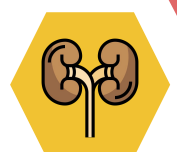
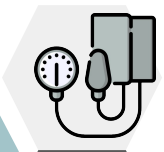
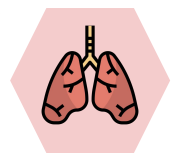
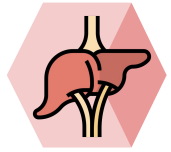


AIDS/HIV



Objectives :

1. Have an overview of the epidemiology of HIV worldwide and in Saudi Arabia
2. Understand the risk factors for HIV
3. Know the life cycle of HIV and have a brief overview of antiretroviral therapy.
4. Describe the infections and opportunistic diseases expected to occur in AIDS

Done by :

Team leader: Salem Al-Ammari

Team members: - Naif Almutairi - Meaad Alnofaie
- Mansour Alobrah. - Norah Alkadi

Revised by :

Yazeed Al-Dossare

Resources :

Doctor's slides + Team 436
Lecturer: Dr. Fahad AL Majid
Same as 436 slides: Yes

متلازمة نقص المناعة المكتسب = AIDS

HIV

There is no cure for HIV virus

Definition:

Infection with Human immunodeficiency Virus which leads to:
 Chronic and -without treatment- usually fatal infection characterized by:
 A} Progressive immunodeficiency
 B} Opportunistic infection



Retrovirus: Retro means, the virus is RNA and can go **back** to DNA thanks to the enzyme reverse transcriptase.

It is an RNA Lentivirus virus which belongs to retrovirus family.

Information in the form of RNA is transcribed into DNA in the host cell.



There are two viruses:



It causes diseases by disrupting the immune system function as measured by CD4 cell depletion called: AIDS (Acquired Immune Deficiency Syndrome).

The hallmark of HIV Disease:

The virus goes to cells that have receptors of CD4 and damages them (cell mediated immunity).

Infection and viral replication within T-lymphocyte expressing the CD4 antigen resulting in:
Progressive depletion in CD4 cell counts. Hallmark of the disease

This effect on CD4 (helper-inducer lymphocyte) will increase the risk of:

- 1) Opportunistic infections such as Pneumocystis Jiroveci
- 2) Neoplasm such as Lymphoma and Kaposi sarcoma

History:



- 1st recognised in USA 1981
- CDC reported the occurrence of:
 - Unexplained occurrence of pneumocystis pneumonia in 5 healthy homosexual in LA
 - Kaposi sarcoma in 25 healthy homosexual men in NY and LA
- later on:
 - The disease became recognised in both male and female with (IVDs) as well as
 - Recipients of blood transfusion and haemophiliacs.

HIV was isolated from patient with lymphadenopathy

ELISA test was developed.

1984

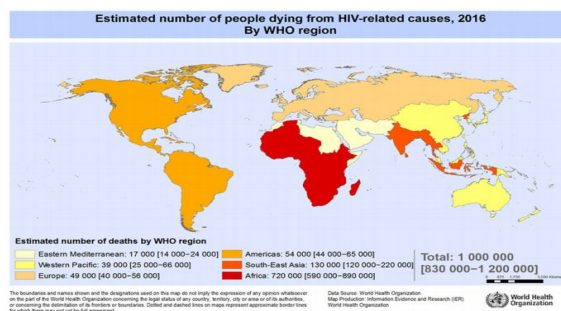
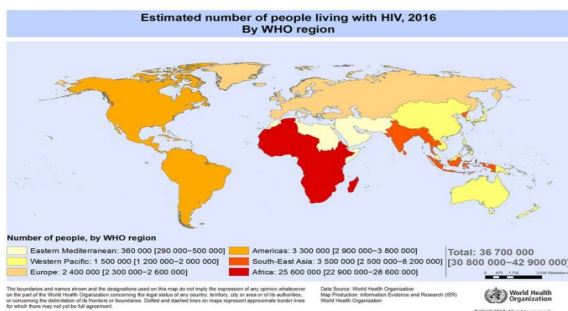
1983

1983

HIV was demonstrated to be the causative agent of AIDS

Global situation

- 75 million people have been infected with the HIV virus.
- 35 million people have died of HIV.
- Globally, 37.9 million people were living with HIV at the end of 2018.
- An estimated 0.8% [0.6-0.9%] of adults aged 15–49 years worldwide are living with HIV.
- African region remains most severely affected: Nearly 1 in every 25 adults (3.9%) living with HIV and accounting for more than two-thirds of the people living with HIV worldwide.



EPIDEMIOLOGY

- Although HIV is not curable, it CAN be prevented in the first place.
- Most deaths come from Africa.

Summary of the global HIV epidemic (2018)

	People living with HIV in 2018	People newly infected with HIV in 2018	HIV-related deaths 2018
Total	37.9 million [32.7 million – 44.0 million]	1.7 million [1.4 million – 2.3 million]	770 000 [570 000 – 1.1 million]
Adults	36.2 million [31.3 million – 42.0 million]	1.6 million [1.2 million – 2.1 million]	670 000 [500 000 – 920 000]
Women	18.8 million [16.4 million – 21.7 million]	–	–
Men	17.4 million [14.8 million – 20.5 million]	–	–
Children (0-9 years)	1.7 million [1.3 million – 2.2 million]	160 000 [110 000 – 260 000]	100 000 [64 000 – 160 000]

Source: UNAIDS/WHO estimates



Transmission

sexual <small>most common route</small>	(heterosexual, msm (man sex with man), others) Heterosexual is the most common mode of transmission worldwide	
Vertical	from pregnant woman to the newborn (MTCT) is the main mode of infection in children. Nowadays, this route can be easily prevented, almost 100% (very successful)	
Blood and body fluid		
IVDU		
Casual contact	No evidence of spread	

HIV+ people can live with HIV- people in the same house and share toilets too. However, careful with anything that may introduce blood (ex: nail clippers).

Pregnancy and HIV infection

Pregnant women infected with HIV infection carries 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)

Today the risk of perinatal transmission is less than 2% with: (viral load should be zero, and CD4 count should be normal)

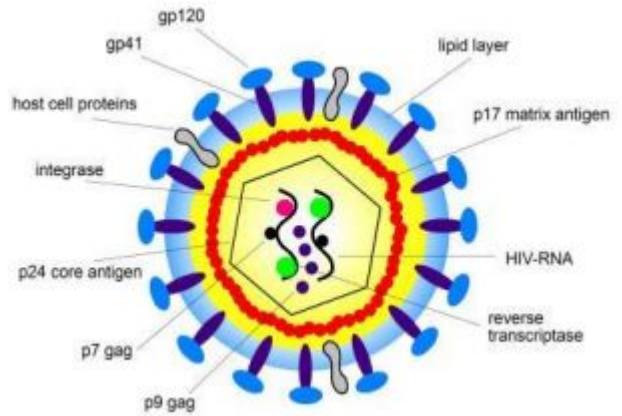
1. Effective antiretroviral therapy (ART)
2. Elective caesarean section -when appropriate-
3. Formula feeding

Structure of the virus

It is an RNA virus

It is an icosahedral *متعدد السطوح* structure of :

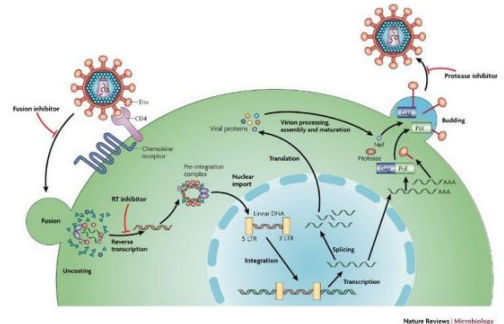
- Lipid Envelope (env) derived from infected cell, containing numerous external spikes formed by two major envelope proteins:
 - The external gp 120
 - The trans membrane gp 41
- Nucleocapsid (gag) with P24 major core protein . The core contains two single strands of RNA.
- Polymerase (pol)



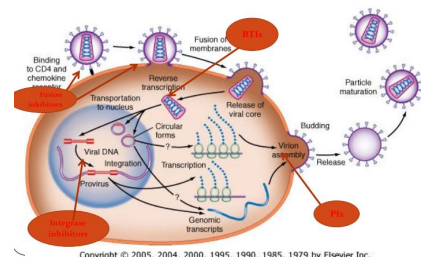
HIV life cycle & replication

[Recommended by the doctor](#)

1. Binding of Viral gp120 protein to CD4 receptor containing cells : T cell, Macrophages, and Microglial cells then, gp 120 and gp41 bind to the chemokines : CXCR5 and CXCR4
2. Fusion between cell membrane and the virion.
3. Penetration
4. Upcoating
5. Reverse transcription Formation of cDNA
6. Integration
7. Transcription of proviral DNA
 - a. formation of genomic RNA
 - b. formation of structural mRNA
8. Translation of structural mRNA
 - a. Formation of viral structural protein
 - b. Packaging of genomic RNA of structural protein
9. Final assembly
 - a. insertion of viral specific glycoprotein into plasma membrane
 - b. Budding
 - c. Release of mature virions
10. Final maturation BY cleavage of gag and pol by polymerase enzyme



HIV life cycle



Pathophysiology

The reason why HIV is very difficult to get rid of is because its genetic material is integrated inside the cells' nuclei, and this is why it would be easier in the future to develop a vaccine (prevent HIV) rather than trying to eliminate it from the body (medications to cure it).

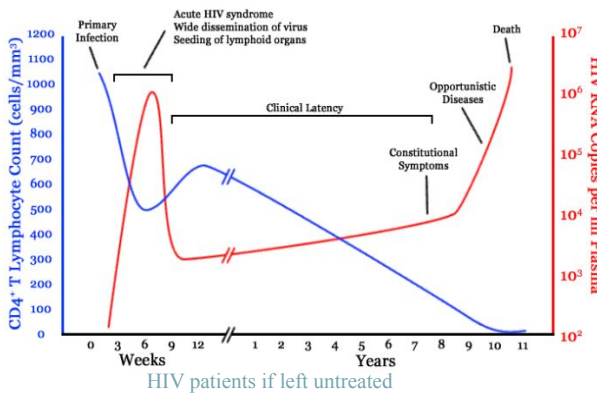
Early stage: Massive replication of the virus in the lymphatic tissues .subsequently

Chronic immune system activation determine the course of the illness.

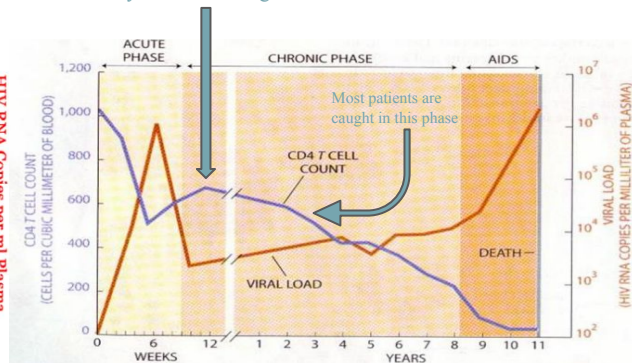
Permanent viral reservoirs containing proviral DNA are established in the latent T cell or macrophages.

<i>Acute infection</i>	<i>Chronic HIV infection</i>
Acute HIV infection: (exposure to symptoms:2-4 wks)	Asymptomatic chronic phase: Active viral replication is ongoing and progressive.
It resembles infectious mononucleosis with: Fever, Pharyngitis, Adenopathy, Rash, myalgia, fatigue, oral ulcer, Diarrhoea, anorexia.	Patient with high HIV RNA may progress to symptomatic disease than those with low HIV RNA level.
THEN, HIV RNA level falls and the symptoms resolve. CD4 cell count rebounds but remains below the baseline	Chronic immune activation lead to increase in various inflammatory markers. This increases the risk of Non-AIDS related comorbidities: CVD, Renal dysfunction, and cancer.

HIV Progression



CD4 count goes up a little when the immune system tries to fight the virus



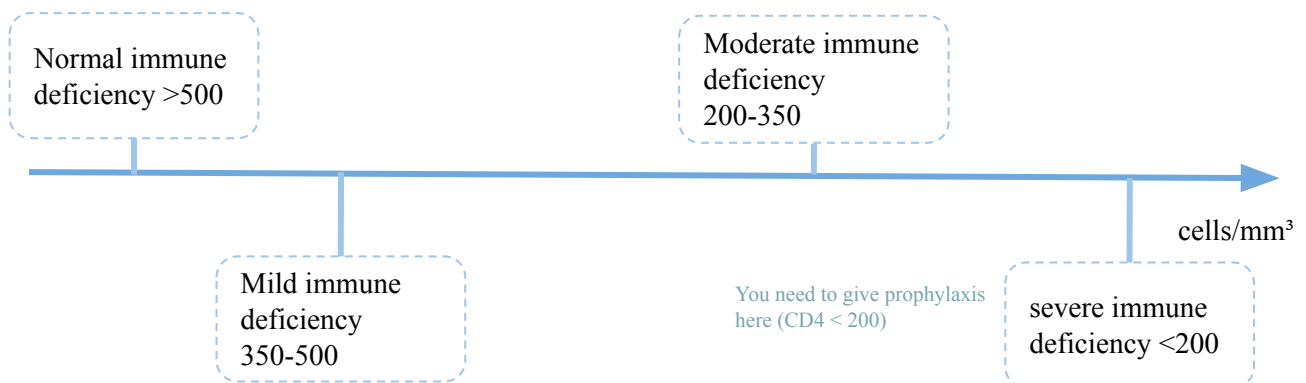
Diagnosis & Confirmation:

<p>HIV Antibody/Antigen immunoassay Test</p> <p>The best for screening, cannot differentiate between HIV 1 and 2</p>	<p>The screening test that is used to screen:</p> <ol style="list-style-type: none"> 1. blood products 2. patients. <p>HIV antibodies take time to develop (4-6 weeks), so the best thing to do is order both antigens and antibodies.</p> <p>It detect both HIV antigen (p24) and antibody. Result in 20 minutes shows up 2 to 4 weeks after infection.</p>
<p>In-home test kits</p>	<p>Kits that test your blood or oral. FDA-approved. Home tests are slightly less sensitive than in-person lab tests.</p>
<p>PCR: (polymerase chain reaction)</p> <p>In case you cannot confirm with other tests, do this one. It is not practical to do it in every patient.</p>	<p>for quantitative RNA assay. Uses:</p> <ol style="list-style-type: none"> 1. diagnose HIV about 10 days 2. Confirmatory test for undetermined cases. 3. To asses the viral load. 4. Babies born to HIV-positive mothers, because their blood contains their mother's HIV antibodies for several months. 5. Blood supplies <p>Not for routine testing: a) Decreased sensitivity at lower viral load b) Significant cost.</p>
<p>INNO-LIA™ (HIV I/II) Score</p> <p>Do this one next after positive screening to confirm. It can tell you which type of HIV (1 or 2)</p>	<p>It is a Line Immuno Assay (LIA®)</p> <ol style="list-style-type: none"> 1. to confirm antibodies against the human (HIV-1) and (HIV-2) 2. differentiates between HIV-1 and HIV-2 <p>Sensitivity 100% specificity : 96%</p>

Immunological staging:

- HIV is a chronic and treatable disease, but not curable.
- Normal CD4 count = 500 - 1500

CD4 positive T lymphocytes level is the main method of assessing the immune status of the HIV positive patient.

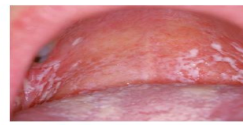
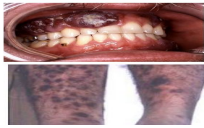


Clinical manifestation



Oropharynx

- 1) oral thrush
- 2) hairy leukoplakia
- 3) mucosal kaposi sarcoma *common in lower limbs.*



Oral thrush in a young healthy man, screen for HIV. Unless it's uncontrolled DM.



Lymph

Generalized lymphadenopathy (TB, Lymphoma)



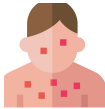
Eye

Fundoscopy : CMV retinitis (CD4 less than 50).



Genitals

ulcers, condylomatous lesions



Skin

condition associated with HIV
seborrheic dermatitis *a normal skin disease that is very common in HIV patients*



Condyloma acuminatum

Condylomatous lesions: genital wart
A pointed papilloma typically found on the skin or mucous membranes of the anus and external genitalia. It's caused by: human papillomavirus HPV

Transmitted through sexual contact.

Common in HIV patients because it's sexually transmitted.



Natural history:

The average time from HIV to AIDS- is about 10 yrs *if left untreated.*

then survival averages 1-2 yrs

BUT there is tremendous individual variability in these time intervals:

- Patients progress from acute HIV infection to death within 1-2 yrs
- and others don't manifesting HIV- related immunosuppression for 20 yrs

Stages of HIV infections

Viral Transmission



The mode of transmission does not affect the natural history of HIV disease.

Acute HIV infection



Acute HIV occurs 1-4 wks after transmission. Most patient manifest asymptomatic mononucleosis like-syndrome which is usually overlooked.

Seroconversion



Development of a positive HIV antibody test within 4 wks and always by 6 months.

Asymptomatic HIV infection



It lasts variable amount of time average 8-10 yrs and is accompanied by a gradual decline in CD4 counts.

COMPLICATION OF HIV/AIDS

Tuberculosis TB in a young healthy man? screen for HIV too.

It is the most common opportunistic infection and a leading cause of death.

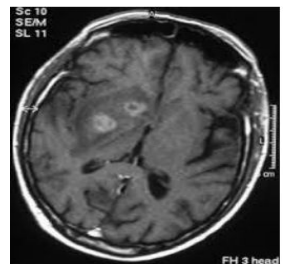


Candidiasis

It causes inflammation and a thick, white coating on the mucous membranes of the mouth, tongue, esophagus or vagina.

Toxoplasmosis CD4 has to be less than 100, requires severe immunodeficiency to develop.

This potentially deadly infection is caused by *Toxoplasma gondii*, a parasite spread primarily by cats. It causes meningoencephalitis.



DX: Serology and MRI.

Treatment: Combination of pyrimethamine plus sulfadiazine
Respond very well.

Cancers

- Kaposi's sarcoma
 - A tumor of the blood vessel walls, common in HIV-positive patients. Rare in none.
 - 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.
- Lymphomas
 - Non-Hodgkin lymphoma

Treatment:

Goals of Antiretroviral Therapy (ART)

You have to give multiple antiviral medications to stop progression.

Eradication of HIV is not possible with currently available antiretroviral medications.

- Improvement of quality of life
- Reduction of HIV-related morbidity and mortality
- Restoration and/or preservation of immunologic function
- Maximal and durable suppression of viral load

Prophylaxis

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

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

Indication of initiation of antiretroviral drugs

1. Chronic infection
 - a. Symptomatic disease.
 - b. Asymptomatic disease with
 - i. CD4 count less than 350
 - ii. Pregnancy
2. Post exposure prophylaxis.

Prevention

Prevention is the most important thing in HIV, and the best way is stay away from extra-marital sexual intercourse.

The only absolute way to Prevent sexual transmission of HIV infection is:
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
- Screen all blood and blood products

The cornerstone of an HIV prevention strategy is:

- Education
- Counseling
- Behaviour modification

More than 25% of infected patient don't know.
What to do?

Routine testing between 13 and 64 ys. (CDC recommendations without written consent)

- Male circumcision for HIV prevention
- Mother-to-child transmission of HIV
- Pre-exposure prophylaxis (PrEP).*

*It's actually post exposure, it will work if you give it within 48-72h following exposure. يجيك يقول مارست معاه وانقطع الوافي، تقوم تعطيه. Also, needle stick injury carries 0.3% of getting HIV, but should give PrEP anyway.

Summary

Definition	Infection with Human immunodeficiency Virus which typically begins with a brief acute retroviral syndrome.
Characterized by	Long latency period, Progressive immunodeficiency, Opportunistic infection. that will end up with AIDS.
Types	HIV I (predominant worldwide), HIV II (slower progression). Hallmark: Progressive depletion in CD4 cell counts which predispose to opportunistic infections such as Pneumocystis Jiroveci and neoplasms such as NON Hodgkin lymphoma & Kaposi sarcoma
Structure	RNA Lentivirus belongs to Retrovirus family with a lipid envelope with the envelope proteins external gp120, transmembrane gp41, nucleocapsid (gag) with P24 major core protein, and polymerases.
Transmission	Sexual Heterosexual is the most common mode of transmission worldwide, Vertical transmission Blood and body fluid, IV Drug Users.
Life cycle	Binding, Fusion, Penetration, Upcoating, Reverse transcription, Integration, Transcription, Translation, Assembly, Maturation.
Disease Course	Viral Transmission → Acute HIV infection (occurs 2-4 weeks after transmission) infectious mononucleosis → Seroconversion (occurs 2-12 weeks after the development of symptoms) → Asymptomatic HIV infection (last 8-10 yrs) → symptomatic HIV infection (last 1-3 years) → AIDS cell count < 200 (Average survival 1-2 years).
Diagnostic Tests	Screening tests; (combo for P24 detection + Elisa for antibodies). Confirmatory tests: (the INNO-LIATM HIV I/II Score is a Line Immuno Assay (LIA®) antibodies against HIV I, HIV II + western blot assays + PCR to confirm the undetermined and asses viral load).
Complications	TB most common, Candidiasis, Toxoplasmosis, Kaposi Sarcoma, Lymphoma non Hodgkin's.
Mother to child transmission	In-utero, 25-40%. Intrapartum, 60-75% most common. Breast feeding, Established infection 14%, Primary infection 29%. now with available treatment the risk has dropped to 1%.
Prevention and Counseling	
Treatment	according to current guidelines you treat any infection immediately and you don't wait until the count drops to 200.

Questions

1. A 25 years old pregnant women at 20th week of gestation presented to the clinic and was diagnosed to have HIV. Laboratory revealed viral load of 100,000 copies, and CD4 count of 450 cells/mm². She is on No medication and get worried about her fetus contacting the infection. Which one of the following is most appropriate next step?

- A. testing for her husband and other children
- B. Induction for abortion
- C. Initiation of antiretroviral therapy
- D. Reassurance and follow up after 4 weeks

2- A 39 year old man IV drug abuser came complaining of fever, night sweats and hemoptysis. AFB stain was positive. Also blood test revealed that he is positive to HIV with 50 cell CD4+. What is your next step in management?

- A. Start antiretroviral then after that start TB medications.
- B. Start antiretroviral till CD4+ become 350 cell then start anti TB.
- C. Now treat only the HIV infection
- D. Start anti TB medication at the same time with antiretroviral therapy

3- A 42-year-old man presents to his GP complaining of deterioration in his vision in the right eye and the presence of floaters. The change in his vision has been causing him to suffer from headaches. He has been HIV positive for ten years. Fundoscopy reveals haemorrhages and exudates on the retina. What is the most likely diagnosis?

- A. Retinal detachment
- B. CMV retinitis
- C. Optic atrophy
- D. Diabetic retinopathy

Questions

4- A 42-year-old man presents to his GP with ‘blotches’ over his legs. He has been HIV positive for ten years. On examination, there are multiple purple and brown papules over his legs and his gums. What is the most likely diagnosis?

- A. Malignant melanoma
- B. Squamous cell carcinoma
- C. Basal cell carcinoma
- D. Kaposi’s sarcoma

5- Which one of the following cells are the target for HIV virus?

- A. CD8 receptor containing cells.
- B. CD3 receptor containing cells.
- C. CD4 receptor containing cells.
- D. CD6 receptor containing cells.

6- One of the following drugs reduces the risk of tuberculosis ONLY in HIV-infected patients with a positive tuberculin skin test (induration of 5 mm or more):

- A. Co-trimoxazole.
- B. Isoniazid preventive therapy (IPT).
- C. Clarithromycin.
- D. Protease inhibitors.

Answer key: 1 (C) | 2 (D) | 3(B) | 4(D) | 5(C) | 6(B)