

HIV & AIDS

Color index :

Grey → extra

Blue → males slides

دعاء قبل المذاكرة

(اللهم إني أسألك فهم النبيين و حفظ المرسلين و
الملائكة المقربين, اللهم اجعل ألسنتنا عامرة بذكرك
و قلوبنا بخشيتك, إنك على كل شيء قدير و
حسبنا الله و نعم الوكيل)

Objectives

HIV main structural components

Mode of transmission

Stages of HIV infection

- Main clinical features of each stage of HIV infection
- Serological profile during the stages of HIV infection

Diagnosis

Management & treatment



HIV life cycle

Human Immunodeficiency Virus (HIV)

- Is a retrovirus that causes human AIDS, and was initially identified in 1983.
- HIV is known to infect mainly **T-helper cells(CD4)**, macrophages, monocytes and dendritic cells which express the surface receptor CD4.
- Destroying **T-helper cells(CD4)** resulting in the loss of cell mediated immunity which leads to severe immunologic impairment, leading to multiple opportunistic infections, unusual cancers and death.

Acquired immunodeficiency syndrome (AIDS)

- Is the **end stage of the disease** that is associated with CD4+ T cell depletion, multiple or recurrent opportunistic infections, and unusual cancer (Kaposi sarcoma).

Characteristics of HIV

- Family of Retroviridae¹

Virion consist of:

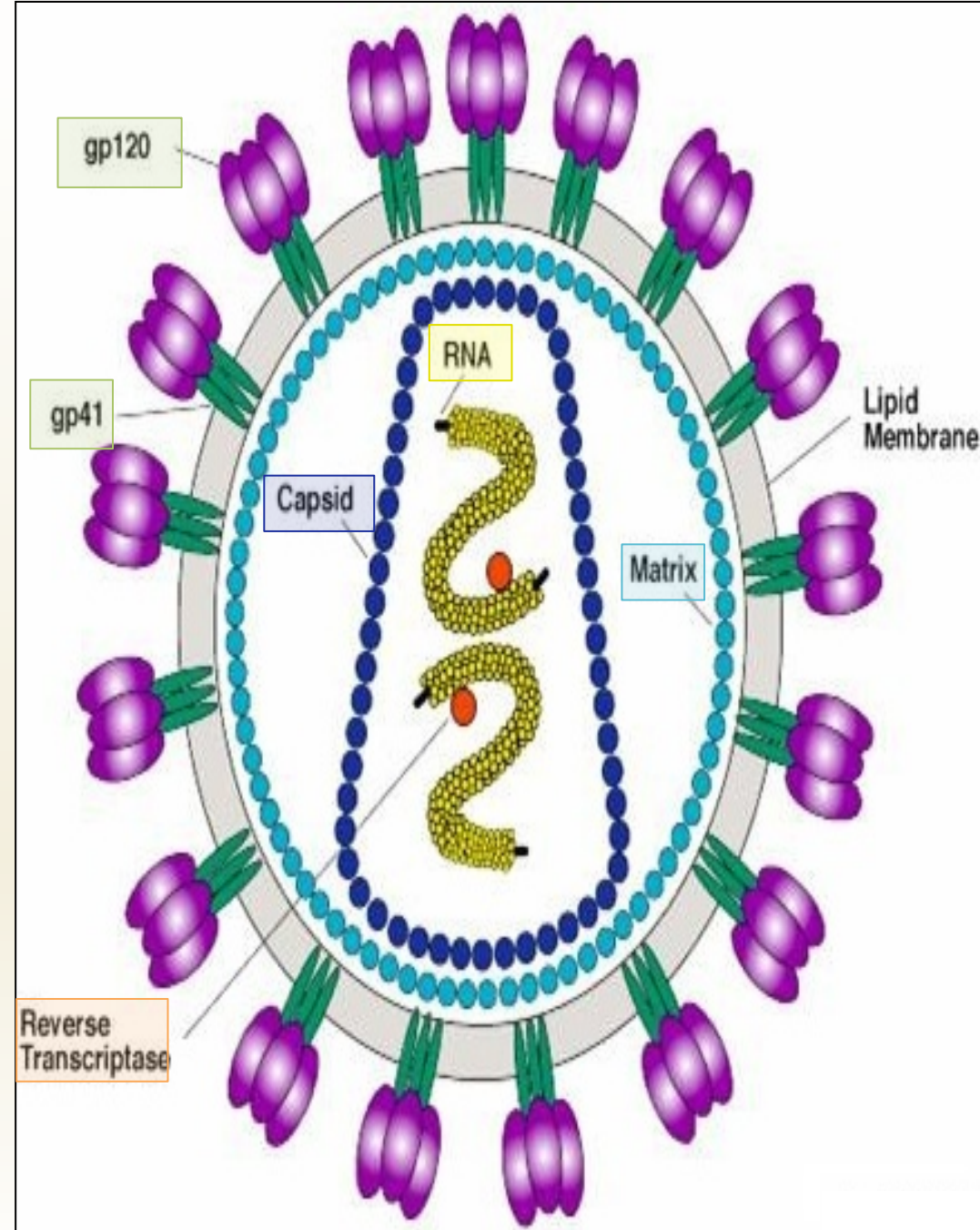
Glycoprotein envelope (gp120, gp41) → to recognize and attach to the epithelial cells

Matrix layer (p17) → To maintain the virus structures

Capsid.

Two identical copies of ssRNA (p24). (diploid virus)

Enzymes (reverse transcriptase², integrase, protease³).



1: Retroviridae: a family of single-stranded RNA 2:reverse transcriptase: a polymerase especially of retroviruses that catalyzes the formation of DNA using RNA as a template 3: protease: any of numerous enzymes that hydrolyze proteins

HIV virus

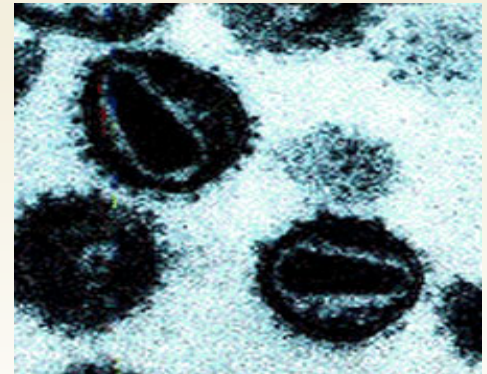
There are two HIV species known to cause AIDS in humans HIV-1 and HIV-2, and the overall sequence homology between HIV-1 & HIV-2 is less than 50%

	HIV-1	HIV-2
Epidemiology	(most common cause of AIDS) Causes HIV infection worldwide	Causes HIV infection in specific regions e.g. West Africa
virulence	Highly virulent	Relatively less virulent.
susceptibility to mutations	Highly susceptible to mutations	Relatively less susceptible to mutations

HIV genome (not important)

The genome consists of 9 genes:

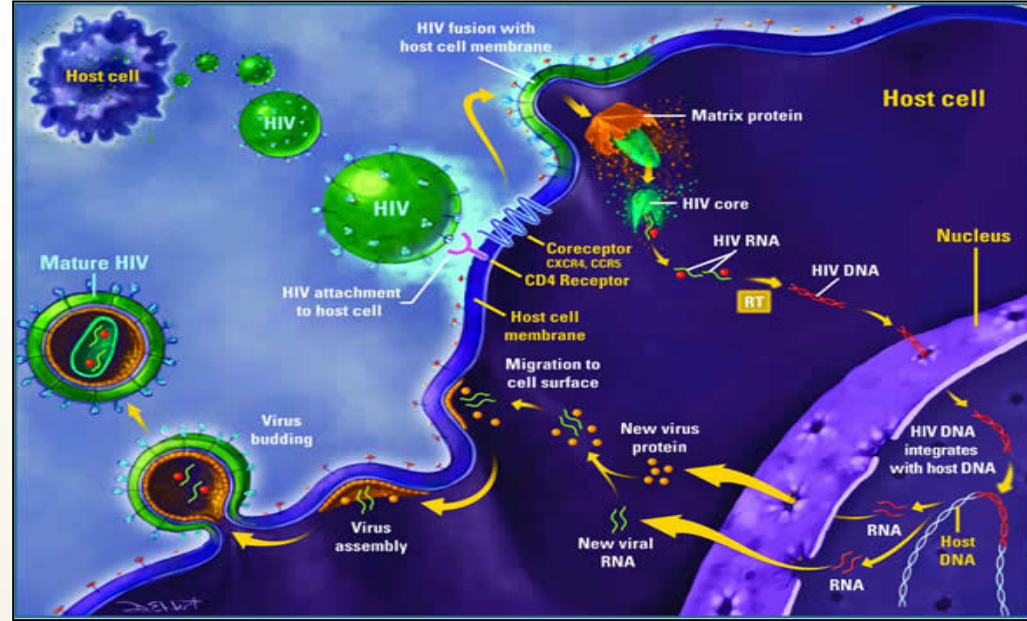
- 3 structural genes (gag, pol, env)
- 6 non-structural genes (tat, nef, rev, vif, vpr, vpu)



HIV life cycle

(Recommended for understanding)

- HIV is an enveloped virus the envelop is derived from host cell membrane with viral glycoproteins such as gp120 & gp 41
- To establish infection HIV most first attach to its host cell → attachment occurs **by interaction between** : gp120 on the surface of the virus + CD4 antigen receptor on the surface of the host cell + co-receptor on the host cell (co-receptor differs for different host cells types)



- After attachment the viral envelope and host cell membrane fuse resulting in entry of the virus into the cell → once the RNA is released into the cytoplasm up the host cell reverse transcriptase makes a DNA copy of the viral RNA genome → as the DNA is being formed reverse transcriptase degrades the RNA strand → a complementary DNA strand is then added by the reverse transcriptase → and the ends of the resulting **ds-DNA segment** are joint non-covalently [treatment with nucleoside analogues or reverse transcriptase inhibitors interferes with these steps]

- The resulting circular DNA is then moved to the nucleus and inserted into the host cell chromosome by the viral integrase enzyme → the integrated viral DNA is now referred to as **proviral DNA** → following integration the proviral DNA may remain dormant or with host cell activation RNA maybe synthesized from the DNA → yielding messenger RNAs and viral genome RNA

- Viral messenger RNA is translated yielding viral enzymes and structural proteins → some of the functional proteins are formed by cleavage of a long polyprotein by the enzyme protease [protease inhibitors interfere with this step]

- gp41 and gp120 are inserted into the host cell membrane and the structural proteins surround the viral RNA to form the core → finally the virion is released by budding

Transmission of HIV

1- Sexually:

The most common mode of HIV infection is sexual transmission (unprotected sex) at the genital mucosa through **direct contact** with infected blood, semen and vaginal secretion. More common in homosexual men Because the rectum is highly vascular and sensitive

2- Parenterally:

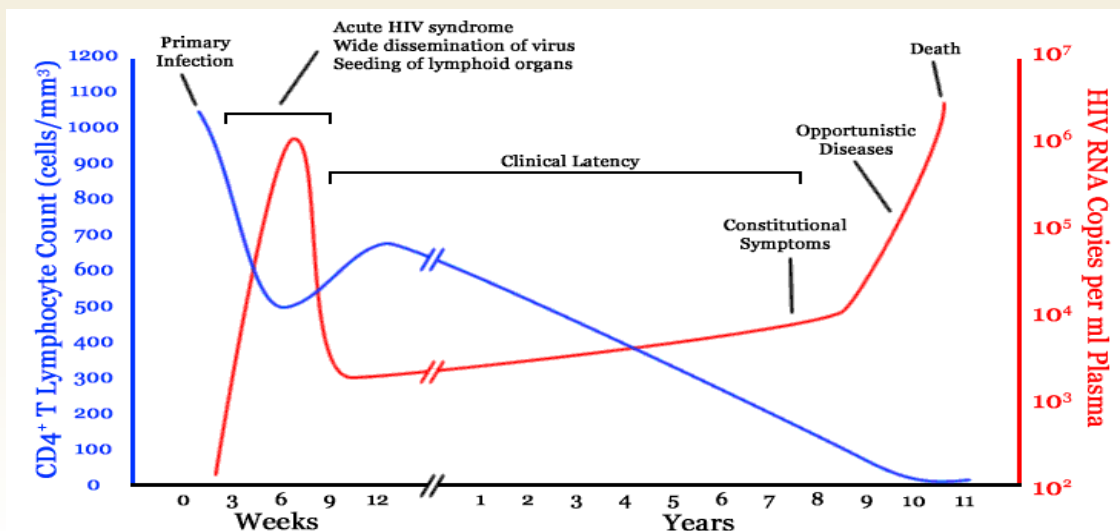
- Direct exposure to infected blood and blood products or body fluids (e.g. receiving blood from infected donor).
- Use contaminated or not adequately sterilized needles and syringes as in (drug abuser, Tattooing, body piercing & dental instruments).
- Through contaminated surgical and Sharing contaminated razors, tooth brushes, and nail cutters.

3- From mother to child:

- Infected mother transmit HIV to their babies transplacentally (vertical 25%) ,but Treatment of the mother with antiretroviral Anti-reverse transcriptase **(Zidovudine)** during **pregnancy** can reduce transmission in most cases.
- Virus spread to child mainly **(50%)** during delivery (perinatally) given Anti-reverse transcriptase **(Nevirapine)** as single dose during delivery can reduce the transmission. breast feeding also an important way of viral transmission (25%). Antiretroviral treatment of the mother and infant after birth can also significantly decrease the risk of HIV infection in the newborn.

Course of HIV-infection

Acute	Chronic	AIDS
Incubation period (2-4 weeks), this phase lasts for about 12 weeks.	Lasts for about 10 years in adults, 5 years in children.	The end stage of the disease.
Rapid viral replication (high viral load RNA in the serum).	Low viral load.	Continuous viral replication (high viral load viral RNA in the serum).
Gradual decrease in CD4 cell count	CD4 count > 500/ml	Marked decrease in CD4 cell count < 200
<ul style="list-style-type: none"> ✓ 25-65% of patients develop symptoms resemble infectious mononucleosis or Flu like syndrome (fever, headache, anorexia, fatigue, lymphadenopathy, & skin rash). ✓ Some of patients may develop aseptic meningitis. ✓ About 13% of the patients will be asymptomatic. 	Totally asymptomatic but the patients still contagious , at the end of this stage patients start to develop PGL and ARC. (explained in the next slide)	Persistent or frequent multiple opportunistic infections e.g. Pneumocystis pneumonia and development of unusual cancer (Kaposi sarcoma)



Chronic HIV

Persistent Generalized Lymphadenopathy

Defined as enlargement of lymph nodes for at least 1 cm in diameter, and **must meet the following conditions:**

1- In two or more extra inguinal area.

2- Persists for at least 3 months.

3- In the absence of any illness or medication known to cause PGL.

AID-Related Complex

Defined as a group of clinical symptoms that come before AIDS and may include the following:

1- Fever of unknown origin that persists > 1 month.

2- Chronic diarrhea, persisting > 1 month

3- Weight loss(Slim disease) > 10% of the original weight

4- Fatigue

5- Neurological disease as myelopathies and peripheral neuropathy.

DIAGNOSIS

- Patient's history with or without clinical symptoms may give hints for a physician whether the patient has ever **exposed to HIV or not**.
- Detection of both HIV Ag & Ab in the patient serum by **ELISA**
- If result is positive, repeat the screening test in duplicate.
- if still giving +ve result will do confirmatory tests (Western Blot) OR detect Blood viral load by PCR
- Blood viral load by PCR is also used to monitor HIV replication and follow up patients treatment.

Western Blot:

To confirm the presence of Anti –HIV to the structural proteins of the virus by **ELECTROPHORESIS**

PCR :

Detection of **HIV RNA** in the blood (viral load) this test is important for HIV diagnosis in:

- 1) **Infant of infected mother and**
- 2) **To monitor the antiviral treatment**

Treatment



Is a combined therapy known as High Active Antiretroviral Therapy (HAART)

- HAART **does not clear the virus**, and should be taken all life.
- HAART treated patients are **still contagious** even if their blood viral load below detection (< 50 copies/ μL).
- **HAART is usually composed of :**
 - 1) two reverse transcriptase inhibitors
 - 2) one protease inhibitor

<u>Reverse Transcriptase Inhibitors</u>	<u>Proteases inhibitors</u>
<ul style="list-style-type: none">• Zidovudine (AZT)• Zalcitabine (ddC)• Stavudine (d4T)• Lamivudine (3TC)	<ul style="list-style-type: none">• Saquinavir• Indinavir• Nelfinavir• Ritonavir

Goals of HIV treatment:



- ❖ To **inhibit** viral replication.
- ❖ To **control** chronic immune activation and keep the immune system close to the normal state.
- ❖ To **prevent** the development of opportunistic infection.
- ❖ To **minimize** the chance of viral transmission especially from mother to neonate.

Treatment will never eradicate the HIV virus.

Management and prevention:

There is no vaccine available yet for HIV

- Practice safer sex .
- Do not share razors, tooth brushes, etc
- Do not share needles and syringes
- Avoid direct exposure to body fluids
- Educate the public about HIV-infection.



OPPORTUNISTIC INFECTIONS

HELLO, I UNDERSTAND YOUR T CELLS ARE OUT FOR A WHILE



CONSTITUTIONAL ILLNESS



AIDS



T-CELL DEATH



HIV VIRION



MALIGNANCY



NEUROLOGIC DISEASE



MCQ's & SAQ's

1- D
2- A
3- D

1- Which of the following antiretroviral Anti-reverse transcriptase is given to a pregnant woman with HIV infection to reduce the risk of transmission to the fetus ?

- A- Saquinavir
- B- Indinavir
- C- Ritonavir
- D- Zidovudine

2- CD4 cell count in AIDS ?

- A- less than 200 cell
- B- > 500/ml
- C- more than 200 cells/mm³
- D- normal

3- HIV confirmatory test ?

- A- ELISA
- B- PCR
- C- electrophoresis
- D- b & c

1) What's a persistent generalized lymphadenopathy?

Ans: Enlargement of the lymph nodes in the absence of any illnesses, in extra inguinal area or persistent for more than 3 months

2) What's the cause of death in AIDS?

Ans: Opportunistic infections

3) Describe your treatment goals in a recently diagnosed HIV patient?

Ans:

- 1) Inhibit viral replication
- 2) Prevent transmission
- 3) keep the immune system close to a normal state

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