MICROBIOLOGY
TEAM 432

LECTURE (5)
HIV & AIDS

OBJECTIVES:

- Were not given.

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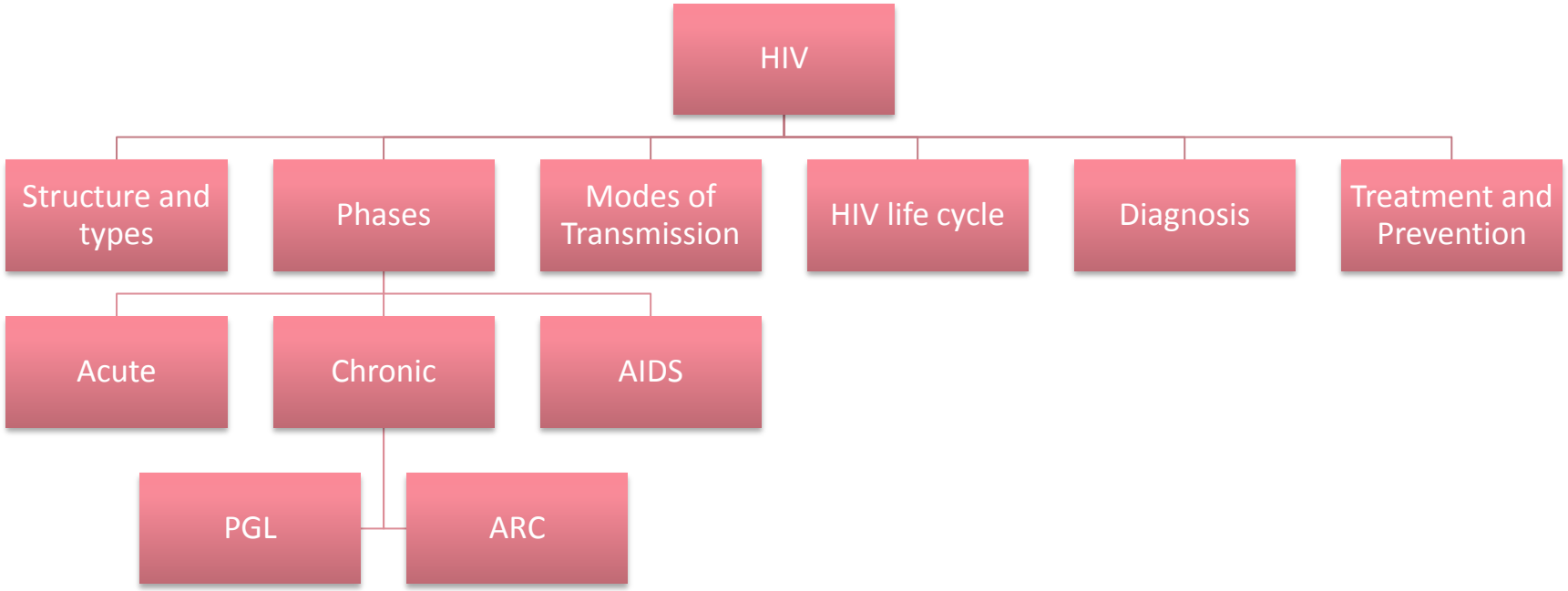
MIND MAP
(HIV & AIDS)

MICROBIOLOGY TEAM 432



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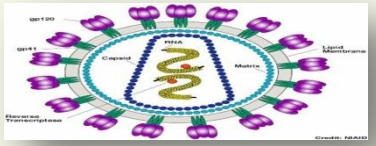
Human Immunodeficiency Virus :

- HIV is known to infect mainly T-helper cells(CD4), macrophages 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 "(Kaposi sarcoma)" and death.

Characteristics of HIV and Structure of HIV :



- Family of **Retroviridae**.
- Virion consist of:
  - **Glycoprotein envelope (gp120, gp41).**
  - Matrix layer(p17).
  - Capsid.(covers the RNA) (p24)
  - **Two copies of ssRNA.**
  - **Enzymes(reverse transcriptase, integrase, protease).**

Types :

- **HIV-1:**
  1. Causes HIV infection worldwide.
  2. Highly virulent. (can cause an infection in low doses)
  3. Highly susceptible to mutations.
- **HIV-2:**
  1. Causes the infection in specific regions e.g. West Africa
  2. Relatively less virulent.
  3. Relatively less susceptible to mutations

Transmission of HIV :

1-**Sexually:**

- The **most common mode** of HIV infection is sexual transmission at the genital mucosa through direct contact with infected blood, semen and vaginal secretion.

2-**Parenterally:**

- Direct exposure to infected blood and blood products.
- Use contaminated needles and syringes as in (drug abuser) and Tattooing.
- Through contaminated surgical and **dental instruments.**
- 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 **perinatally A- mainly (50%) during delivery** , **given Anti-reverse transcriptase (*Nevirapine*) as single dose during delivery can reduce the transmission** . B-breast feeding also an important way of perinatal transmission (25%).Antiretroviral treatment of the mother and infant after birth can also significally decrease the risk of HIV infection in the newborn.

HIV genome

The genome consists of 9 genes:

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

Virus Inactivation

➢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

HIV life cycle:

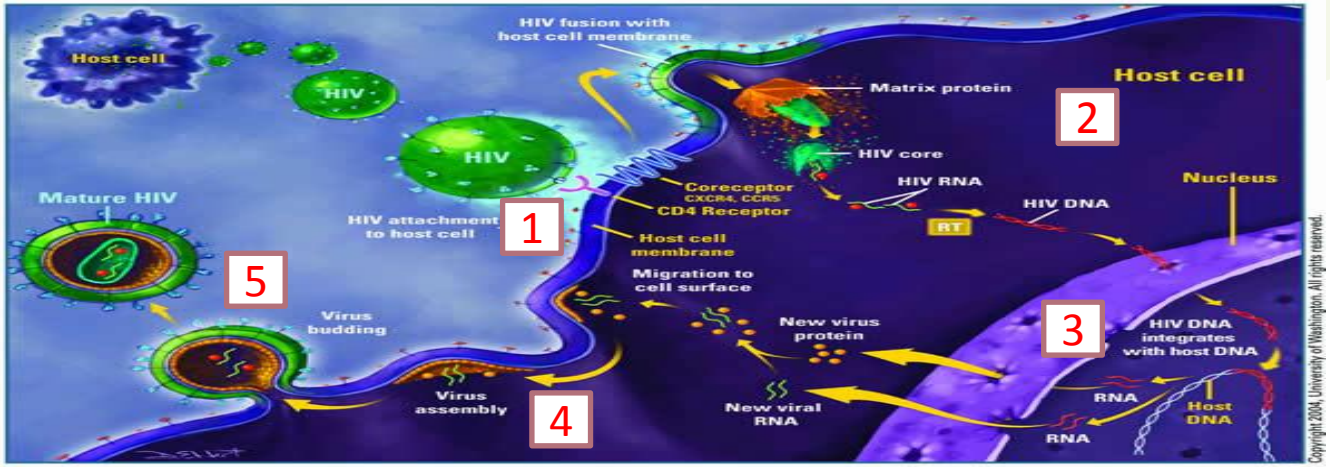
1-Binding and Fusion: HIV binds to a specific type of CD4 receptor on the surface of the CD4 cell by its own gp120 (for attachment) and gp 41 (which insures the binding and entry) .once bound HIV can fuse with the host cell (CD4 cell) to release its genetic material into the cell.

2-Reverse Transcription and Integration: when in the cell further layers are removed till all what's left is the RNA. A special enzyme called reverse transcriptase changes it to host cell Pro-viral DNA , which enters the nucleus and then integrated into the host DNA via an enzyme called integrase.

3-Transcription: When the host cell becomes activated, the virus uses the host enzymes to create more of its genetic material (RNA) which then leaves the nucleus to the cytoplasm

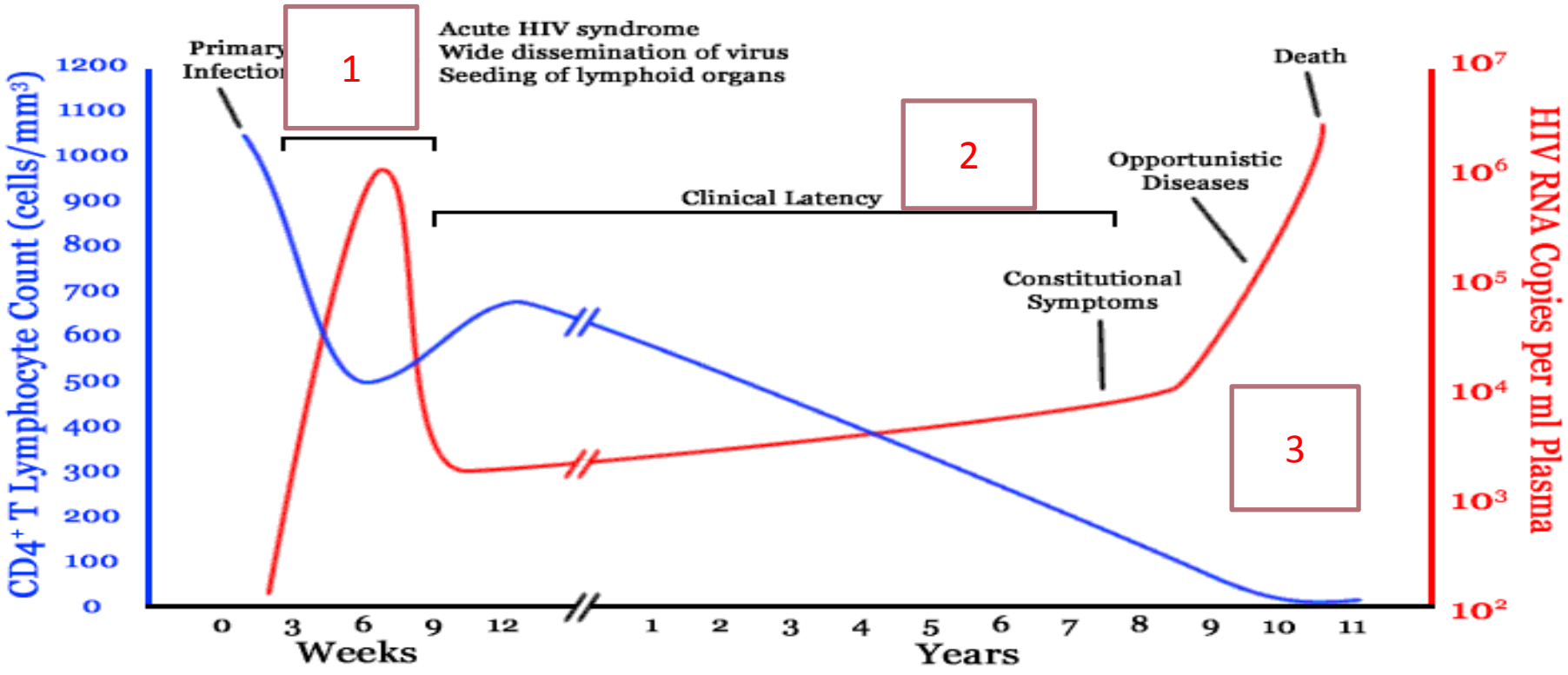
4-proteins Assembly: A special enzyme called protease cuts the longer HIV proteins into individual proteins. When these come together with the virus's genetic material, a new virus has been assembled.

5-Budding: This is the final stage of the virus's life cycle. In this stage, the virus pushes itself out of the host cell, taking with it part of the membrane of the cell. This outer part covers the virus and contains all of the structures necessary to bind to a new CD4 cell and receptors and begin the process again.



The Course of HIV-infection (can be divided into 3 stages):

1. The acute phase
2. The chronic phase
- 1- (PGL)
- 2-(ARC)
3. AIDS



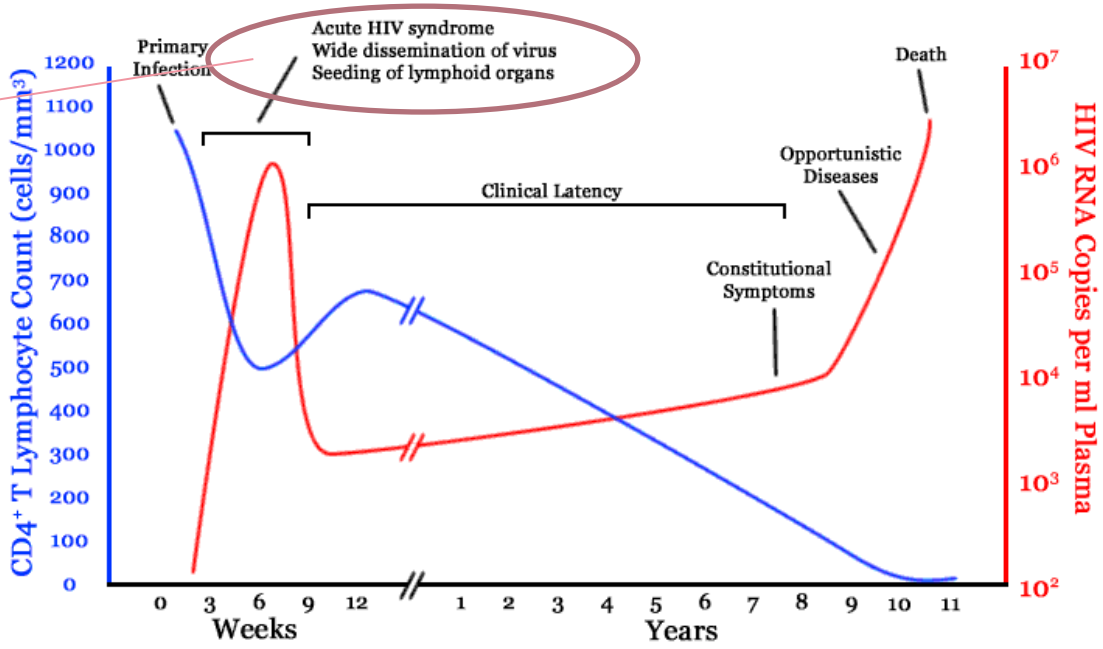
Acute phase:

Incubation period (2-4 weeks) ,this phase Lasts for about 12 weeks. (its from the moment of contact with the visrus till symptoms occur , lasts for ~3months)

- Rapid viral replication (high viral load RNA in the serum).
- Gradual decrease in CD4 cell count.
- 25-65% of patients develop symptoms resemble infectious mononucleosis or Flu like syndrome (fever, headache, anorexia, fatigue, lymphadenopathy , mylagia ,sore throat & skin rash) which resolved in 2 weeks.
- Some of patients may develop aseptic meningitis.
- About 13% to 40% of the patients will be asymptomatic.

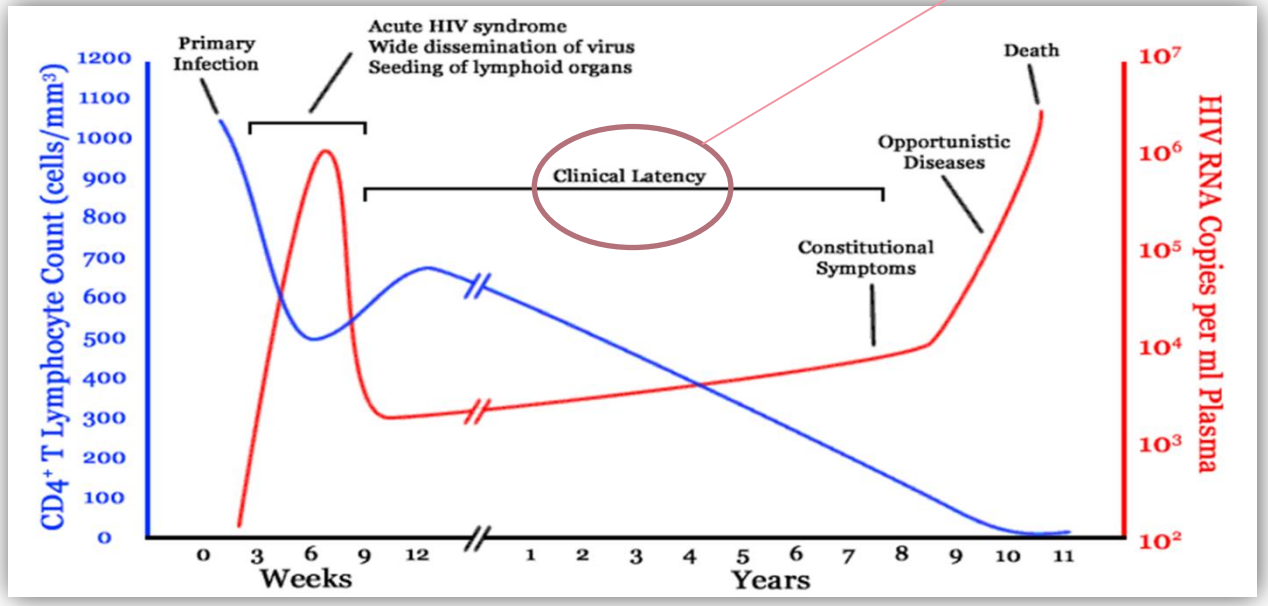
In the acute phase :

- RNA → very high in load
- CD4 declining to ~600/mm^3 as a consequence the immune system can still protect from the opportunistic infection



Chronic Phase:

- Lasts for about 10 to 15 years in adults and around 5 years in children.
- Low viral load.
- CD4 count > 500/ml
- Totally **asymptomatic** but the patients still contagious ,at the end of this stage patients start to develop PGL and ARC.
- HIV is very contagious even from day one.
- HIV is trapped in cells during the chronic phase.



- CD4 cells will increase.
- Viral load is low.
- But at the end of the chronic phase (PGL and ARC phase) the viral load will increase and CD4 count will decrease.

A-Persistent generalized lymphadenopathy (PGL):

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

- In two or more extra inguinal area. (The physician should look for two lymph nodes in two different regions other than inguinal for example, submandibular and axillary)
- Persists for at least 3 months.
- In the absence of any illness or medication known to cause PGL.

B- AIDS Related Complex (ARC):

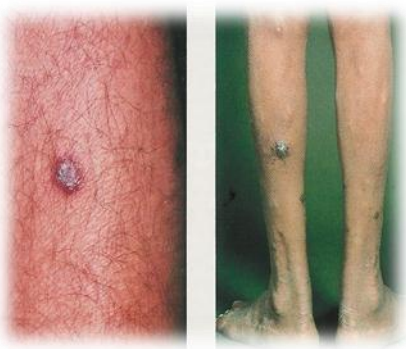
Is a group of clinical symptoms that come before AIDS and may include the following:

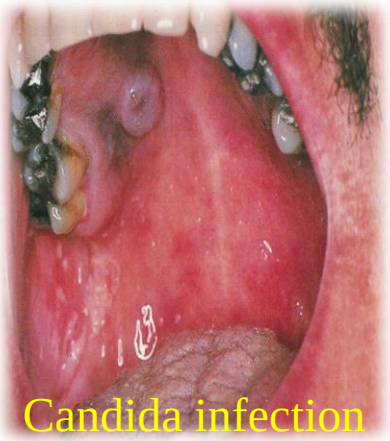
- Fever of unknown origin that persists > 1 month.
- Chronic diarrhea, persisting > 1 month.
- Weight loss(Slim disease) > 10% of the original weight.
- Fatigue.
- Neurological disease as myelopathies and peripheral neuropathy .

Slim disease

AIDS:

- **The end stage of the disease.**
- Continuous viral replication (high viral load viral RNA in the serum).
- Marked decrease in CD4 cell count < 200 if it was more than 200 then opportunistic infections can't occur.
- Persistent or frequent multiple opportunistic infections e.g Pneumocystis pneumonia and development of unusual cancer (Kaposi sarcoma)

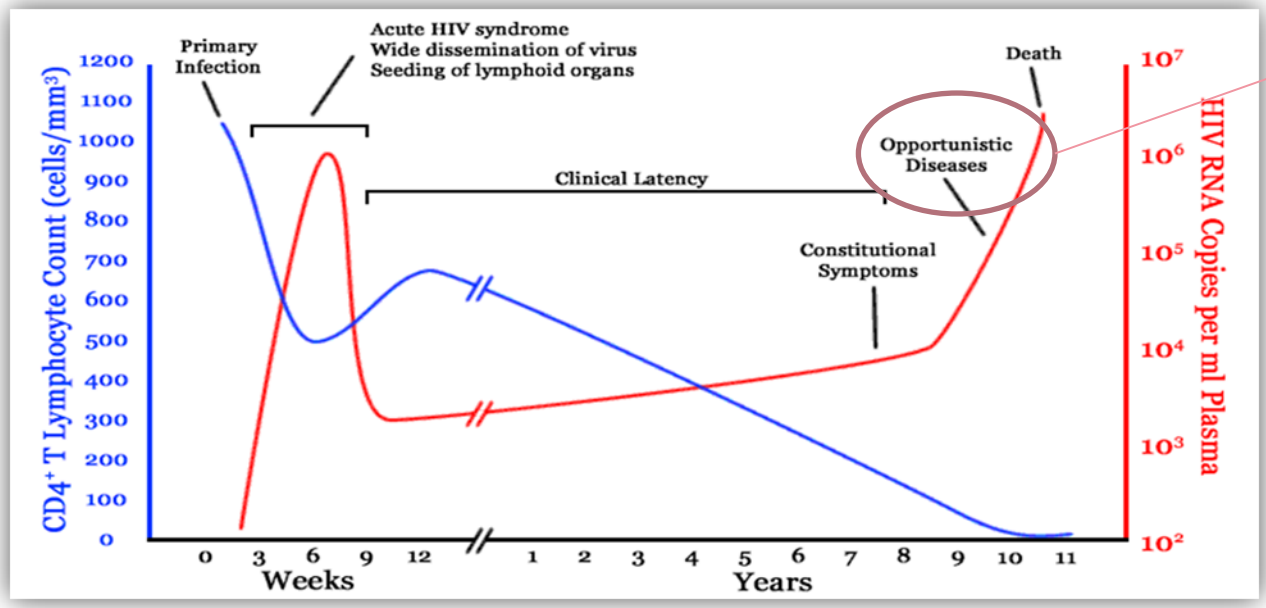




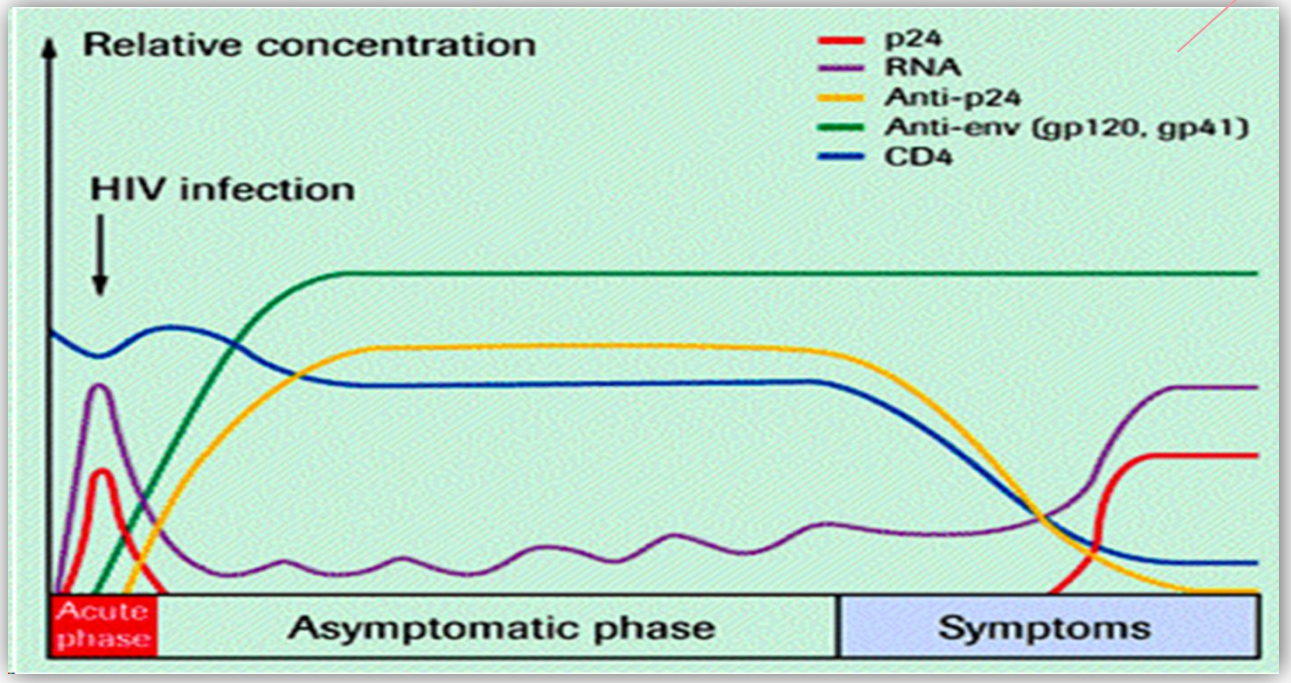
OPPORTUNIST INFECTIONS AND TUMORS IN AIDS	
viruses	disseminated CMV (including retina, brain, peripheral nervous system, gastrointestinal tract) HSV (lungs, gastrointestinal tract, CNS, skin) JC virus (brain – PML) EBV (hairy leukoplakia, primary cerebral lymphoma)
bacteria*	mycobacteria (e.g. *Mycoplasma avium*, *M. tuberculosis* – disseminated, extrapulmonary) *Salmonella* (recurrent, disseminated) septicemia
protozoa	*Toxoplasma gondii* (disseminated, including CNS) *Cryptosporidium* (chronic diarrhea) *Isospora* (with diarrhea, persisting more than one month)
fungi	*Pneumocystis jiroveci* (pneumonia) *Candida albicans* (esophagitis, lung infection) *Cryptococcus neoformans* (CNS) histoplasmosis (disseminated, extrapulmonary) *Coccidioides* (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



- Notice that during the end stage of HIV infection patient get AIDS.
- Viral load is very high and CD4 cells are very low in count.



- Viral load (purple) is detected before the Ag (p24 capsid protein) in acute stage.
- Viral load in chronic (asymptomatic phase) is low and the antigen **(p24) will disapper.**
- Anti-envelop antibodies will be stable and high through out the patient's life.
- **P24 will appear during AIDS.**

Blood markers in the acute stage:

- 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 two antibodies, **Anti-envelop** (**Anti-gp120**) & **Anti-core (Anti-p24).**
- **The 1st choice marker for detection HIV in the acute phase is HIV RNA.**

Blood markers in the chronic stage:

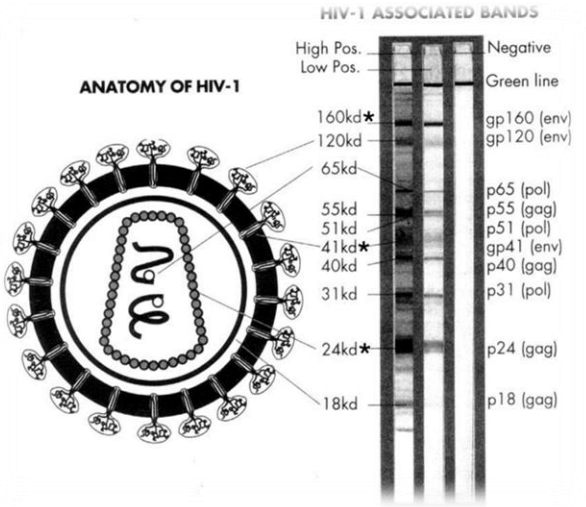
- Viral load **(HIV RNA)** increases gradually, and **HIV core antigen (p24)** may appear in blood.
- Anti-envelop **(Anti-gp120)** & Anti-core (**Anti-p24**) are positive.
- **CD4+ T cell** count gradually **decreased** but still more than 200 cells/mm^3

Blood markers in AIDS stage:

- 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/mm^3).

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.
- Screening patient's serum by ELISA for both (HIV Ag & HIV Ab) if the result is +ve we repeat the specimen twice in duplicate if still giving +ve result will do confirmatory tests (Western Blot). (So 3 times by ELISA and 1 by Western Blot = 4 times for each specimen)
- Blood viral load by PCR is also used as confirmatory test and to follow up patients response to treatment.



Electrophoresis

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.**

Treatment:

- Is a combined therapy known as high active antiretroviral therapy (HAART).
- NOTE: HAART does not clear the virus, and should be taken all life. (It only delays the end stage from occurring)
- NOTE: HAART treated patients are still contagious even if their blood viral load below detection (< 50 copies/µL).
- HAART is usually composed of two reverse transcriptase inhibitors and one protease inhibitor.

A.Reverse Transcriptase Inhibitors:

AZT	Zidovudine
NVP	Nevirapine
ddC	Zalcitabine
ddI	Didanosine
d4T	Stavudine
3TC	Lamivudine

B.Protease inhibitors:

- Saquinavir
- Indiniavir
- Ritonavir
- Nelfinavir

Goals of HIV treatment:

- To inhibit viral replication.
- As in chronic infection ,ART is effective in suppressing serum viral RNA levels and increasing CD4 cell counts in the vast majority of patients, furthermore , initiation of ART earlier after HIV infection may be associated with a greater chance of immune reconstitution to normal or nearly normalCD4 cell levels .
- 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.

Prevention and control:

- 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.

SUMMERY :

- HIV virus is composed of diploid genome (2 molecules of RNA).

- Acute phase : CD4 is decreased and high viral load.
- Chronic phase: CD4 is increased and viral load will decrease .
- End of chronic phase and beginning of AIDS: CD4 is very low and viral load is very high.

- Remember that there is **no** opportunistic infections during the acute phase.

- During latent Phase, virus replicates in lymph nodes.

- Diagnosis is made by ELISA then positive→ repeat the specimen twice in duplicate→ results are confirmed by Western bloat and PCR

- If the patient was infected very recently, we measure the viral load , but routinely we start by measuring Ag and Ab levels in the serum.

Questions

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Q1- HIV belongs to the Retroviridae family and is made up of ?

A. Two single stranded RNA
B. Double stranded DNA
C. Single stranded RNA

Q2-In the acute Phase CD4 cells show?

A. Increase in number
B. Gradual decrease in number
C. Steep drop in number

Q3- What immune cells does HIV infect?

A. CD4 positive cells
B. Macrophages
C. Both a and b

Q4-What is Acute HIV Syndrome?

A. When HIV progresses into AIDS
B. The stage immediately after HIV infection when patient falls ill
C. The final fatal disease for AIDS patient

1-A
2-B
3-C
4-B

For any suggestions or problems please contact
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Thank you