverse transcriptase to transcribe RNA into DNA.

SIV is a virus that infects monkeys and not humans. Just as HIV infects humans but not monkeys.
Added just because it was mentioned in the slides

Types of HIV viruses	
HIV1	**HIV2**
Predominate worldwide.	**Closely resemble HIV-1 but is a much slower progression to AIDS. It predominates in western Africa.**

❖ The hallmark of HIV Disease:

Infection and viral replication within T-lymphocyte expressing the CD4 antigen resulting in:

- **Defect in CD4 responsiveness (Qualitative)**
- **Progressive depletion in CD4 cell counts (Quantatative)**
- **This effect on helper-inducer lymphocyte will increase the risk of:**
  - **Opportunistic infections such as Pneumocystis Jiroveci**
  - **Neoplasm such as Lymphoma and Kaposi sarcoma**

Note that: When the number of CD4 cells falls below 200 cells/mm3, the patient is considered to have progressed to AIDS.

HIV is a fragile virus. It cannot live for very long outside the body.

***If your intrested in reading about the history of HIV click here**

❖ Epidemiology

Skip if you want

- **HIV infection/AIDS is a global pandemic with cases. reported everywhere, ranging 30—36M**
- **More than 95% reside in low and middle –income countries, and around 50% are females, also 3.5 million are children (< than 15).**
- **Epidemic was first recognised in USA and shortly thereafter in western Europe.**
- **More than 2/3rd of all people with HIV live in africa.**
- **Asia: 4.9 million people living with HIV, with prevalence highest in southeast Asia 4.0 million**
- **HIV prevalence is decreasing in Myanamar,Combodia and Thailand , but Increasing in Indonesia and Vietnam.**
- **Epidemic is expanding in E. Europe and central asia: 1**

GLOBAL HIV STATISTICS

- **18.2M people were accessing antiretroviral therapy**
- **2.1M people became newly infected with HIV (end 2015)**
- **1.1M people died from AIDS-related illnesses**
- **78M people have become infected with HIV since the start of the epidemic**
- **35M people have died from AIDS-related illnesses since the start of the epidemic**

1. In molecular biology, CD4 (cluster of differentiation 4) is a glycoprotein found on the surface of immune cells such as T helper cells, monocytes, macrophages, and dendritic cells.
2. Subpopulation of CD4+ lymphocytes that cooperate with other lymphocytes (either T or B) to initiate a variety of immune functions

❖ Transmission

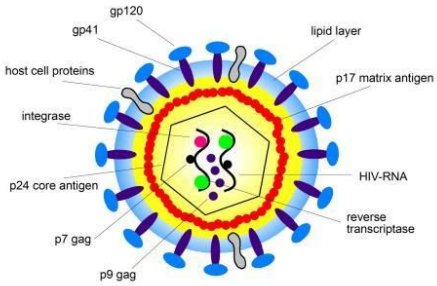
❖ **HIV is primerly found in the blood, semen, or vaginal fluid of an infected person, so it is transmitted through:**

- **Sexual (heterosexual[3] ,msm[4] ,others)**
- **Vertical transmission from pregnant woman to the newborn (MTCT[5]) is the main mode of infection in children.**
- **Blood and body fluid. (Breast milk, pre-cum, & Rectal fluids)**
- **Intravenous Drug User (IVDU).**
- **No evidence of spread by: casual contact or by insects such as by mosquito.**

❖ Structure of HIV virus

❖ **It is an RNA virus, icosahedral structure made of:**

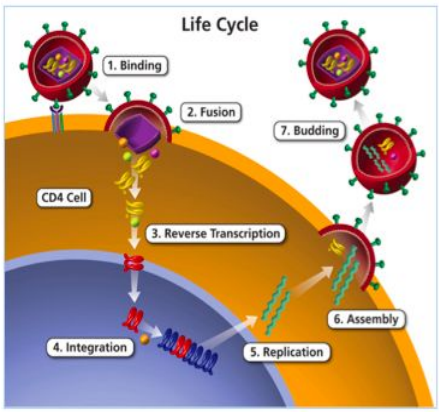
1. **Lipid Envelope derived from infected cell, containing numerous external spikes formed by two major envelope proteins:**
   - **The external gp120**
   - **The trans membrane gp41**
2. **Nucleocapsid (gag) with P24 major core protein. The core contains two single strands of RNA.**
3. **Polymerase[6].**



❖ HIV life cycle & replication

1) Binding (via gp120)

- **HIV use gp120 to bind the CD4 receptor that are located in T-cells**
- **Also, it used co-receptor[7] such as:**
  - **CXCR4.** Found in T cells only
  - **CCR5.**



1 Binding (gp120protein bind to receptor on the CD4 cell)
2 Fusion (HIV envelope fuse with CD4 cell membrane)
3 Reverse transcreptiase (HIV-RNA into HIV-DNA)
4 Integeration (HIV-DNA join CD4 cell DNA)
5 Replication (Creat HIV protein, by transcription & translation)
6 Assembly (Cut HIV protein to join HIV RNA)
7 Budding (New HIV Leaves cell)

2) Penetration
3) Uncoating
4) Reverse transcription (Formation of cDNA)
5) Integration
6) Transcription of proviral DNA
A) formation of genomic RNA
b) formation of structual mRNA

7) Translation of structural mRNA
a) Formation of viral structural protien
b) Packaging of genomic RNA of strucrural protien
8) Final assembly
a) insertion of viral specific glycoprotein into plasma membrane
b) Budding c) Release of mature virions
9) Final maturation (cleavage of gag and pol by polymerase enzyme)

3.Heterosexual is the most common mode of transmission worldwide.
4.Men who have sex with men
5.Mother to child transmission
6.Enzyme that synthesizes nucleic acids
7.CCR5 and CXCR4 are structurally related chemokine receptors belonging to the superfamily of the seven-transmembrane G-protein coupled receptors.

❖ HIV clinical staging:

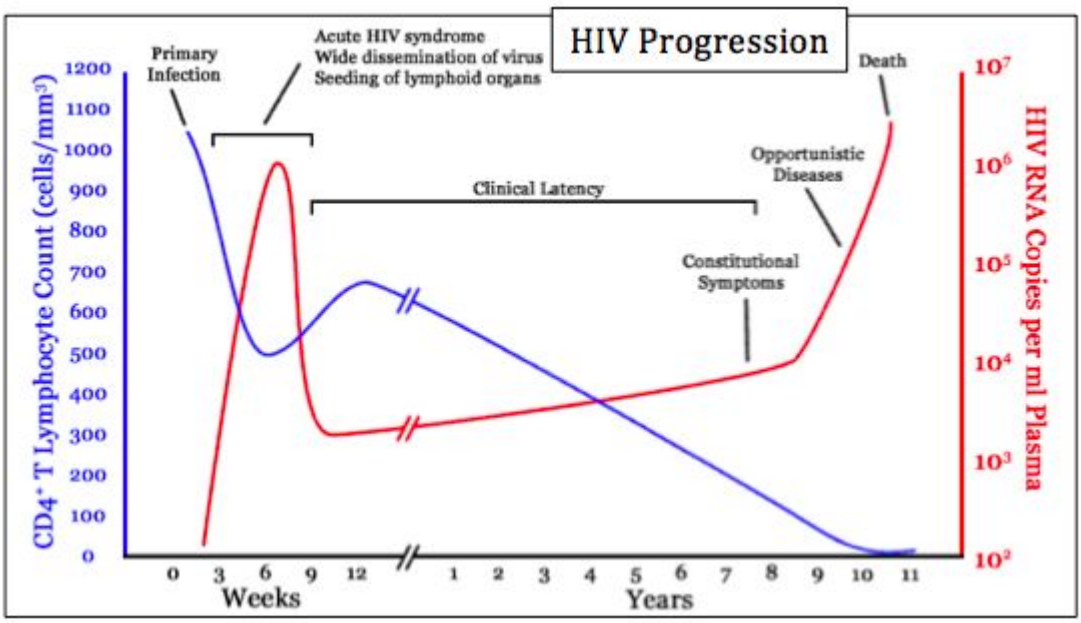
- **Primary HIV infection: Asymptomatic, & Acute retroviral syndrome**
- **Stage1: Asymptomatic, & Persistent generalized lymphadenopathy**

Clinical staging in a nutshell	
HIV-associated symptoms	**WHO clinical stage**
Asymptomatic	**1**
Mild symptoms[8]	**2**
Advanced symptoms[9]	**3**
Sever symptoms[10]	**4**

❖ WHO immunological classification For established HIV infection

CD4 positive T lymphocytes level is the main method of assessing the immune status of the HIV positive patient: (Normal 500-1500/mm3)

Not significant immunosuppression	**>500/mm3**
Mild immunosuppression	**350 – 499/mm3**
Advanced immunosuppression	**200–349/mm3**
Severe immunosuppression	**<200/mm3**

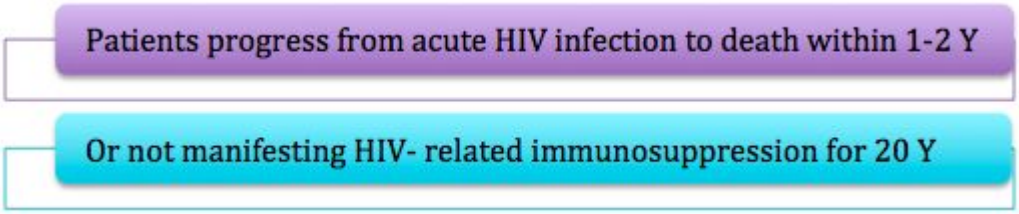


8. Includes: Unexplained moderate weight loss, recurrent URTI, Recurrent oral ulceration
9. Includes: severe weight loss, chronic diarrhea for > 1 month, persistent fever
10. Cervical carcinoma, HIV encephalopathy, Cryptococcosis, Cytomegalovirus disease

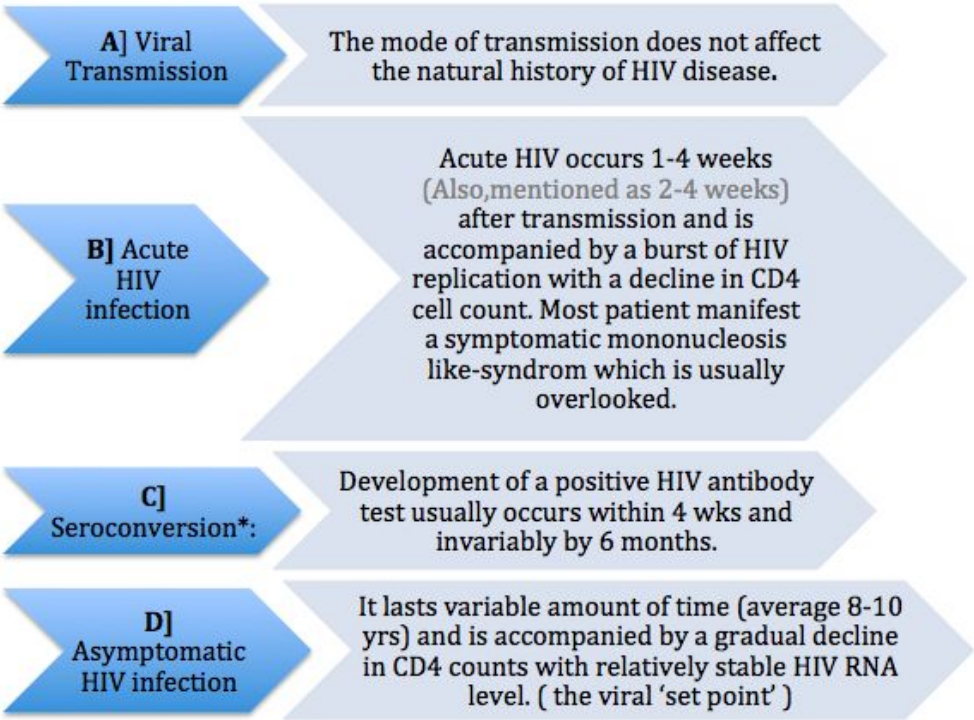
Natural history

The average time from acquisition of HIV to an AIDS- defining illness is about 10 Years then survival averages 1-2 Years.

But, there is tremendous individual variability in these time intervals



Stages of HIV infections:



Clinical Presentation

Acute HIV infection:

- **From exposure to symptoms: 2-4 wks.**
- **It resembles infectious mononucleosis with: --Fever, Pharyngitis, Adenopathy**
  -Rash, myalgia, fatigue, oral ulcer
  -GIT symptoms: diarrhea, anorexia.
- **Result:**

1) Massive response with evolution of HIV-specific immunity (CD8-cytotoxic T lymphocyte.)
2)HIV RNA level falls and the symptoms resolve.

- **CD4 cell count rebounds but remains below the bassline.**

Asymptomatic chronic phase:

- **Active viral replication is ongoing and progressive.**
- **Patient with high HIV RNA may progress to symptomatic disease than those with low HIV RNA level.**
- **Chronic immune activation lead to increase in various inflammatory markers.**
- **This increase the risk of Non-aids related comorbidities: CVD, Renal dysfunction**

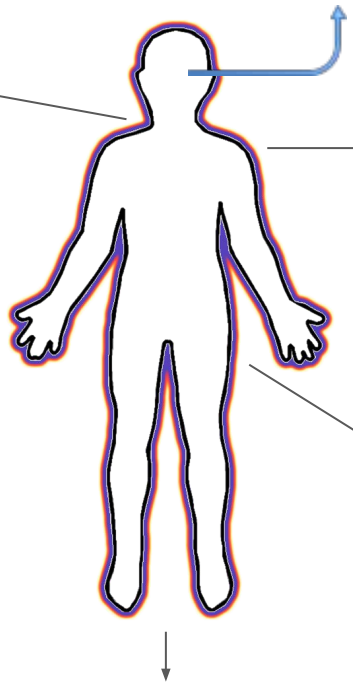
*Seroconversion is the period of time during which HIV antibodies develop and become detectable.

Clincial Manifestation

Eyes
Funduscopy: Cytomegalovirus retinitis. "CD4 less than 50"

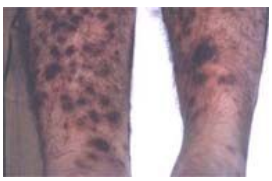
Oropharynx
1) oral trush

2) hairy leukoplakia

Skin
A condition associated with HIV
seborrheic dermatitis

3) mucosal kaposi sarcoma



Lymph node:
Generalized lymphadenopathy
(TB, Lymphoma).

Genital exam:
Ulcers, condylomatous lesions, women for discharge and cervical lesions.

COMPLICATION OF HIV/AIDS

- **Tuberculosis (TB): TB is the most common opportunistic infection and a leading cause of death.**
- **Candidiasis: Causes inflammation and a thick white coating on the mucous membranes of the mouth, tongue, esophagus or vagina.**
- **Toxoplasmosis: This potentially deadly infection is caused by Toxoplasma gondii, a parasite spread primarily by cats.**
  It causes meningoencephalitis.
- **Cryptosporidiosis: Patient contracts cryptosporidiosis when ingest contaminated food or water. The parasite grows in the intestines and bile ducts, leading to severe, chronic diarrhea in people with AIDS.**
- **Cancers common to HIV/AIDS:**
  1. **Kaposi's sarcoma. A tumor of the blood vessel walls, this cancer is rare in HIV negative but common in HIV-positive patients.**
     Kaposi's sarcoma usually appears as pink, red or purple lesions on the skin and mouth and can also affect the internal organs, including the digestive tract and lungs.
  2. **Lymphomas (non Hodgkin's lymphoma)**

Diagnosis

- **ELISA[11] (also known as EIA): is the screening test, used to screen blood products and patients.**
- **Combo test: will detect HIV1 and HIV2 antibodies and P24 antigen.**

Sensitivity of more than 99.5%

The fourth generation test:

- ***EIA[12] test*: combine detection of antibody to HIV and detection of p24 antigen. Extremely sensitive but specificity is not optimal "low risk" only 10% who are positive turn to be real positive.**

Confirmation:

- **The INNO-LIA™ HIV I/II Score: is a Line Immunoassay (LIA®), to confirm:**
  1. **The presence of antibodies against the human immunodeficiency virus type (HIV-1) and (HIV-2) in human serum or plasma.**
  2. **Also, <u>differentiates between HIV-1 and HIV-2 infections.</u>**

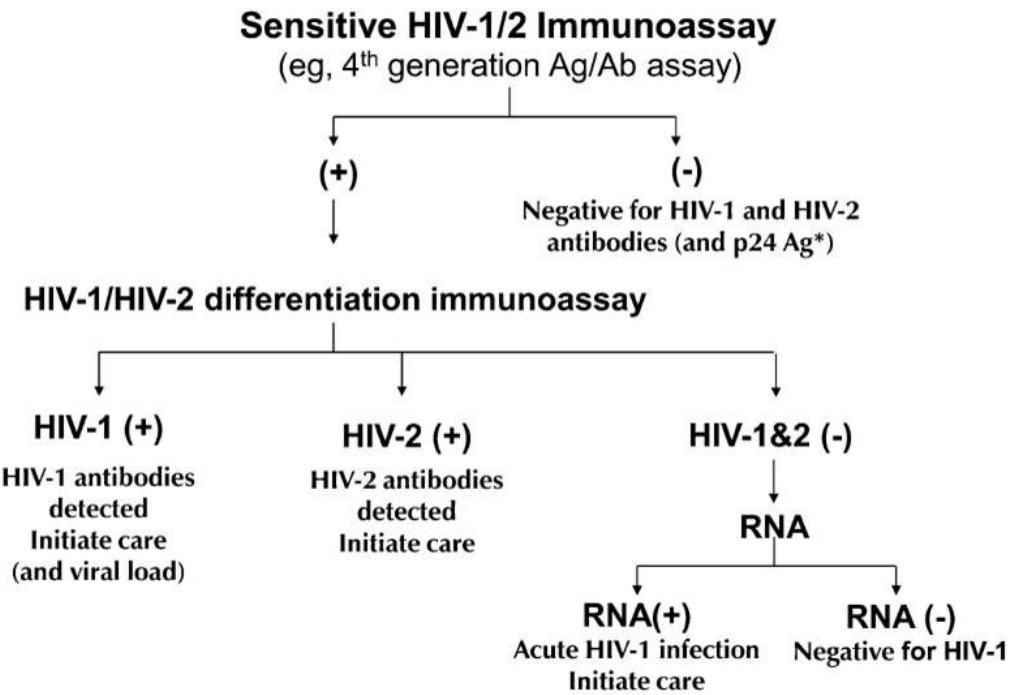
Sensitivity 100% / specificity: 96%

- **Western blot test: Western blot is lousy at detecting recently acquired HIV, and that's a problem since this is the most contagious period in all of HIV infection.**
  There is a problem with the indeterminate cases. (Window period).
- **Polymerase chain reaction (PCR) for quantitative RNA assay and used as:**

1) Confirmatory test for undetermined cases.
2) To assess the viral load.
3) Babies born to HIV-positive mothers, because their blood contains their mother's HIV antibodies for several months.
4) Blood supplies

Not for routine testing: (why is PCR not always used)
a) Decreased sensitivity at lower viral load
b) Significant cost.

Algorithm testing for HIV



11. enzyme immunoassay (Another word for ELISA)
12. enzyme-linked immunosorbent assay

Treatment

Is the goal of antiretroviral therapy to eradicate HIV?
No it's not, as its not currently possible, however, the aim is to:

I. **Improvement of quality of life**
II. **Reduction of HIV-related morbidity and mortality**
III. **Restoration and/or preservation of immunologic function**
IV. **Maximal and durable suppression of viral load**

Prophylaxis:

If CD4 is below 200, patient at high risk to develop:

1) Pneumocystis jirovecii: Causing Pneumonia
Prophylaxis: **co-trimoxazole**
2) **Mycobacterium Avium-Intracellulare: CD4 count less than 50 cells/mm3**
Prophylaxis: co-trimoxazole 500 mg orally twice a day.

Antiretroviral Drugs:	
A) Nucleoside Analogue Reverse transcriptase (RTI)	Abacavir (ABC) Emtricitabine (FTC) Lamivudine (3TC) Tenofovire Zidovudine
B) Non-nucleoside RTI	Delavirdine Efavirenz Nevirapine
C] Protease Inhibitors (PIs)	Atazanavir Darunavir
D] Integrase inhibitor:	Raltigravir

Indication of initiation of antiretroviral drugs

- **Chronic infection**

a) Symptomatic disease.
b) Asymptomatic disease with
1) CD4 count less than 350
2) Pregnancy

- **Post exposure prophylaxis.**

Prevention

- **Abstinence from sexual relation completely**
- **Safer sexual contact:**

Use of condom... 10% failure rate.

- **Circumcision:**

Results in 50% reduction of HIV acquisition

- **Stop using IDUs**[13]
- **Screen all blood and blood products**

- **The corner stone of an HIV prevention strategy is:**

1) Education 2) Counselling 3) Behaviour modification

More than 25% of infected patient do not know. What can we do?
Control and Prevention recommends that everyone between the ages of 13 and 64 get tested for HIV at least once as part of routine health care.

13. Injecting Drug User

Pregnancy and HIV infection

Pregnant women infected with HIV infection caries risk to infect her baby by:

1) **In utero (25-40%)**
2) **Intrapartum (60-75%)**
3) **Breast feeding:**
   - **A) Established infection 14%**
   - **B) Primary infection 29%**

- **Current evidence suggests most transmission occur during the intrapartum period.**
- **Overall risk for mother to child transmission (MTCT) is 16- 25 % (without antiretroviral Rx)**

Very interesting topic "Not included"

- Did you know that some people are actually immune to HIV?
- Well its true, it's called **innate resistance to HIV.**
- A small proportion of humans show partial or apparently complete innate resistance to HIV. It is estimated that the proportion of people with some form of resistance to HIV is less than 1%.
- The main mechanism is a mutation of the gene encoding CCR5, which is a protein on the surface of white blood cells that is involved in the immune system as it acts as a receptor for chemokine's, which acts as a co-receptor for HIV.
- Also, Scientists at the University of Minnesota studying HIV-1 discovered some people have a specific variation of a gene, APOBEC3H, which produces an antiretroviral protein that inhibits the replication of HIV.
- If you want to read more check this link

13. Injecting Drug User

MCQ's

1) The specific binding of HIV to the CD4 surface molecules of the host cell membrane is brought about by:

A. gp 120
B. gp 41
C. p32
D. p55

2) What clinical condition listed below is associated with AIDS-indicated in Oropharynx region:

A. condylomatous lesions
B. hairy leukoplakia
C. seborrheic dermatitis
D. kaposi sarcoma

3) The decision to begin antiretroviral therapy in an asymptomatic patient is based on:

A. The CD4 cell count
B. The plasma viral load
C. The intensity of the patient clinical symptoms
D. All the above

4) A 27-year-old man has fever, macular rash, and lymphadenopathy. He had unprotected sex with a male partner 2 weeks before the onset of these symptoms and has just learned that the partner is infected with HIV. The patient's rapid HIV test is negative.
What is the best test to evaluate this patient for HIV infection?

A. HIV enzyme-linked immunoabsorbent assay (ELISA)
B. PCR for HIV RNA
C. Western blot testing
D. Glycoprotein 120 using ELISA
E. PCR for HIV DNA

Answers: 1.A, 2.B, 3.A, 4.B

Thank you

If you have any question please contact with us at:
Internalmedicineteam434@gmail.com