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MED 443
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TEAM 443
MICROBIOLOGY

L4- HIV & AIDS

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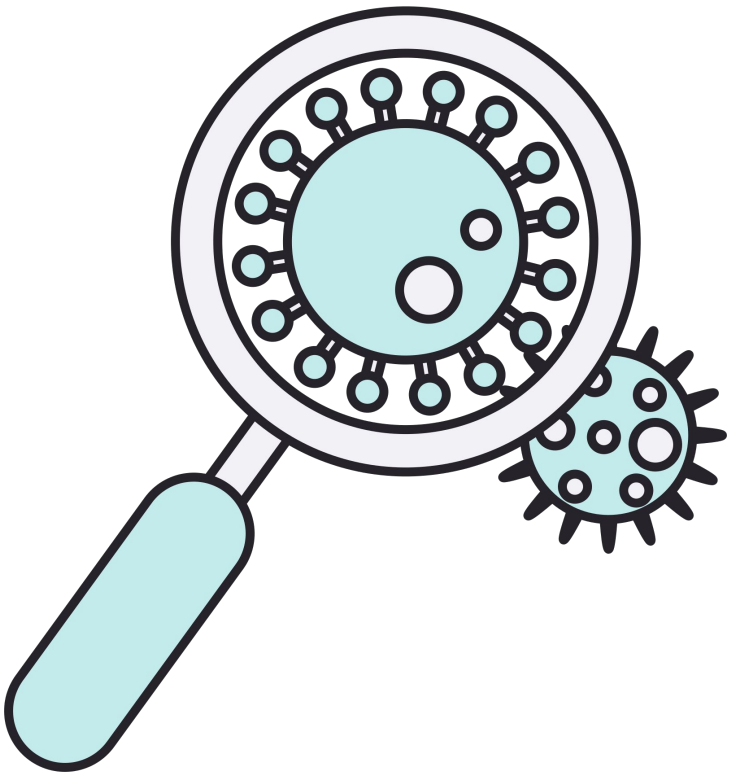


OBJECTIVES

1. HIV main structural components
2. Mode of transmission
3. Stages of HIV infection (main clinical features of each stage & serological profile)
4. Diagnosis
5. Management & treatment

Outline

- Introduction to HIV & AIDS
- HIV main structural components & life cycle
- Mode of transmission
- HIV pathogenesis
- Stages of HIV infection
- Persistent generalized lymphadenopathy (PGL)
- AIDS related complex (ARC)
- Serological profile
- Diagnosis
- Management & treatment

Introduction to HIV

HIV

- Is a retrovirus that causes human AIDS, and was initially identified in 1983.
- HIV infects mainly **CD4+ T cells** , macrophages, and dendritic cells which express the surface receptor CD4.
- Destroying CD4+ T cells leads to severe immunologic impairment & eventually death.

and treatment **doesn't eradicate** the virus, it only improves symptoms & prolong patient life

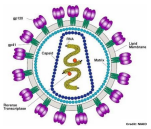
AIDS

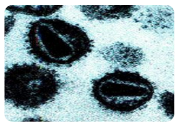
what are the features of this stage?

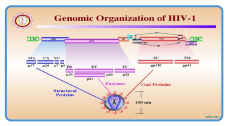
Acquired immunodeficiency syndrome (AIDS) Is the 1-**end stage of the disease** that is associated with CD4+ T cell depletion, multiple or recurrent 2- **opportunistic infections**, and **unusual** cancer 3- (**Kaposi sarcoma**).

Characteristics of HIV

Family of **Retroviridae**, virion consist of:







- **Glycoprotein envelope** (**gp120**, gp41).
  bind to CD4 T cell.
- Capsid (p24).
- **Two** copies of **ss-RNA**.
- The genome consists of 9 genes:
  - 3 structural genes (gag, pol, env)
  - 6 non-structural genes (tat, nef, rev, vif, vpr, vpu)
- **Matrix layer** (p17).
- **Enzymes:**
  - **Reverse transcriptase: converts** viral **RNA** into **DNA**.
  - **Integrase:** integrates viral DNA with host DNA (**provirus**), persisting infection.
  - **Protease:** viral protein maturation.
    Assemble the virus

HIV Species

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

HIV-1

discussed in this lecture

- Causes HIV infection **worldwide**.
- Highly virulent.
- Highly susceptible to mutations.

HIV-2

- Causes the infection in **specific regions** e.g. West Africa.
- Relatively **less virulent.**
- Relatively less susceptible to mutations.

Transmission of HIV

Sexually (unprotected sex)	The virus is present in blood, semen and vaginal secretions.
Parenterally	○ Direct exposure to infected blood or body fluids (e.g. receiving blood from infected donor). not anymore due to screenings. ○ Using contaminated or not adequately sterilized tools in surgical or cosmetic practice (dental, tattooing, body piercing). ○ Sharing contaminated needles, razors, or tooth brushes. HIV is sensitive and dies quickly outside the body.
Perinatally (from mother to baby)	○ Infected mothers can transmit HIV to their babies **transplacentally** (25%), but Treatment of the mothers with the reverse transcriptase inhibitor (**Zidovudine**) during **pregnancy** can reduce transmission in most cases. ○ Virus spread to child perinatally mainly (50%) during delivery, but given the reverse transcriptase inhibitor (**Nevirapine**) as single dose during **delivery** can reduce the transmission. (emergency use only, never had previous treatment) ○ **Breastfeeding** is also an important way of perinatal transmission (25%).

Stages of HIV Infection

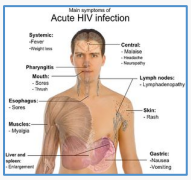
The course of HIV infection is divided into 3 stages based on CD4+ T cell count and presence of opportunistic infections:

Acute phase | **Chronic phase** (PGL & ARC) | **AIDS**

Acute phase | **Chronic phase** (PGL & ARC) | **AIDS**

Acute phase

Overview



- ○ Patient is **contagious**. patient is **contagious** in **all stages**
- ○ Incubation period 2 weeks and lasts for about 12 weeks.
- ○ Mostly **asymptomatic**, but in about 25-65% of the cases, **patients may develop symptoms resemble infectious mononucleosis or Flu** like (fever, headache, anorexia, fatigue, lymphadenopathy, skin rash) which resolved in 2 weeks.
- ○ Rapid viral replication (**high viral load** $>10^6$ copies/mL).
- ○ **Gradual decrease in CD4+ T cell count**.

Blood Markers

- ○ Normal to slightly decrease no of CD4+ T cells.
- ○ **Appearance** of the viral RNA, and then the core antigen (p24 antigen) which indicate active viral replication.
- ○ Appearance of 2 antibodies: Anti-envelop (Anti-gp120 & gp41) & Anti-core (Anti-p24)
- ○ **The 1st choice marker for detection HIV in the acute phase is HIV RNA.** (first to appear)

Stages of HIV Infection

Chronic phase

treatment prolong this stage

Overview	○ Lasts for about > 10yrs in adults, and 5 years in children. (but with treatment patient will live for much longer until they die from a different cause) ○ Totally asymptomatic but the patients is **still contagious**. ○ Relatively **low viral load** (<10^4 copies/mL). but at the end of this stage it will start to increase to reach AIDS. ○ **CD4+ T cell count** decrease but still **> 200** cells/mm^3
Blood Markers	○ Viral load (HIV RNA) increases gradually, but HIV core antigen (p24) may not appear in blood. ○ Anti-envelop (Anti-gp120 & gp41) & Anti-core (Anti-p24) are positive. ○ **CD4+ T cell count** gradually decreased but still **more than >200 cells/mm^3**

At the end of this stage, two syndromes appear:

Persistent generalized lymphadenopathy (PGL)

○ Is defined as **enlargement of lymph nodes** for at least 1 cm in diameter in the absence of any illnesses or medications that known to cause PGL.
○ Clinical features:
- ↠ In 2 or > lymph nodes **out** of the inguinal area. (**except** inguinal area)
- ↠ Persists for at least 3 months.

AIDS-related complex (ARC)

Is a group of clinical symptoms that come before AIDS and may include the following:
- ↠ Fever of unknown origin that persists > 1 month.
- ↠ Chronic diarrhea, persisting > 1 month
- ↠ Weight loss > 10% of the original weight (slim disease).
- ↠ Fatigue, night sweating, and malaise.
- ↠ Neurological disease as myelopathy and peripheral neuropathy.

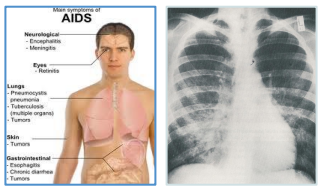
Acute phase | Chronic phase (PGL & ARC) | AIDS

AIDS

how do we know we reach AIDS? CD4 < 200

Overview	○ The end stage of the disease. ○ Continuous viral replication (**high viral load**). ○ Marked decrease in **CD4+ T cell count < 200 cell/mm3**. ○ Defects in cellular immunity. ○ **Persistent or frequent multiple opportunistic infections** as: ↠ **Viral: CMV, EBV**. ↠ **Bacterial**: **Mycobacterium**, Mycoplasma. ↠ Protozoa: **Toxoplasma**, **cryptosporidium**. ↠ Fungi :**Pneumocystis pneumonia** (**was never known before AIDS**, disseminated candida infection. ○ Unusual cancer (**Kaposi sarcoma**).
Blood Markers	○ High viral load (HIV RNA), and HIV core antigen (p24) appears in blood. ○ Detection of both HIV RNA & the antigen p24 indicative of active viral replication ○ Anti-envelop (Anti-gp120) & Anti-core (Anti-p24) are positive. ○ CD4+ T cell count decreased to very low levels (<200 cells/mm3).

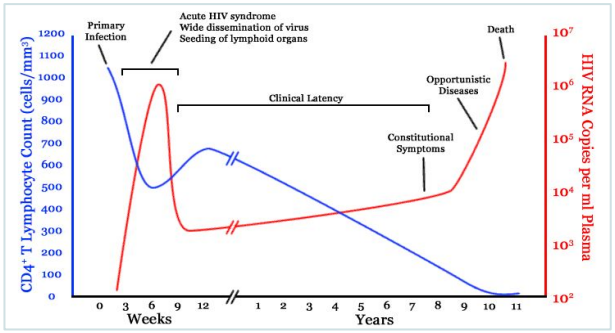
Kaposi sarcoma / Candida infection



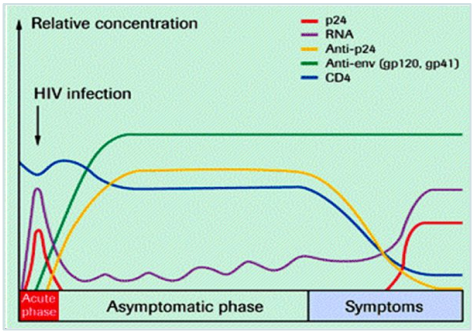
Pneumocystis pneumonia

HIV Infection

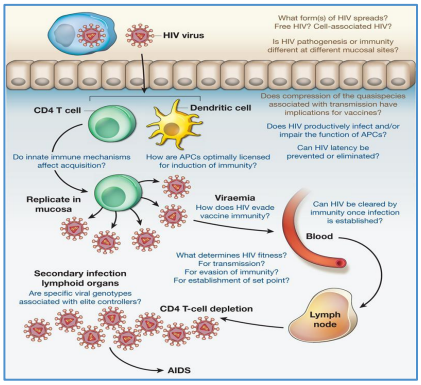
Serological profile of HIV



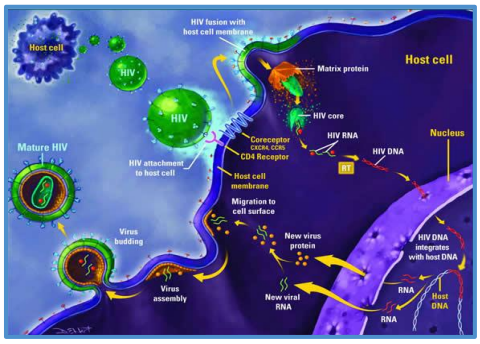
HIV RNA copies ***VS*** CD4+ T cell counts



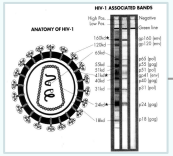
HIV Pathogenesis



HIV life cycle



HIV Diagnosis

History	Patient's history with or without clinical symptoms may give/provide hints for a physician whether the patient has ever exposed to HIV or not.
Screening	○ Screening/detection of both HIV Ag & Ab in the patient serum by **ELISA**. ○ **If** the result is **+ve** we **repeated** the specimen twice (screening test) in duplicate ○ **If** still giving **+ve** (repeatedly reactive) result will do **confirmatory tests.**
Confirmation 	○ **Western blot**: To confirm the presence of Anti –HIV to the structural proteins of the virus by ELECTROPHORESIS ○ PCR: For detection of HIV RNA in the blood (viral load). this test is important for HIV diagnosis in infant of infected mother and also to monitor the antiviral treatment ○ Recombinant immunoblot assay (RIBA)
Follow up	Blood viral load by **PCR** is also used to monitor HIV replication and follow up patients response to treatment.

Management & Prevention

No vaccine is available to prevent HIV infection, and thus the best strategies to control the spread of HIV infection are the following:

- Religious education (teaching the risk of making prohibited relations).
- Public health education (teaching the risk of using shared materials).
- Practice safer sex by having one sexual partner.
- Advise of using condoms when is necessary.

HIV Treatment

Is a combined therapy known as high active antiretroviral therapy (HAART). NOTE:

- ↠ HAART doesn't clear (**doesn't eradicate**) **the virus from the body,** and should be taken all life.
- ↠ HAART treated patients are still **contagious** even if their blood viral load below detection level (< 50 copies/mL).
- ↠ HAART is usually composed of 2 type of reverse transcriptase inhibitors & 1 protease inhibitor

- HIV is easily inactivated by treatment for 10 min at 37°C with any of the following disinfectant as: 10% Household bleach, Sodium hypochlorite, 50% Ethanol, 35% Isopropanol, 0.5% Paraformaldehyde, 0.3% Hydrogen peroxide

Male Slides	Nucleoside analog RT inhibitors for HIV-1 & HIV-2	Non-nucleoside analog RT inhibitors for HIV-1 only
Reverse transcriptase inhibitors	○ Zidovudine (AZT) ○ Zalcitabine (ddC) ○ Stavudine (d4T) ○ Lamivudine (3TC)	○ Nevirapine ○ Delavirdine ○ Efavirenz
Proteases inhibitors include	○ Saquinavir ○ Indinavir ○ Nelfinavir ○ Ritonavir	

Goal of HIV treatment

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

MCQs - SAQ

Q1 - Kaposi sarcoma is characteristic for :			
A- HSV	B- HPV	C- HIV-2	D- HIV-1
Q2 - main cell infected by HIV?			
A- macrophages	B- dendritic	C- CD4 T cell	D- epithilium
Q3 - what does integrase do ?			
A- assemble the virus	B- Provirus (integration of viral genome into host DNA)	C- convert RNA to DNA	D- bind virus to host receptor
Q4 - chronic stage HIV patient with persistent generalized lymphadenopathy has lymph nodes anywhere on the body except :			
A- inguinal	B- back of neck	C- axillary	D- supraclavicular
Q5 - pregnant mother during delivery was discovered to have HIV, what treatment should be given ?			
A- Zidovudine	B- Nevirapine	C- indenavir	D- ritonavir
Q6 - for HIV screening a population we use :			
A- PCR	B- western blot	C- RIBA	D- ELISA
Q7 - for confirmation of HIV we use :			
A- ELISA	B- western blot	C- history	D- :-)
Q8 - when is the patient contagious in HIV infection			
A- acute	B- chronic	C- AIDS	D- ALL
Q9 - CD4 T cell level in chronic phase			
A- >200 cells/mm	B- < 200 cells/mm	C- < 50 cells/mm	D- > 3000 cells/mm
Q10 - 1st marker for detecting HIV in acute phase :			
A- HIV RNA	B- anti core	C- HIV antigen	D- HIV antibody

1- D | 2- C | 3- B | 4- A | 5- B | 6- D | 7- B | 8- D | 9- A | 10- A

TEAM 443
MICROBIOLOGY

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اللهم إني استودعك ما قرأت وما حفظت فرده إليّ عند حاجتي إليه انك على كل شيء قدير

Any future corrections will be in the editing file, so please check it frequently