

HIV & AIDS

By

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Objectives

The students should be able to know:

- 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

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

Human immunodeficiency virus (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 and eventually death.

Acquired immunodeficiency syndrome (AIDS)

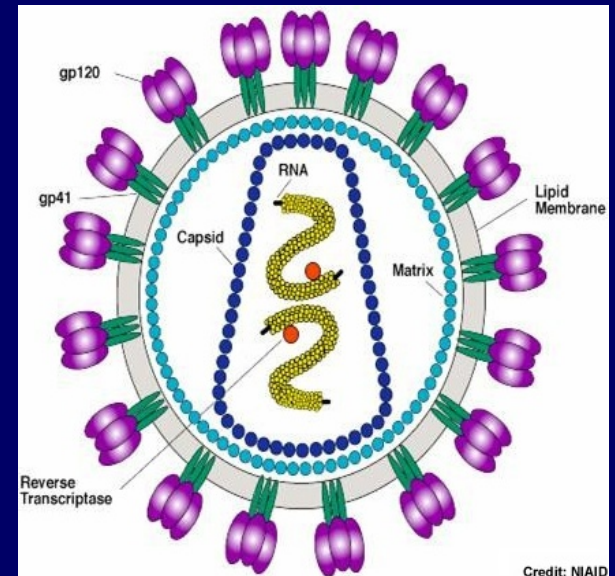
- Is the end stage of the disease that is associated with CD4+ T cell depletion, multiple or recurrent opportunistic infections, and unusual cancer (Kaposi sarcoma).

Characteristics of HIV

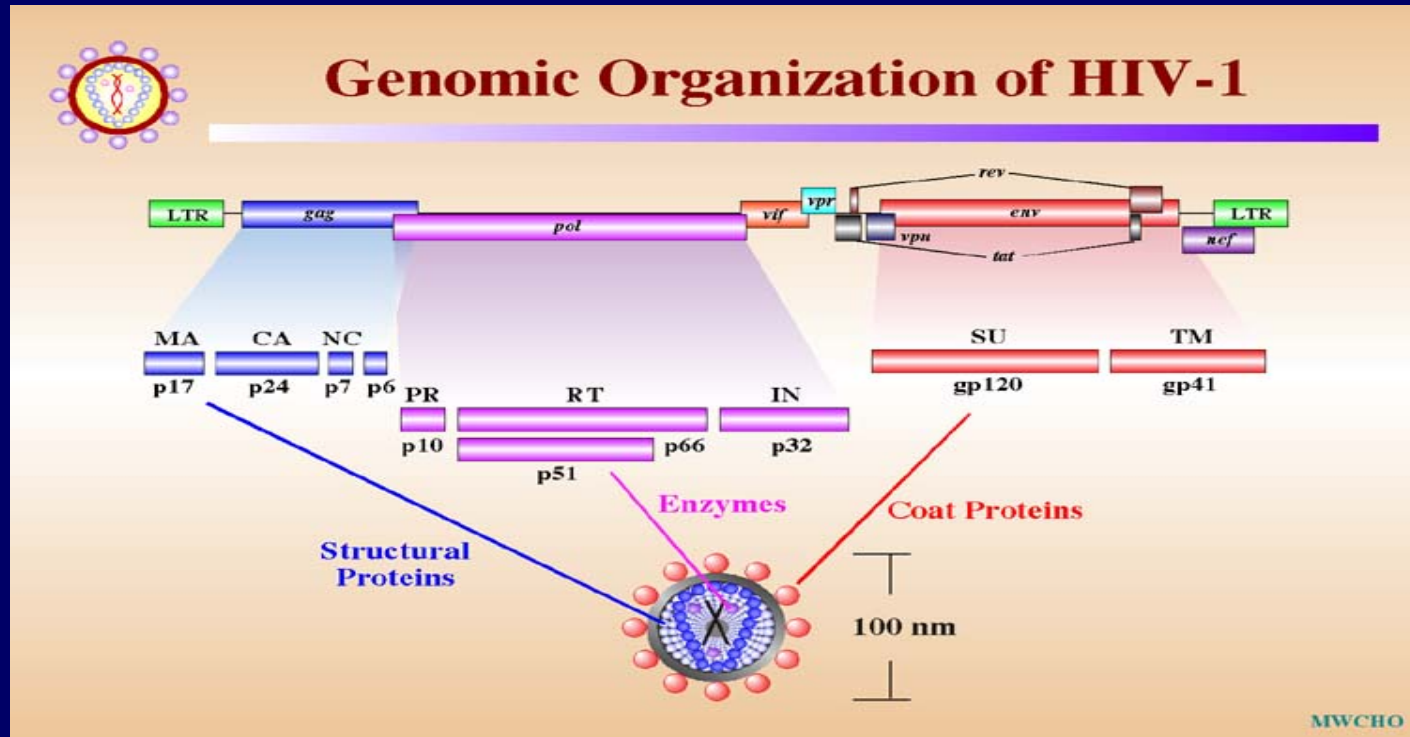
- Family of *Retroviridae*.

Virion consist of:

- Glycoprotein envelope (gp120, gp41).
- Matrix layer (p17).
- Capsid (p24).
- Two copies of ss-RNA.
- Enzymes:
 - Reverse transcriptase: converts viral RNA into DNA.
 - Integrase: integrates viral DNA with host DNA (provirus), persisting infection.
 - Protease: viral protein maturation.



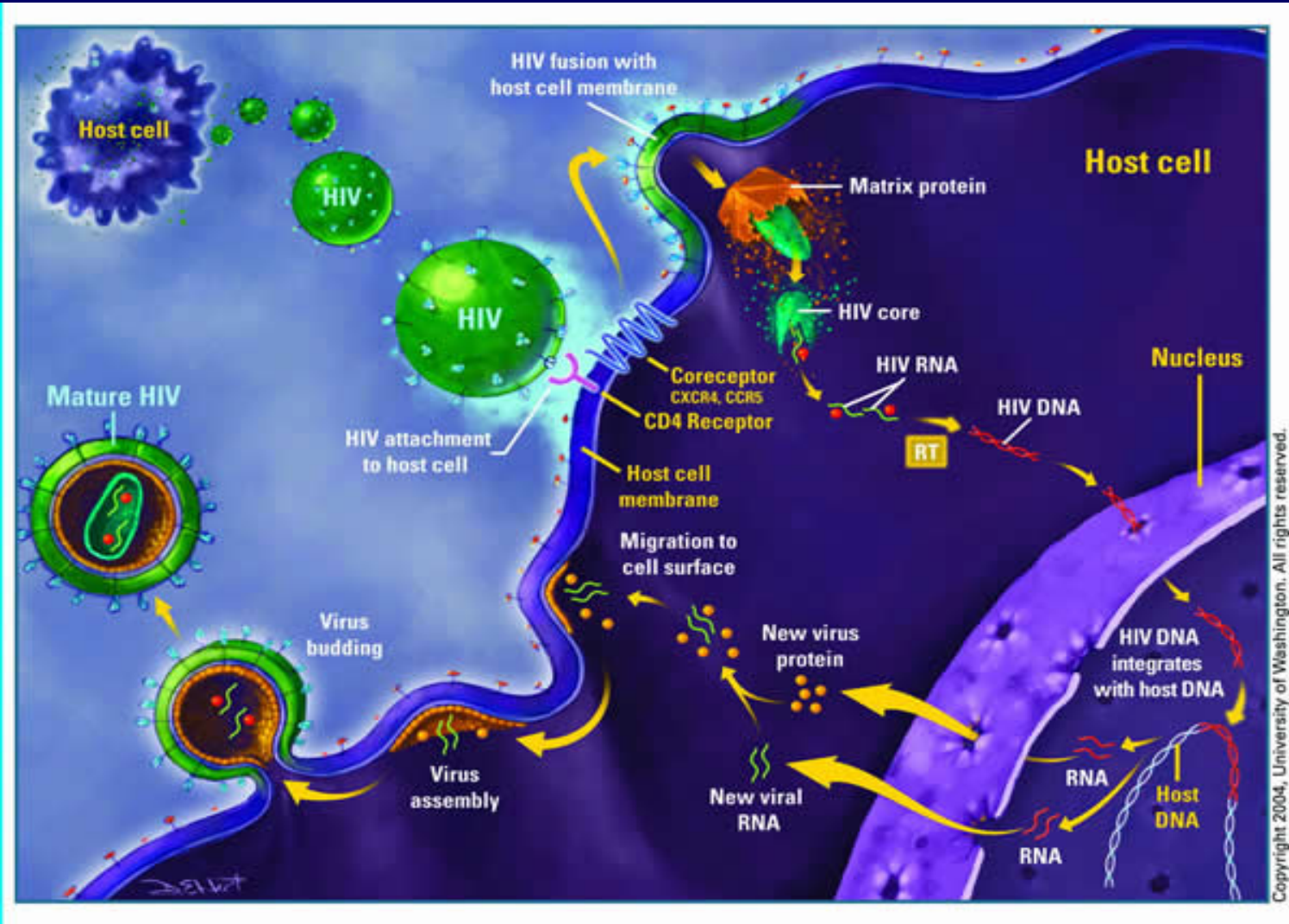
HIV genome



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



HIV species

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:
 - 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

1- Sexually (unprotected sex):

- The virus is present in blood, semen and vaginal secretions.

2- Parenterally:

- Direct exposure to infected blood or body fluids (e.g. receiving blood from infected donor).
- Using contaminated or not adequately sterilized tools in surgical or cosmetic practice (dental, tattooing, body piercing).
- Sharing contaminated needles, razors, or tooth brushes.

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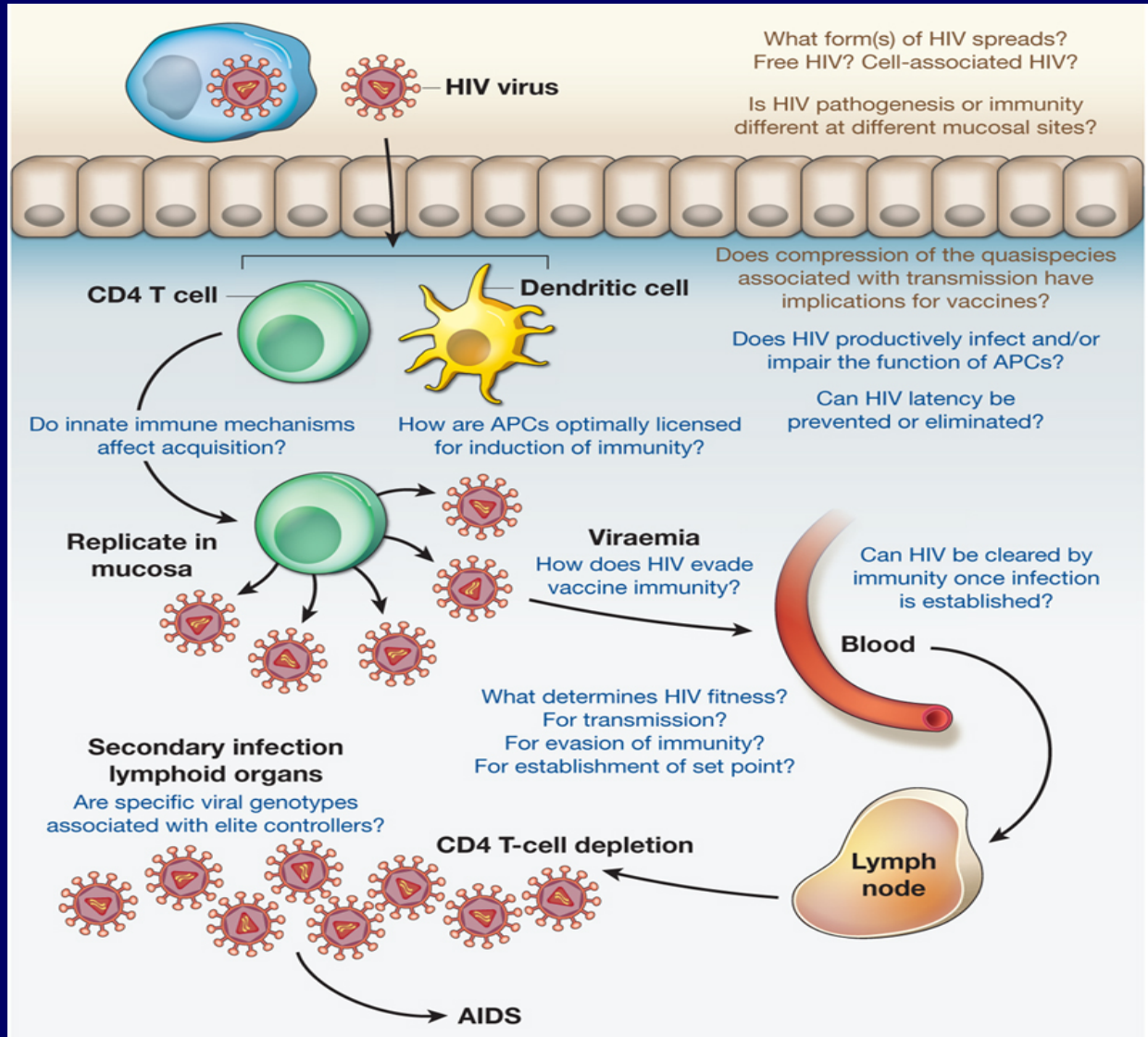
3- Perinatally (from mother to baby):

- 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.
- Breastfeeding is also an important way of perinatal transmission (25%).

Virus Inactivation

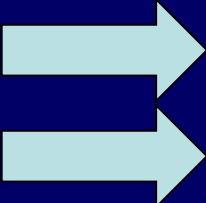
- HIV is **easily** inactivated by treatment for 10 min at 37°C with any of the following:
 - 10% House hold bleach, Sodium hypochlorite
 - 50% Ethanol
 - 35% Isopropanol
 - 0.5% Paraformaldehyde
 - 0.3% Hydrogen peroxide

HIV pathogenesis



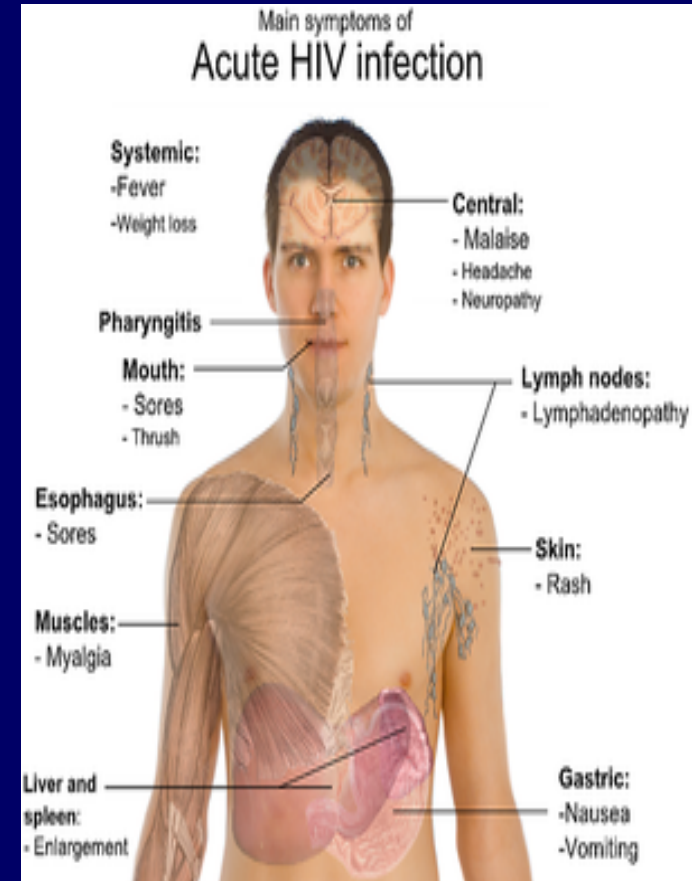
Stages of HIV infection

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

- The acute phase
- The chronic phase 
 - 1- (PGL)
 - 2- (ARC)
- AIDS (the end stage of the disease)

Acute phase:

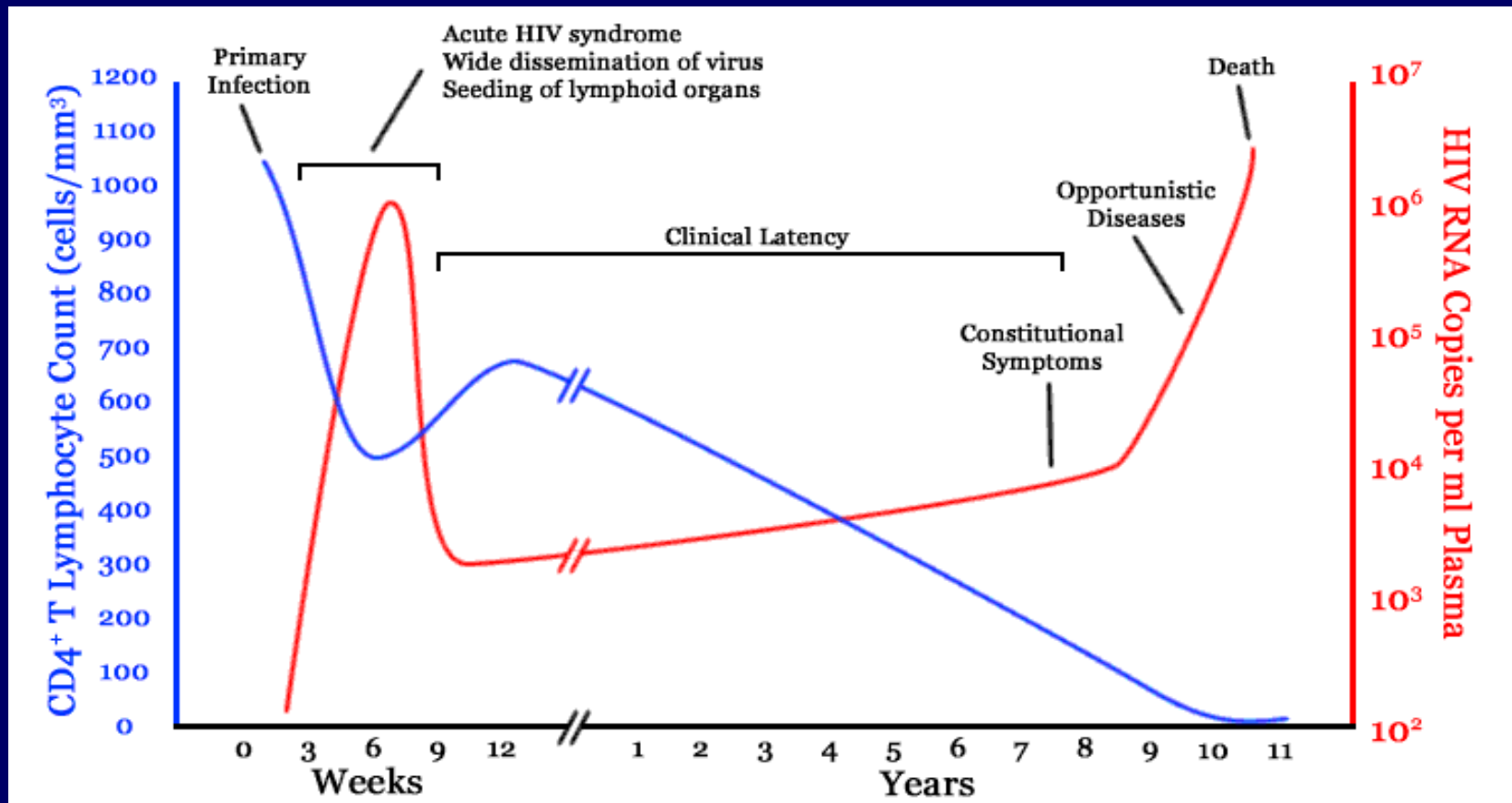
- Incubation period 2 weeks and lasts for about 12 weeks.
- Mostly asymptomatic, but in about 25-65% of the cases, patients may develop symptoms resemble infectious mononucleosis or Flu (fever, headache, anorexia, fatigue, lymphadenopathy, skin rash) which resolved in 2 weeks.
- Rapid viral replication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



Blood markers 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.**

HIV RNA copies VS CD4+ T cell counts



Chronic phase:

- Lasts for about 10 yrs in adults, and 5 yrs in children.
- Totally asymptomatic but the patients is still contagious.
- Relatively low viral load ($<10^4$ copies/mL).
- CD4+ T cell count > 200 cells/mm³.
- **At the end of this stage, two syndromes appear:**
 - 1. Persistent generalized lymphadenopathy (PGL).**
 - 2. AIDS-related complex (ARC).**

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 two or more lymph nodes out of the 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.

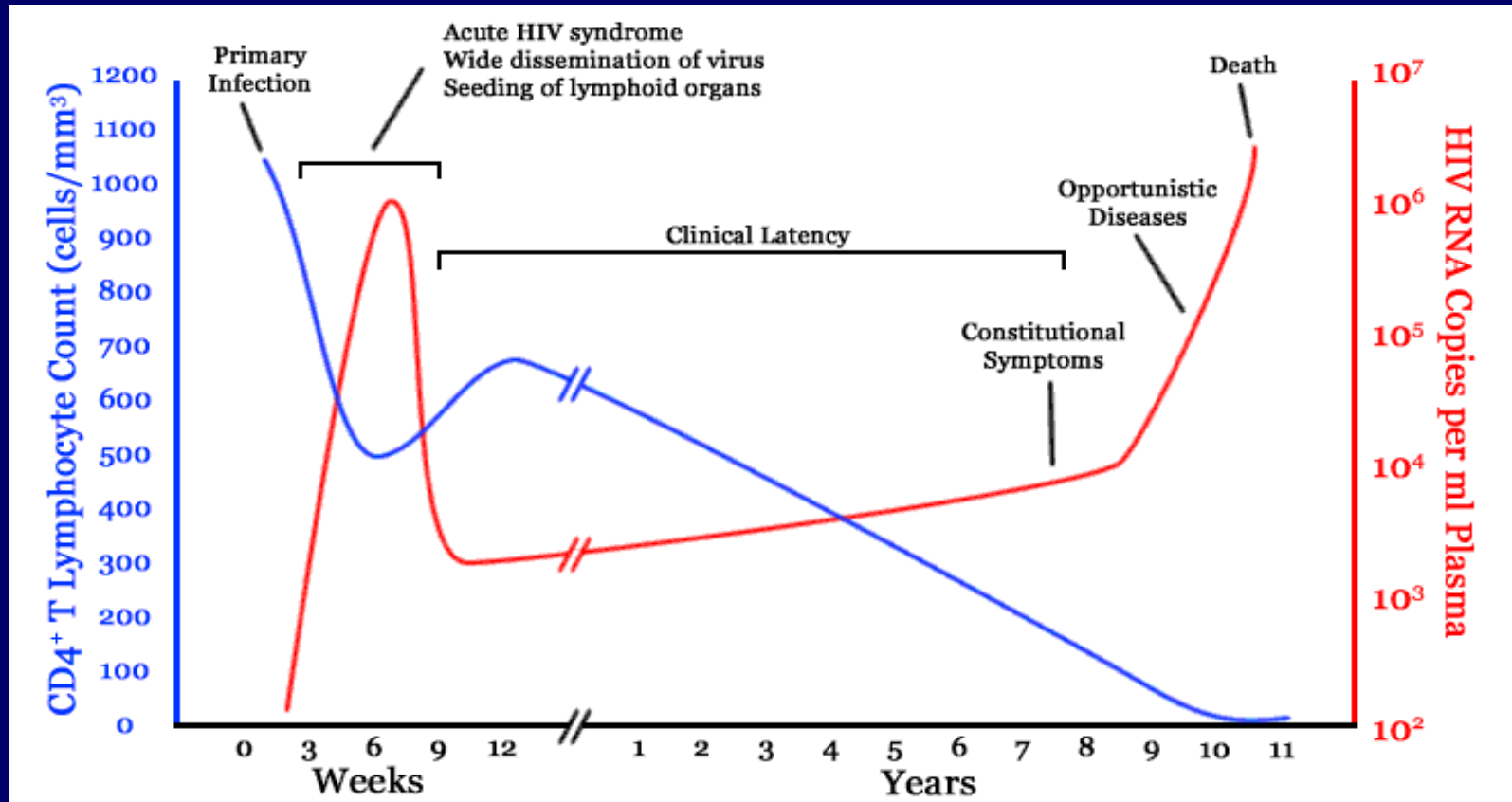
Slim disease



Blood markers in the chronic stage:

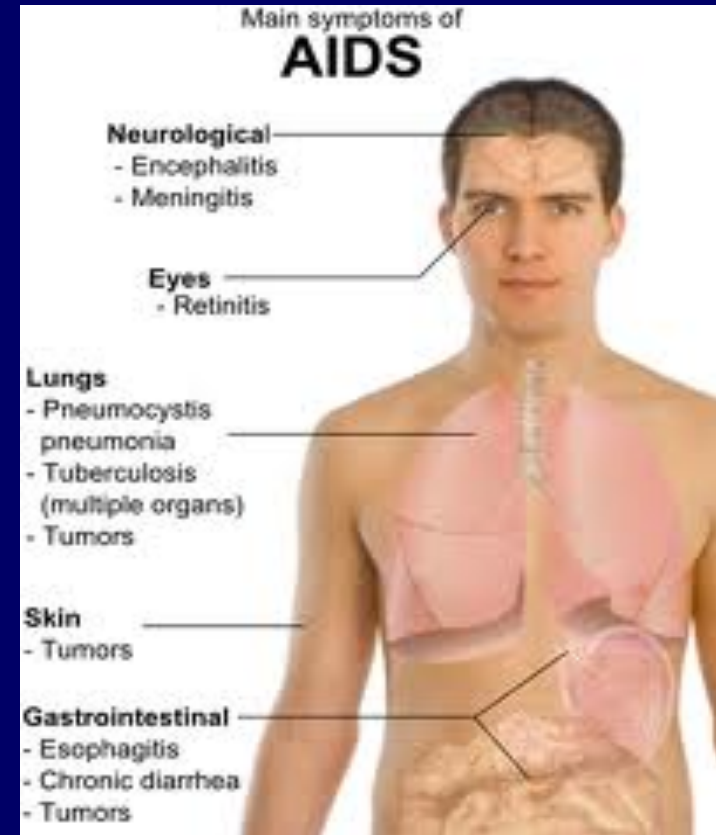
- Viral load (**HIV RNA**) increases gradually, but **HIV core antigen (p24)** may not appear in blood.
- Anti-envelop (**Anti-gp120**) & Anti-core (**Anti-p24**) are positive.
- **CD4+ T cell** count **gradually decreased** but still more than 200 cells/mm³

HIV RNA copies VS CD4+ T cell counts



AIDS phase:

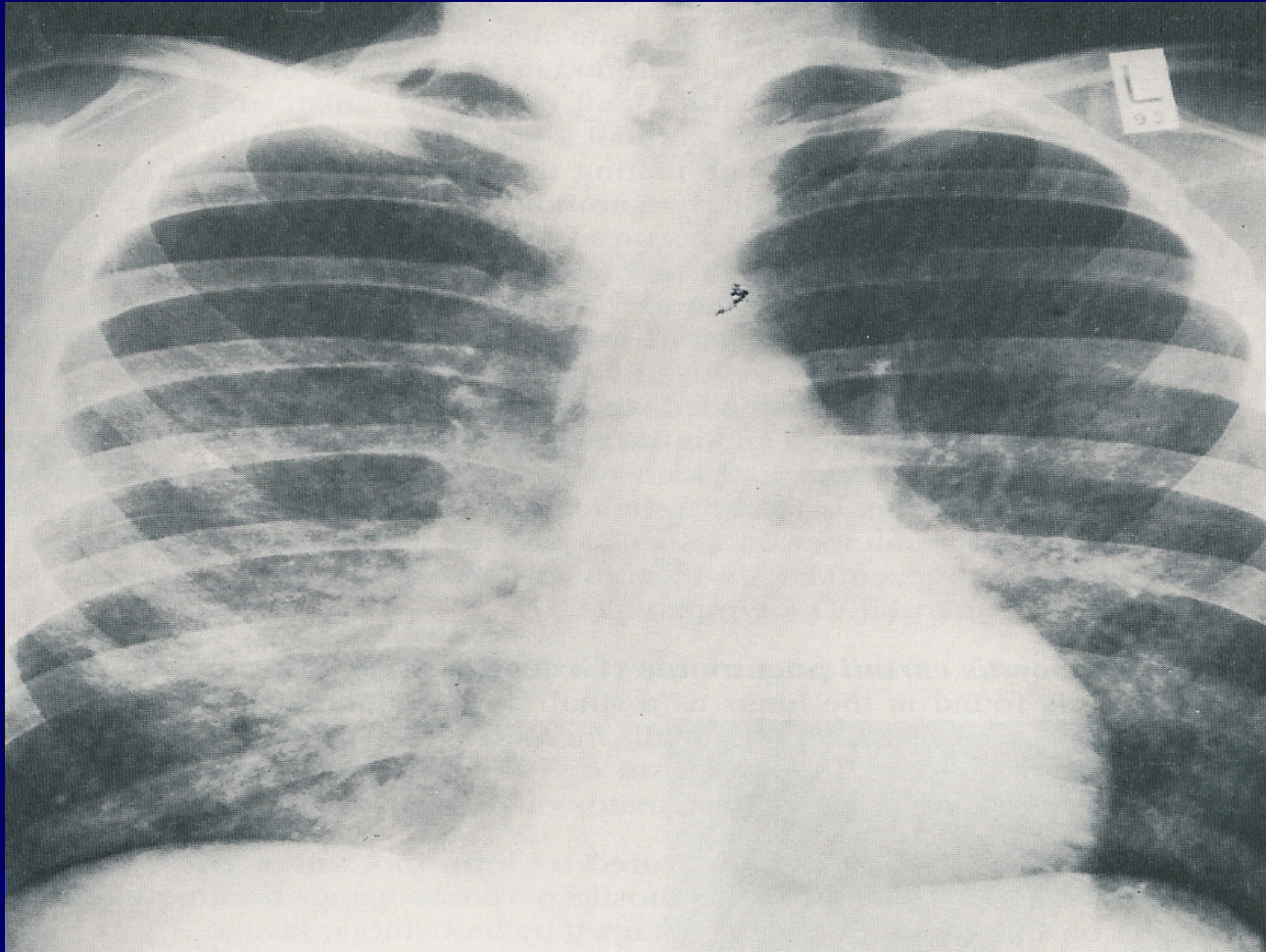
- The end stage of the disease.
- Continuous viral replication (high viral load).
- Marked decrease in CD4+ T cell count <math>< 200 \text{ cell/mm}^3</math>.
- Defects in cellular immunity.
- Persistent or frequent multiple opportunistic infections.
- Unusual cancer (Kaposi sarcoma).



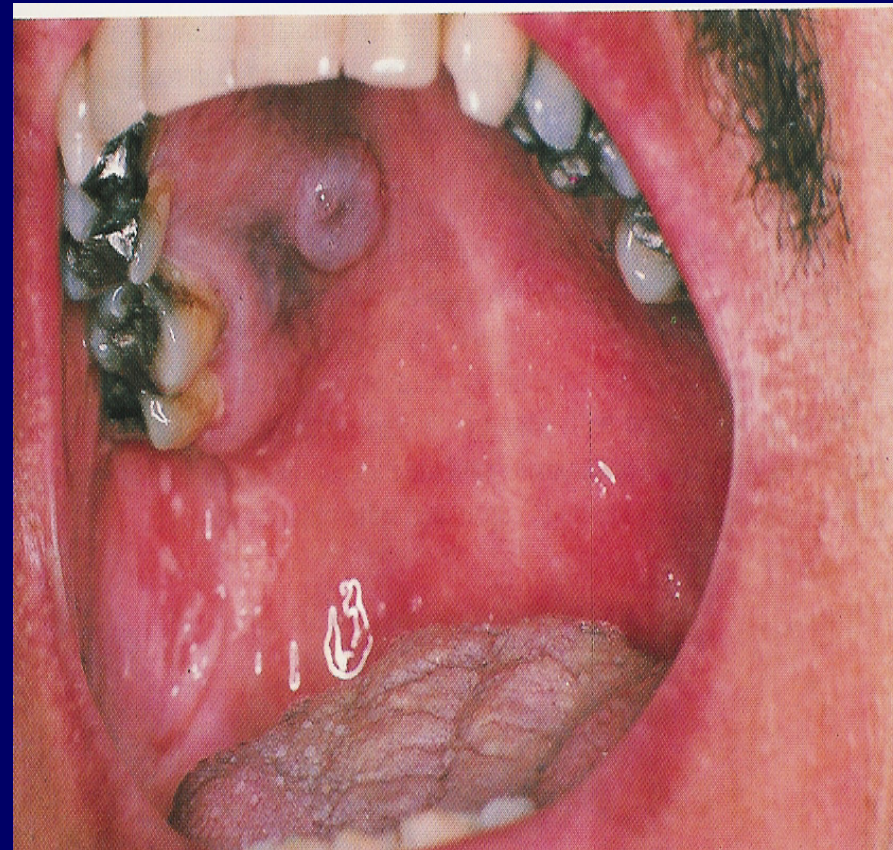
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OPPORTUNIST INFECTIONS AND TUMORS IN AIDS	
viruses	<p>disseminated CMV (including retina, brain, peripheral nervous system, gastrointestinal tract)</p> <p>HSV (lungs, gastrointestinal tract, CNS, skin)</p> <p>JC virus (brain – PML)</p> <p>EBV (hairy leukoplakia, primary cerebral lymphoma)</p>
bacteria*	<p>mycobacteria (e.g. <i>Mycoplasm</i>a <i>avium</i>, <i>M. tuberculosis</i> – disseminated, extrapulmonary)</p> <p><i>Salmonella</i> (recurrent, disseminated) septicemia</p>
protozoa	<p><i>Toxoplasma gondii</i> (disseminated, including CNS)</p> <p><i>Cryptosporidium</i> (chronic diarrhea)</p> <p><i>Isospora</i> (with diarrhea, persisting more than one month)</p>
fungi	<p><i>Pneumocystis jiroveci</i> (pneumonia)</p> <p><i>Candida albicans</i> (esophagitis, lung infection)</p> <p><i>Cryptococcus neoformans</i> (CNS)</p> <p>histoplasmosis (disseminated, extrapulmonary)</p> <p><i>Coccidioides</i> (disseminated, extrapulmonary)</p>
tumors	<p>Kaposi's sarcoma**</p> <p>B cell lymphoma (e.g. in brain, some are EBV induced)</p>
other	<p>wasting disease (cause unknown)</p> <p>HIV encephalopathy</p>
<p>*also pyogenic bacteria (e.g. <i>Haemophilus</i>, <i>Streptococcus</i>, <i>Pneumococcus</i>) causing septicemia, pneumonia, meningitis, osteomyelitis, arthritis, abscesses etc.; multiple or recurrent infections, especially in children</p> <p>**associated with HHV8, an independently-transmitted agent; 300-times as frequent in AIDS as in other immunodeficiencies</p>	

Pneumocystis pneumonia



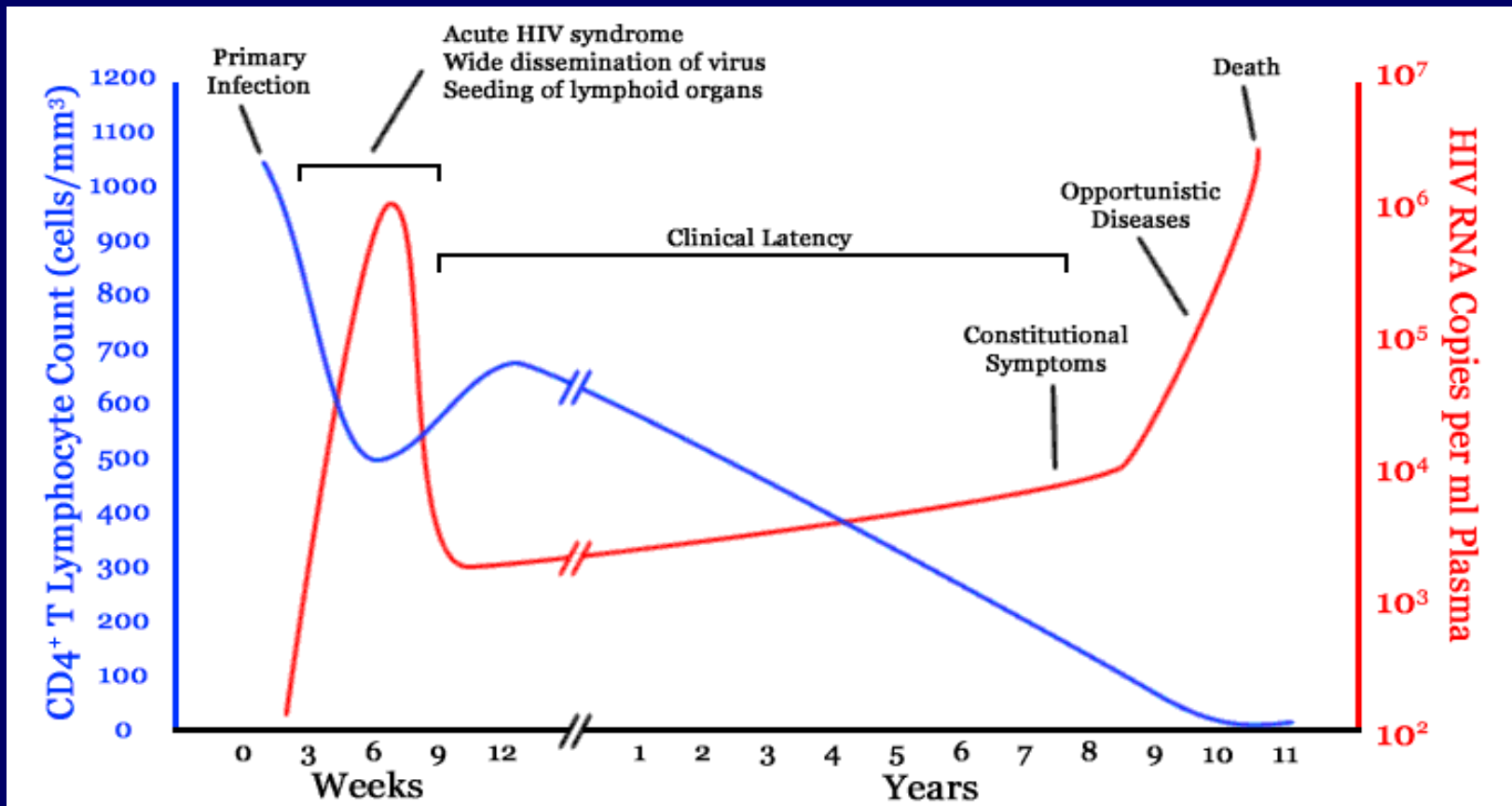
Kaposi sarcoma / Candida infection



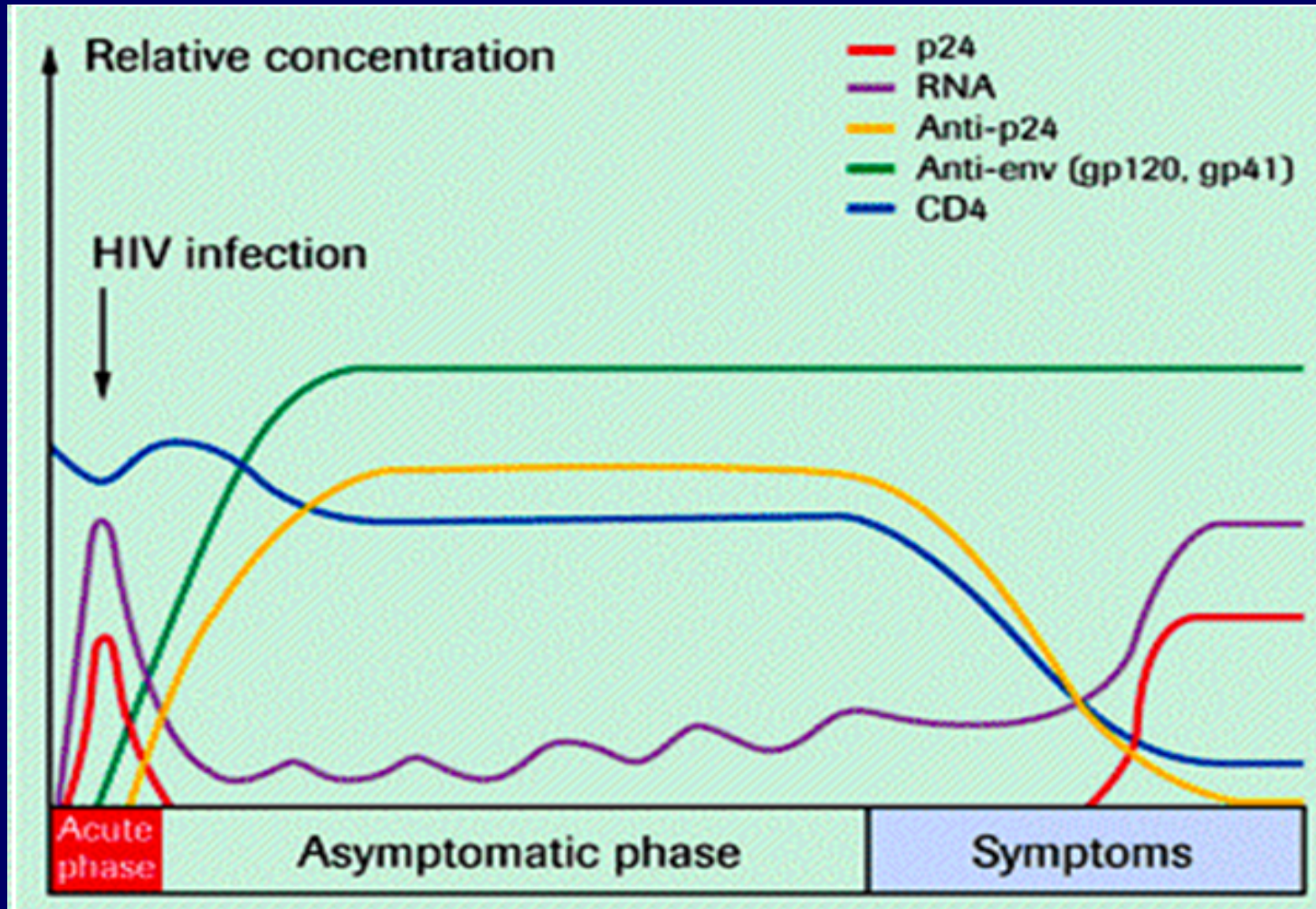
Blood markers in AIDS stage:

- 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/mm³).

HIV RNA copies VS CD4+ T cell counts



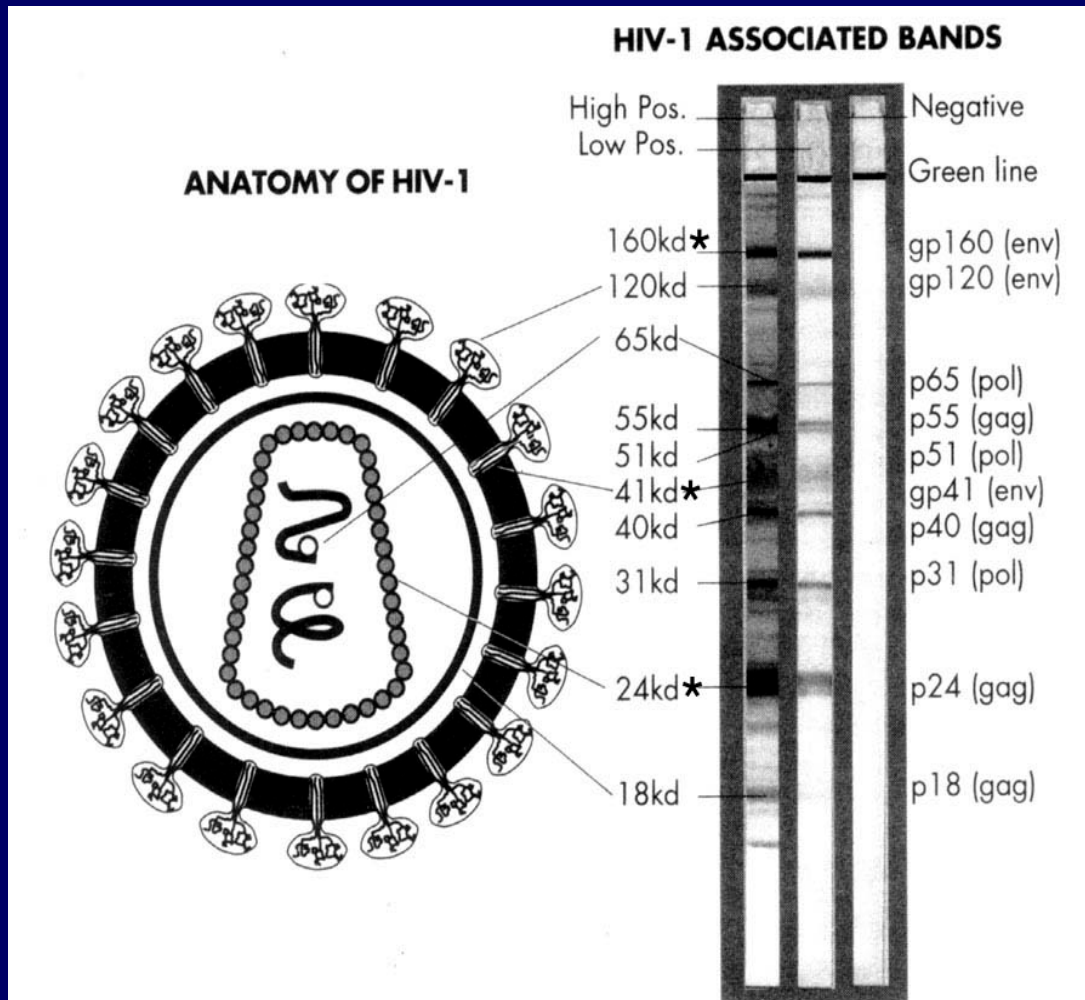
Serological profile of HIV infection



Diagnosis

- Patients history with or without clinical symptoms provides 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 repeatedly reactive (positive), do confirmatory tests (Western blot, recombinant immunoblot assay (RIBA), or PCR).
- Blood viral load by PCR is also used to monitor HIV replication and follow up patients treatment.

HIV western blot



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.

Treatment

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

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- There are two types of reverse transcriptase inhibitors:
 - Nucleoside analog RT inhibitors for HIV-1 & HIV-2:
 - Zidovudine (AZT) - Zalcitabine (ddC)
 - Stavudine (d4T) - Lamivudine (3TC)
 - Non-nucleoside analog RT inhibitors for HIV-1 only:
 - Nevirapine - Delavirdine - Efavirenz
- Proteases inhibitors include:
 - Saquinavir - Indinavir
 - Nelfinavir - Ritonavir

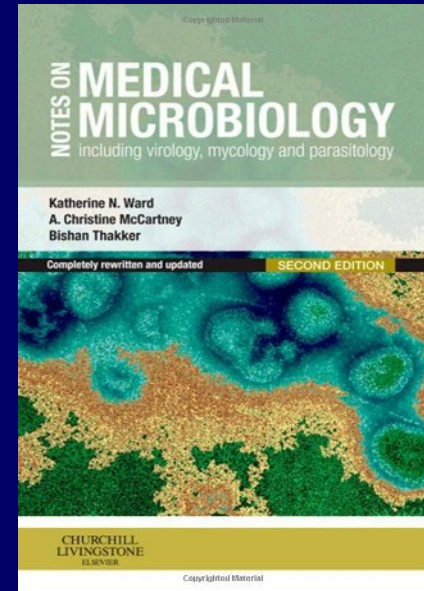
Goals of HIV treatment

- 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.

Reference books

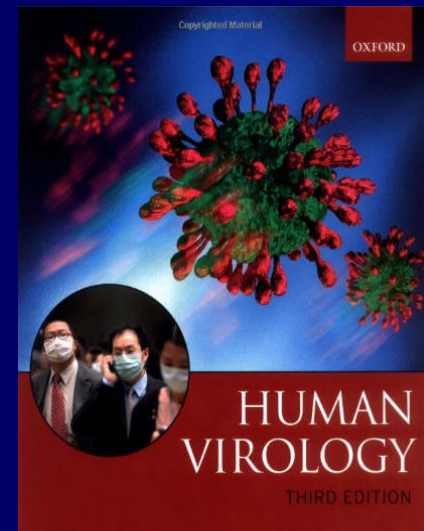
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Thank you for your attention !

Questions ?