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)

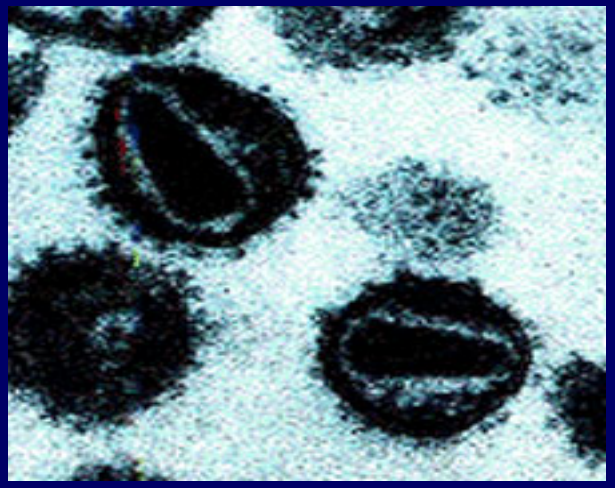
- Is the end stage of the disease that is associated with CD4+ T cell depletion, multiple or recurrent opportunistic infections, and unusual cancer (Kaposi sarcoma).

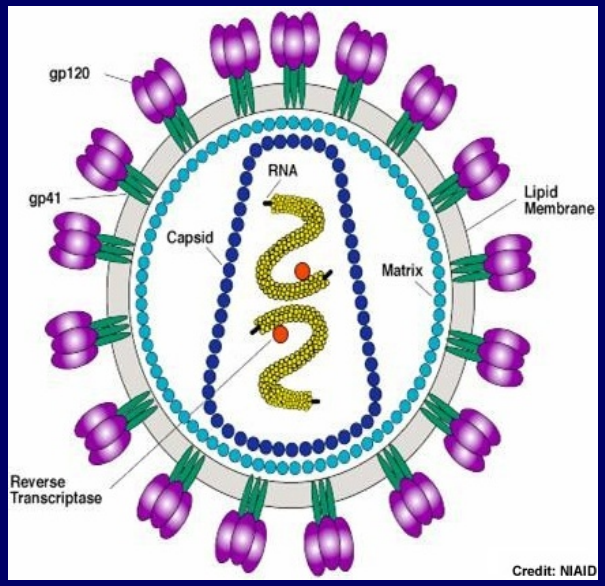
Characteristics of HIV

- Family of *Retroviridae.*

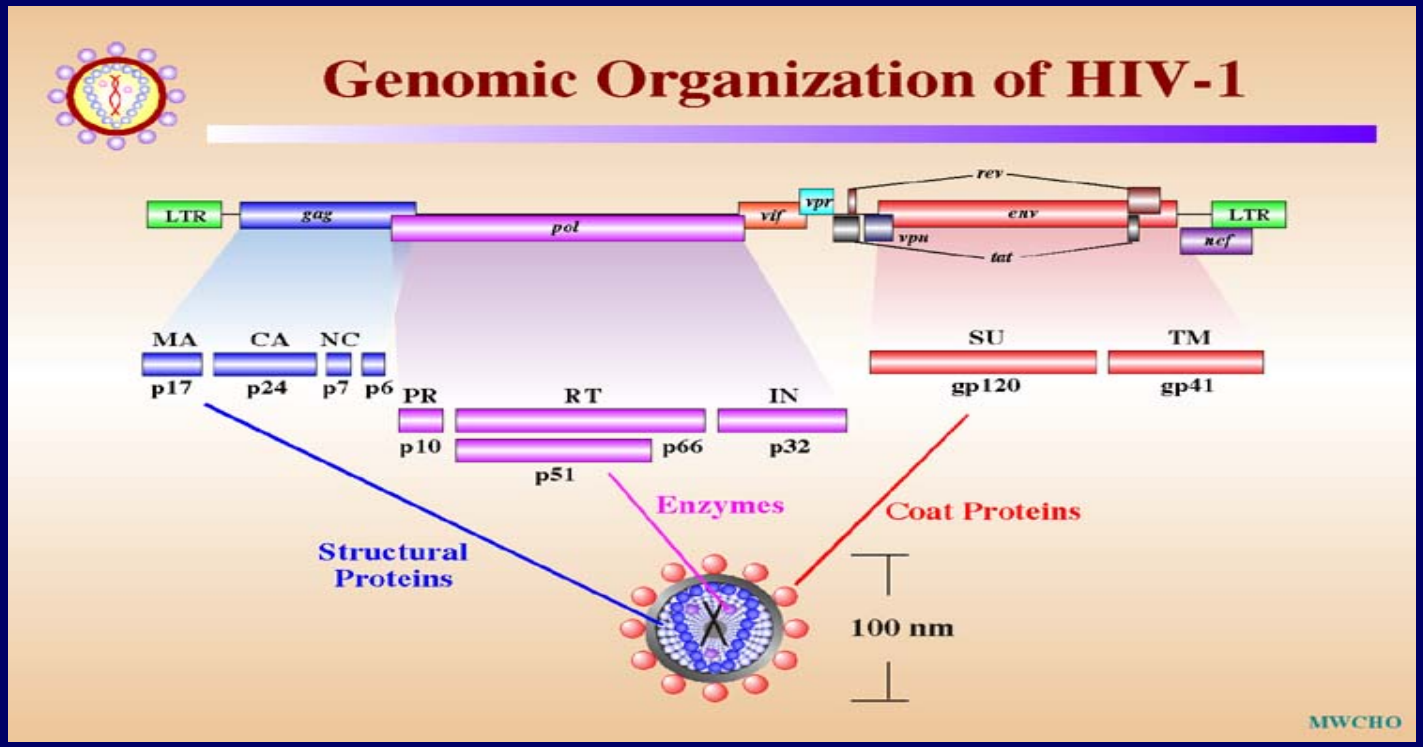
Virion consist of:

- 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.





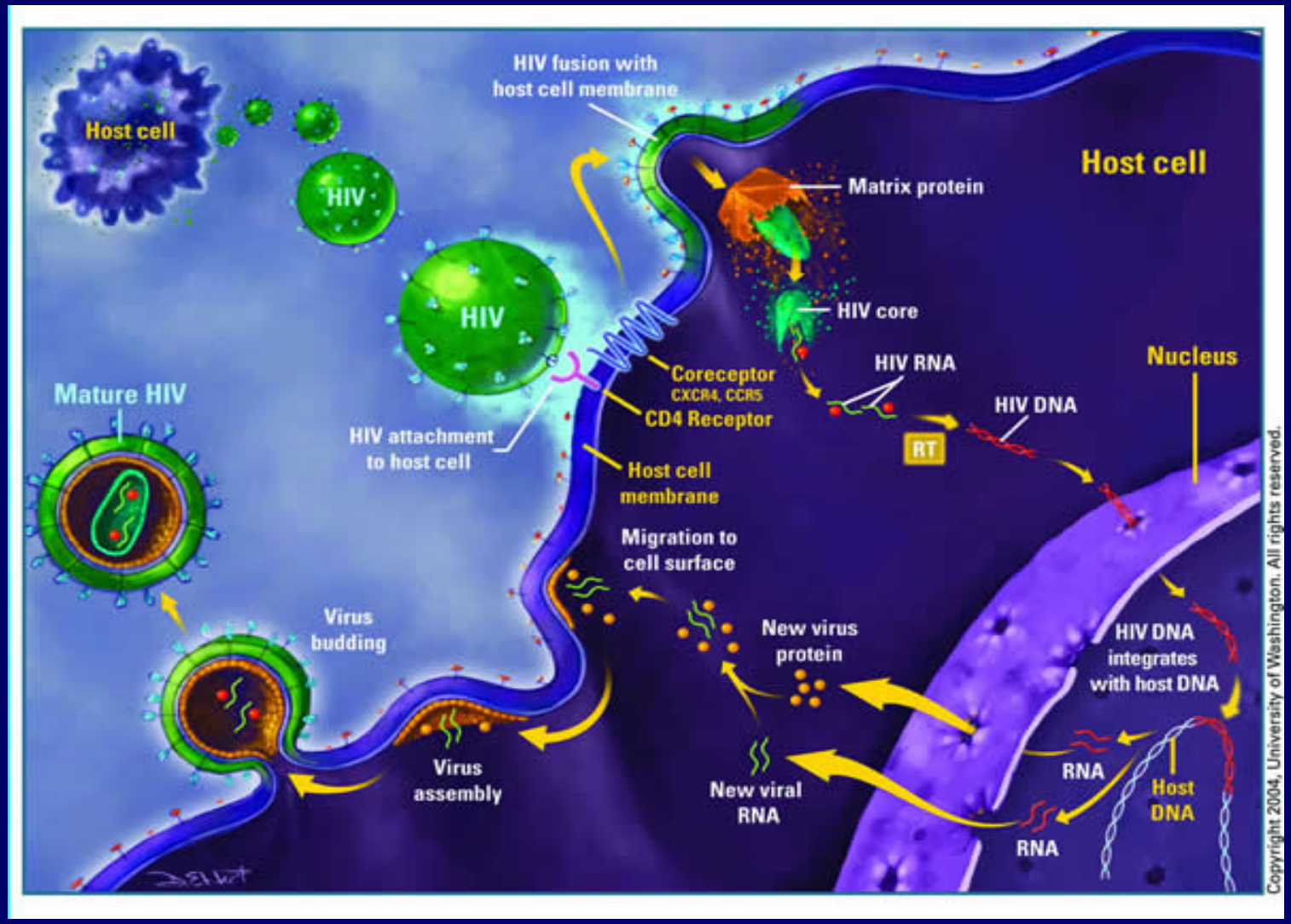
HIV genome



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- Parenteraly:

- 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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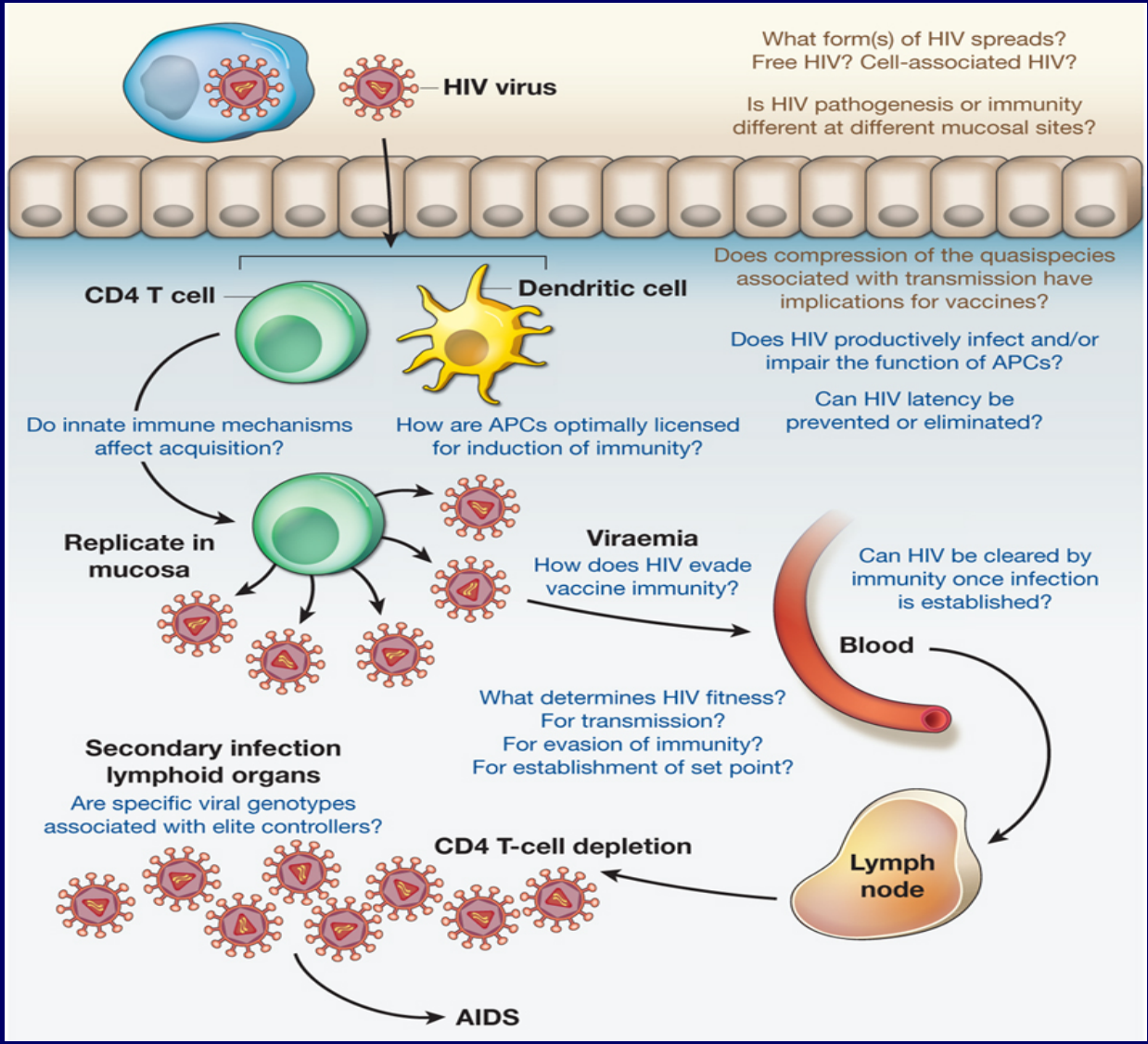
3- Perinatally (from mother to baby):

- 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



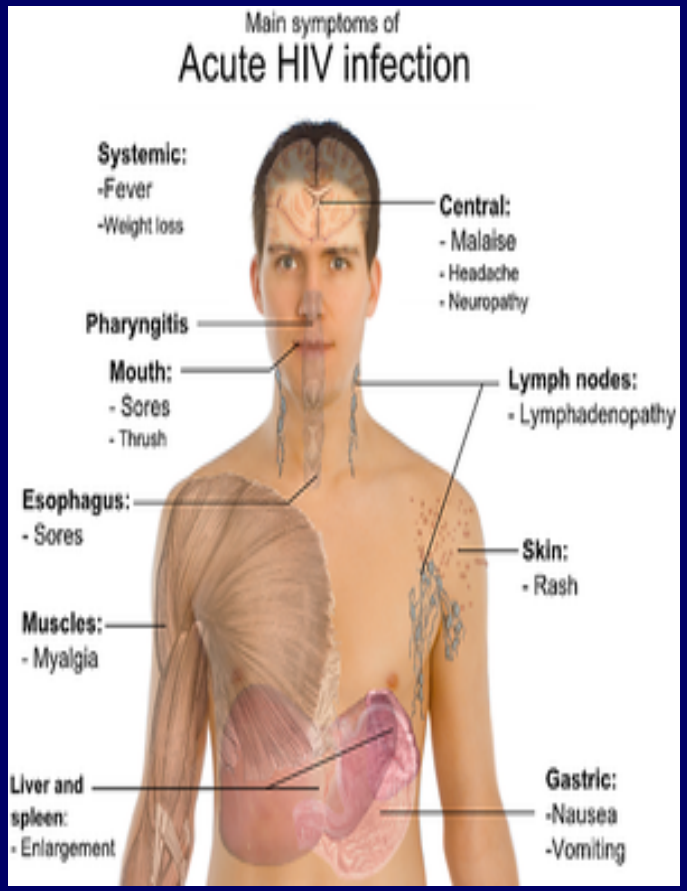
Stages of HIV infection

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:

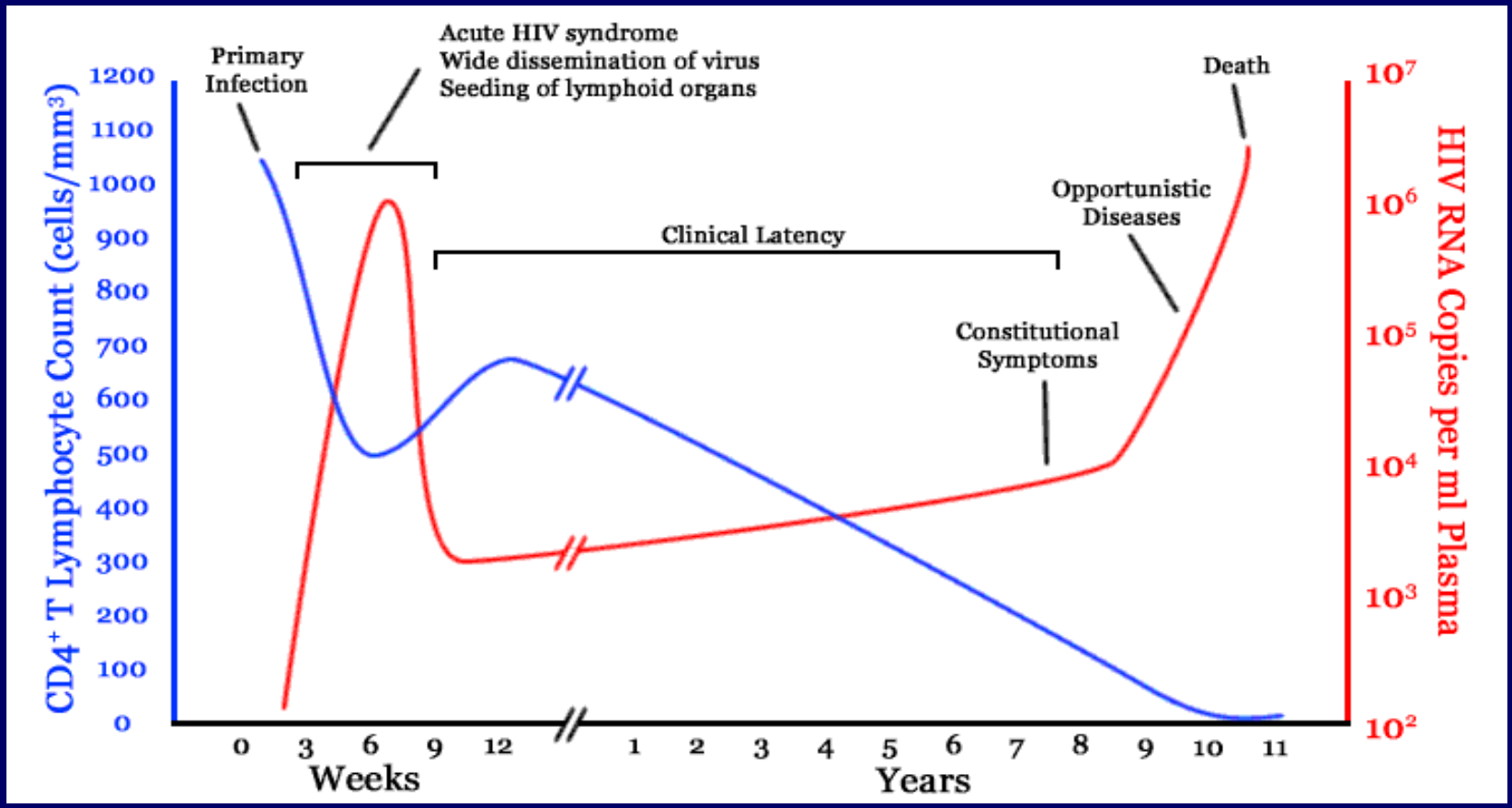
- Incubation period 2 weeks and lasts for about 12 weeks.
- Mostly asymptomatic, but in about 25-65% of the cases, patients may develop symptoms resemble infectious mononucleosis or Flu (fever, headache, anorexia, fatigue, lymphadenopathy, skin rash) which resolved in 2 weeks.
- Rapid viral replication (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



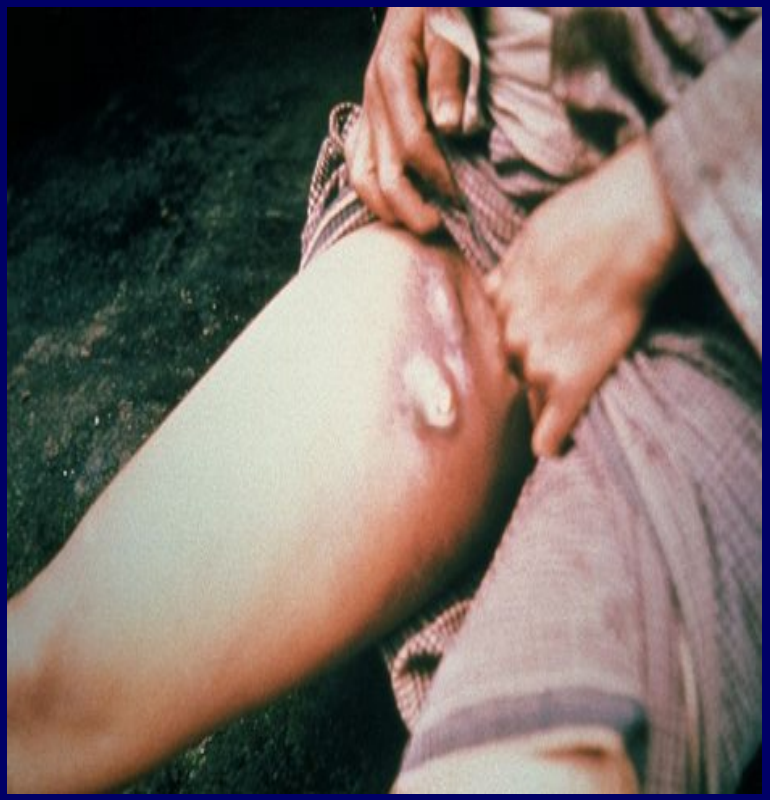
Chronic phase:

- 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/mm^3.
- 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:

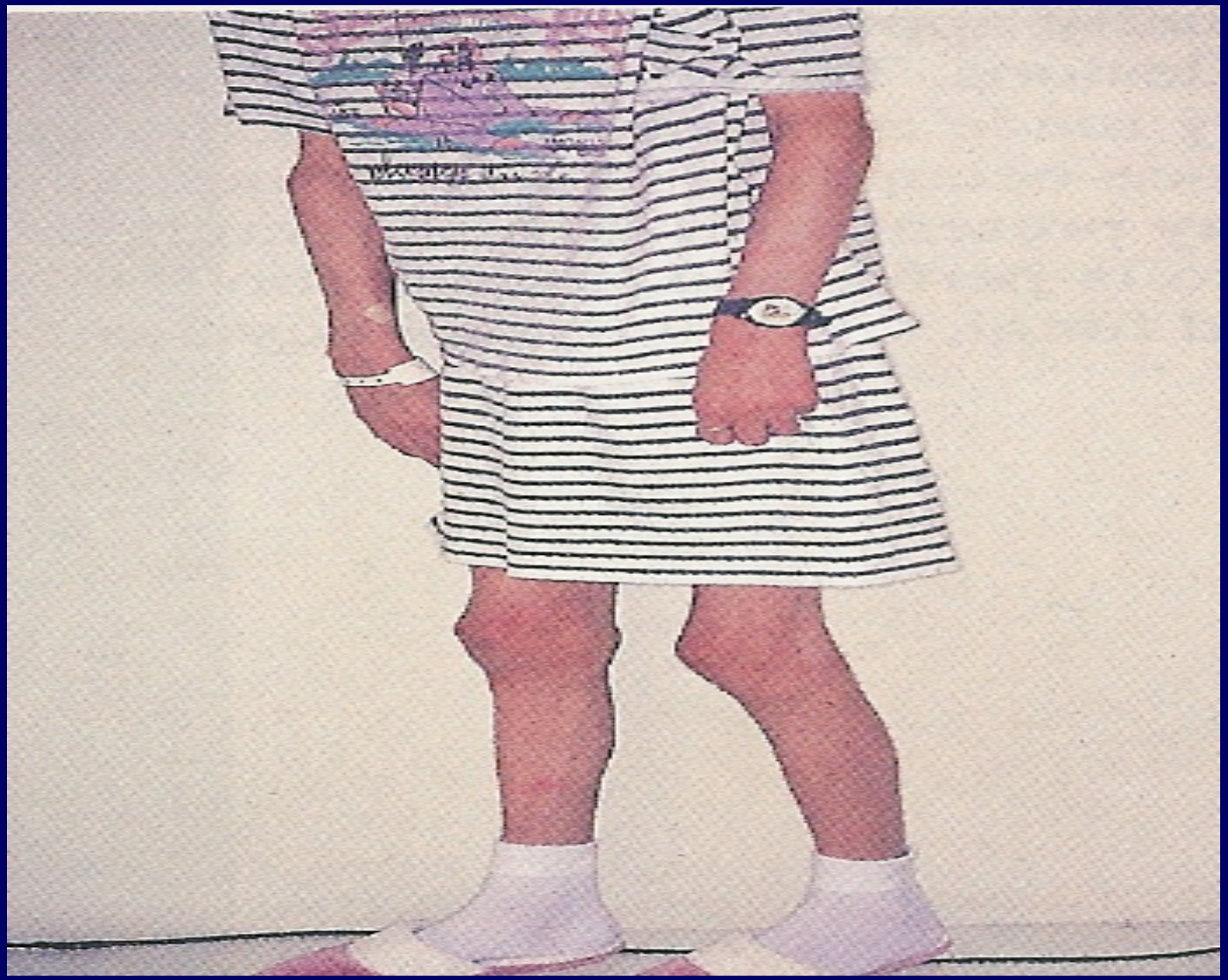
- In two or more lymph nodes out of the inguinal area.
- Persists for at least 3 months.

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.

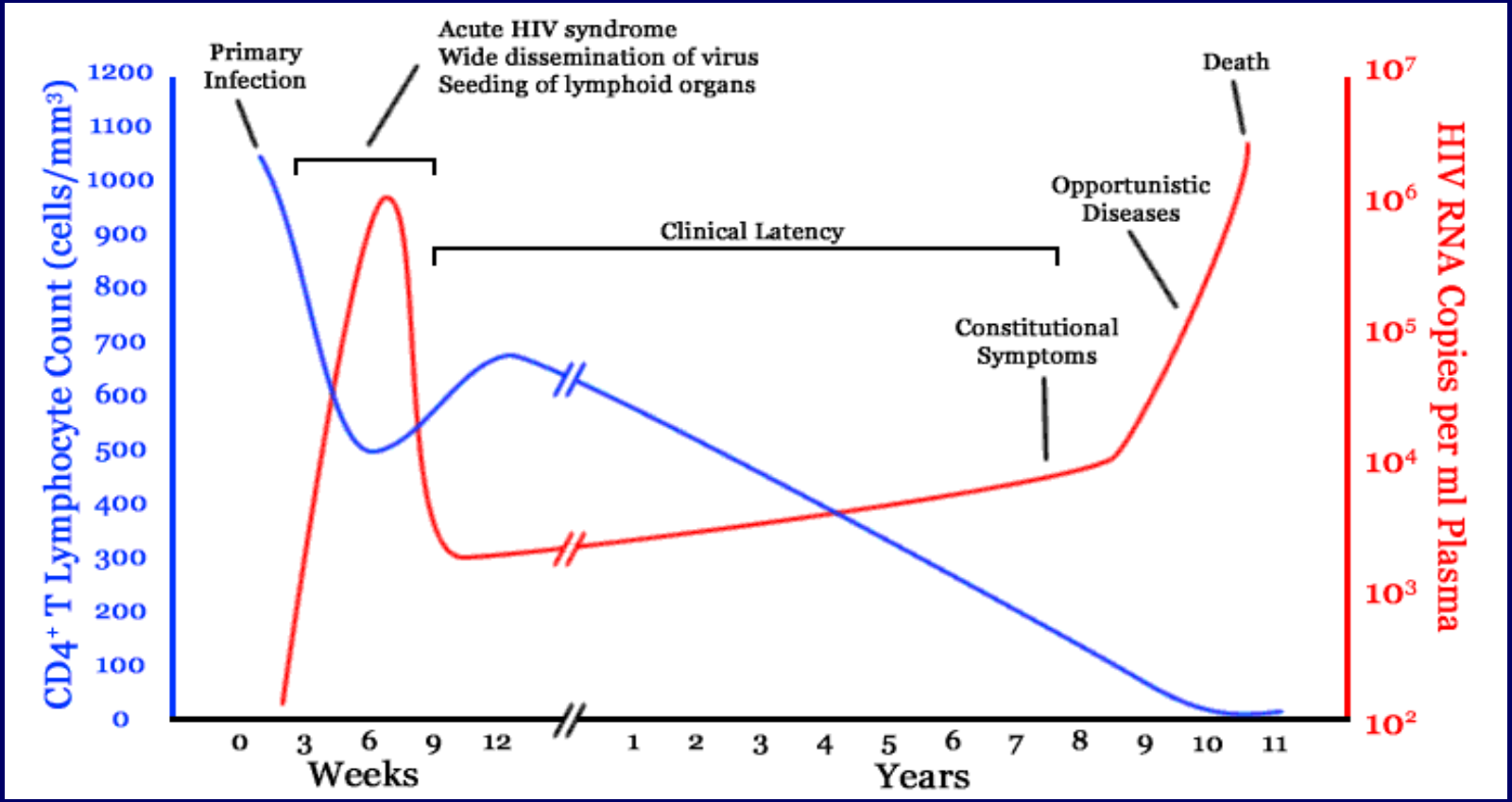
Slim disease



Blood markers in the chronic stage:

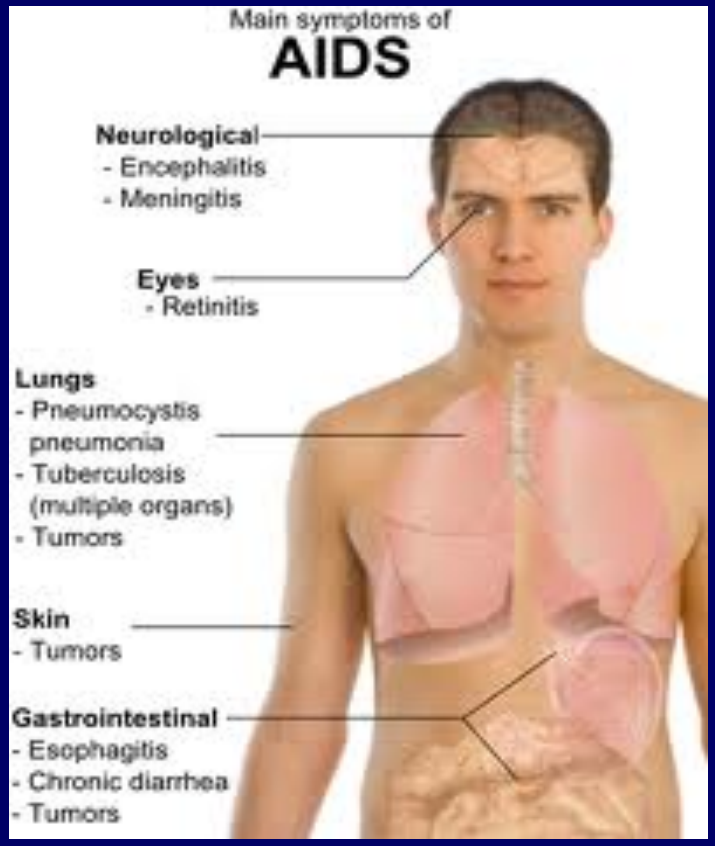
- Viral load **(HIV RNA)** increases gradually, but **HIV core antigen (p24)** may not appear in blood.
- Anti-envelop **(Anti-gp120)** & Anti-core (**Anti-p24**) are positive.
- **CD4+ T cell** count gradually **decreased** but still more than 200 cells/mm^3

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 < 200 cell/mm^3.
- Defects in cellular immunity.
- Persistent or frequent multiple opportunistic infections.
- Unusual cancer (Kaposi sarcoma).



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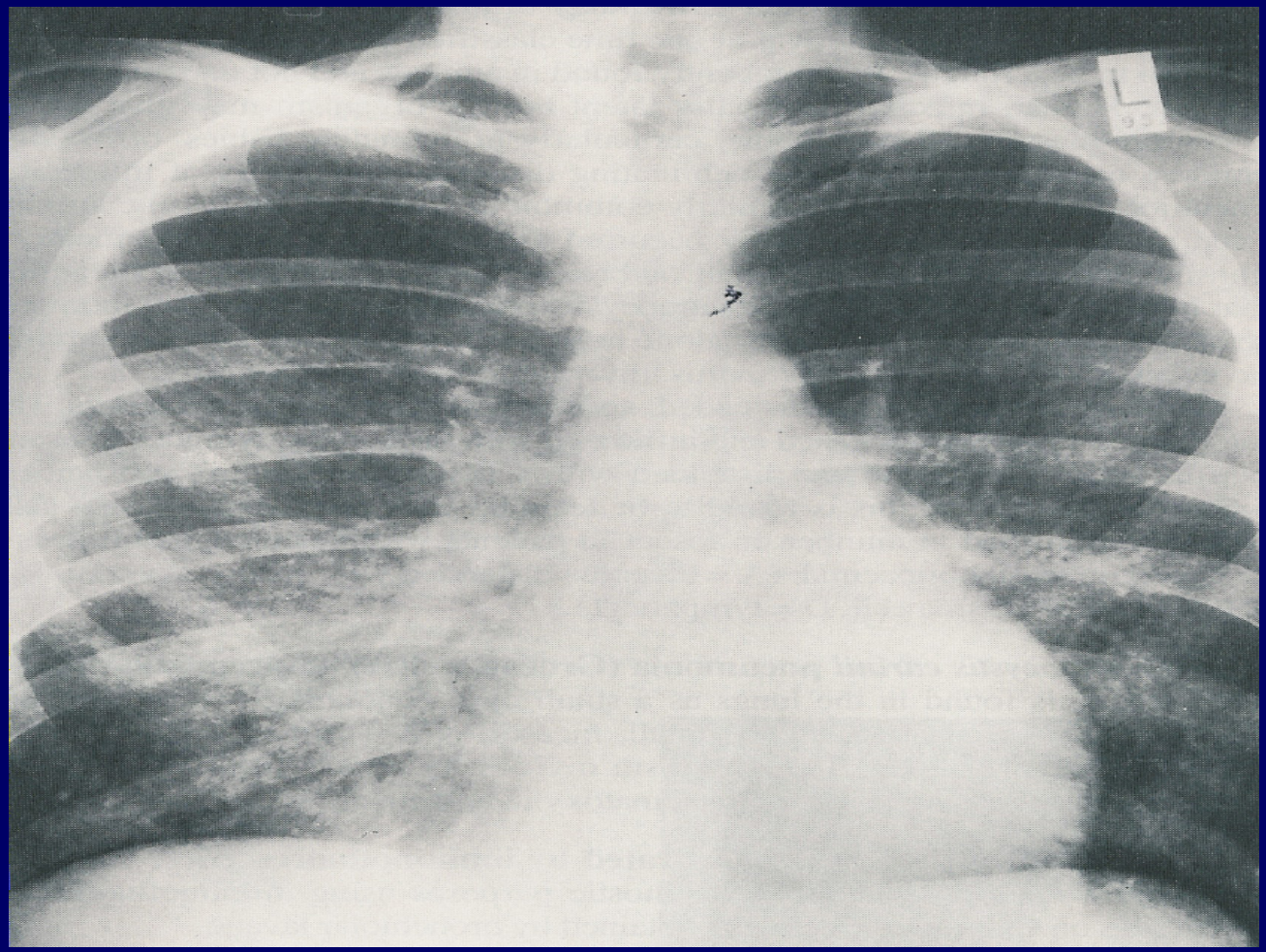
OPPORTUNIST INFECTIONS AND TUMORS IN AIDS	
viruses	disseminated CMV (including retina, brain, peripheral nervous system, gastrointestinal tract) HSV (lungs, gastrointestinal tract, CNS, skin) JC virus (brain – PML) EBV (hairy leukoplakia, primary cerebral lymphoma)
bacteria*	mycobacteria (e.g. *Mycoplasma 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

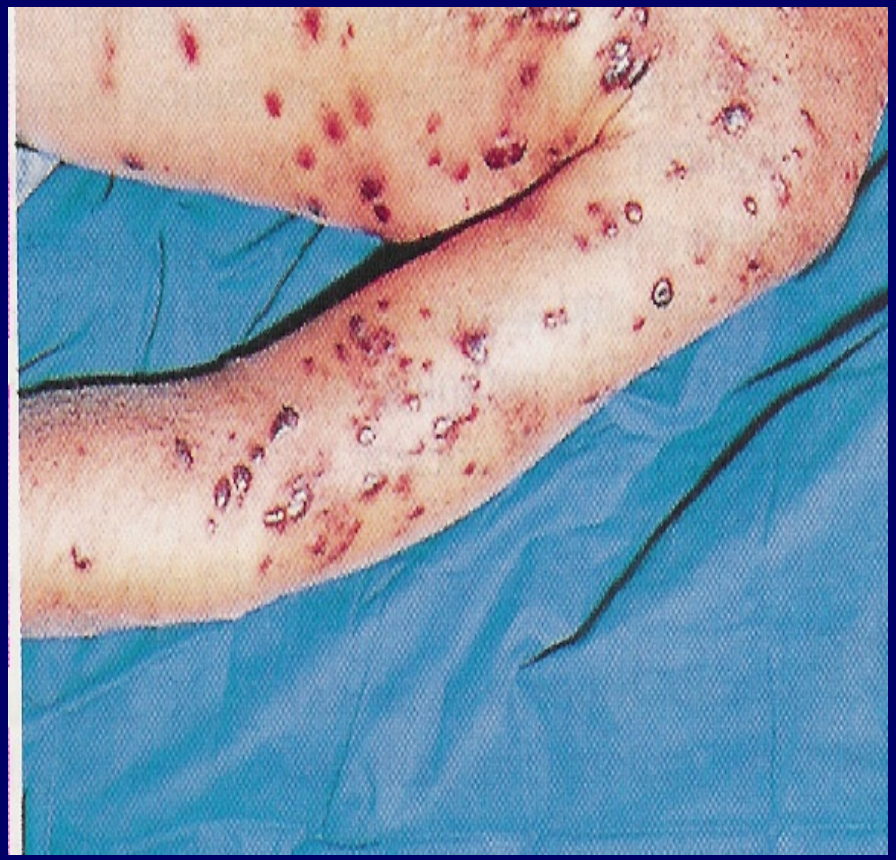
*also pyogenic bacteria (e.g. *Haemophilus, Streptococcus, Pneumococcus*) causing septicemia, pneumonia, meningitis, osteomyelitis, arthritis, abscesses etc.; multiple or recurrent infections, especially in children

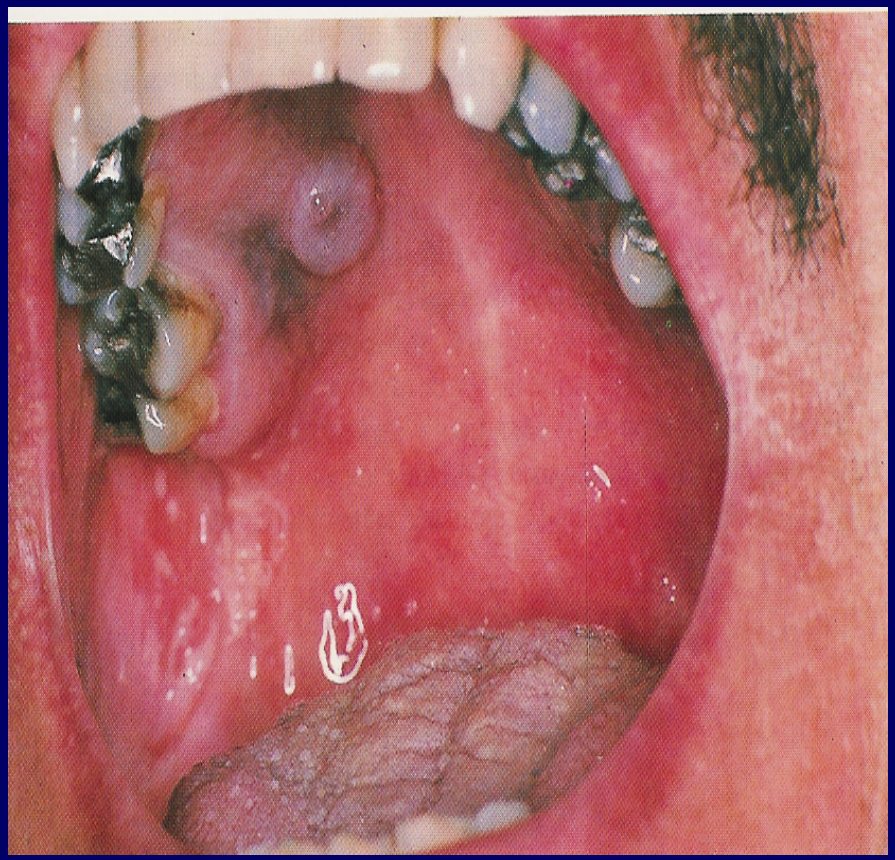
**associated with HHV8, an independently-transmitted agent; 300-times as frequent in AIDS as in other immunodeficiencies

Pneumocystis pneumonia



Kaposi sarcoma / Candida infection

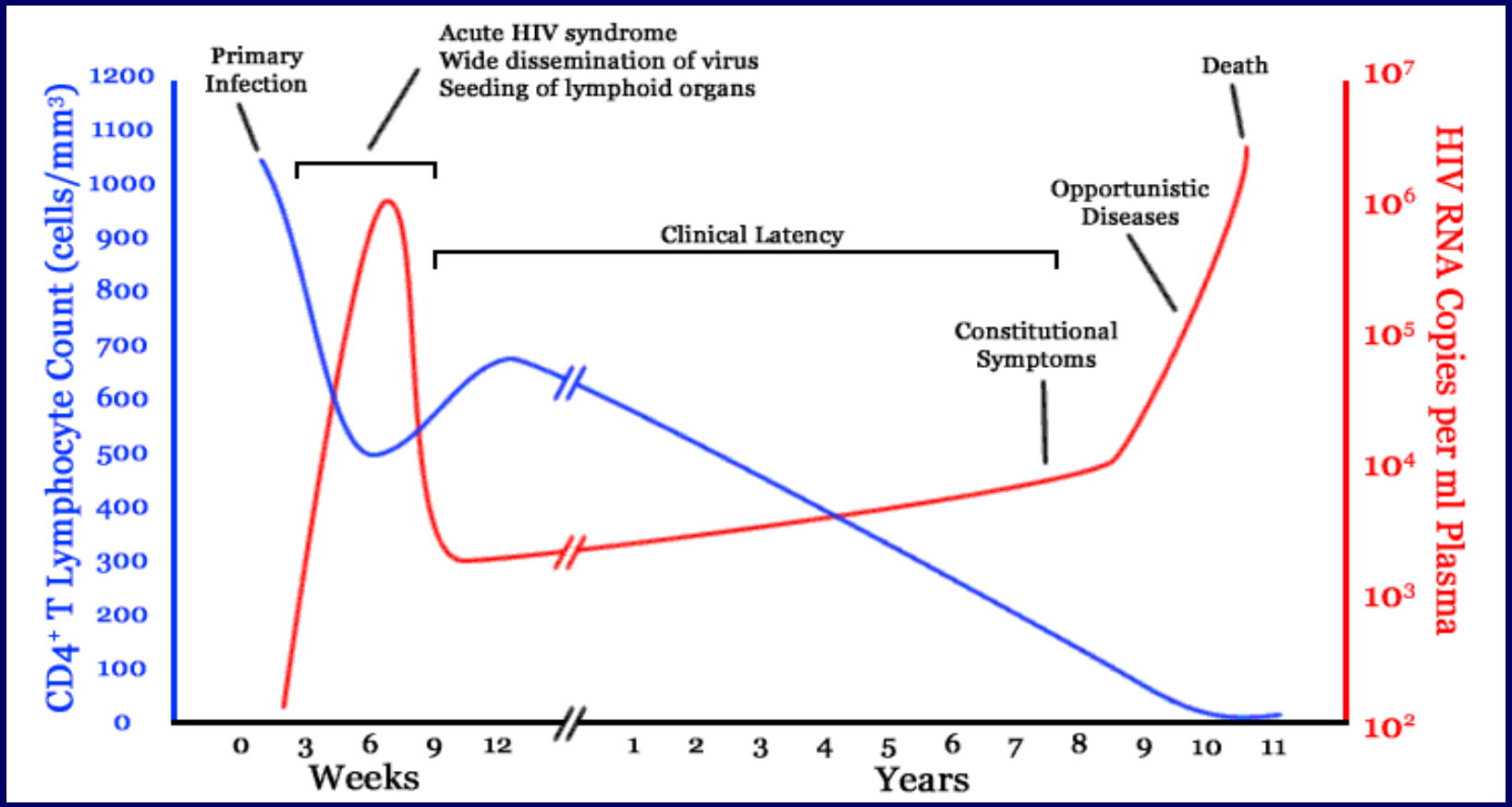




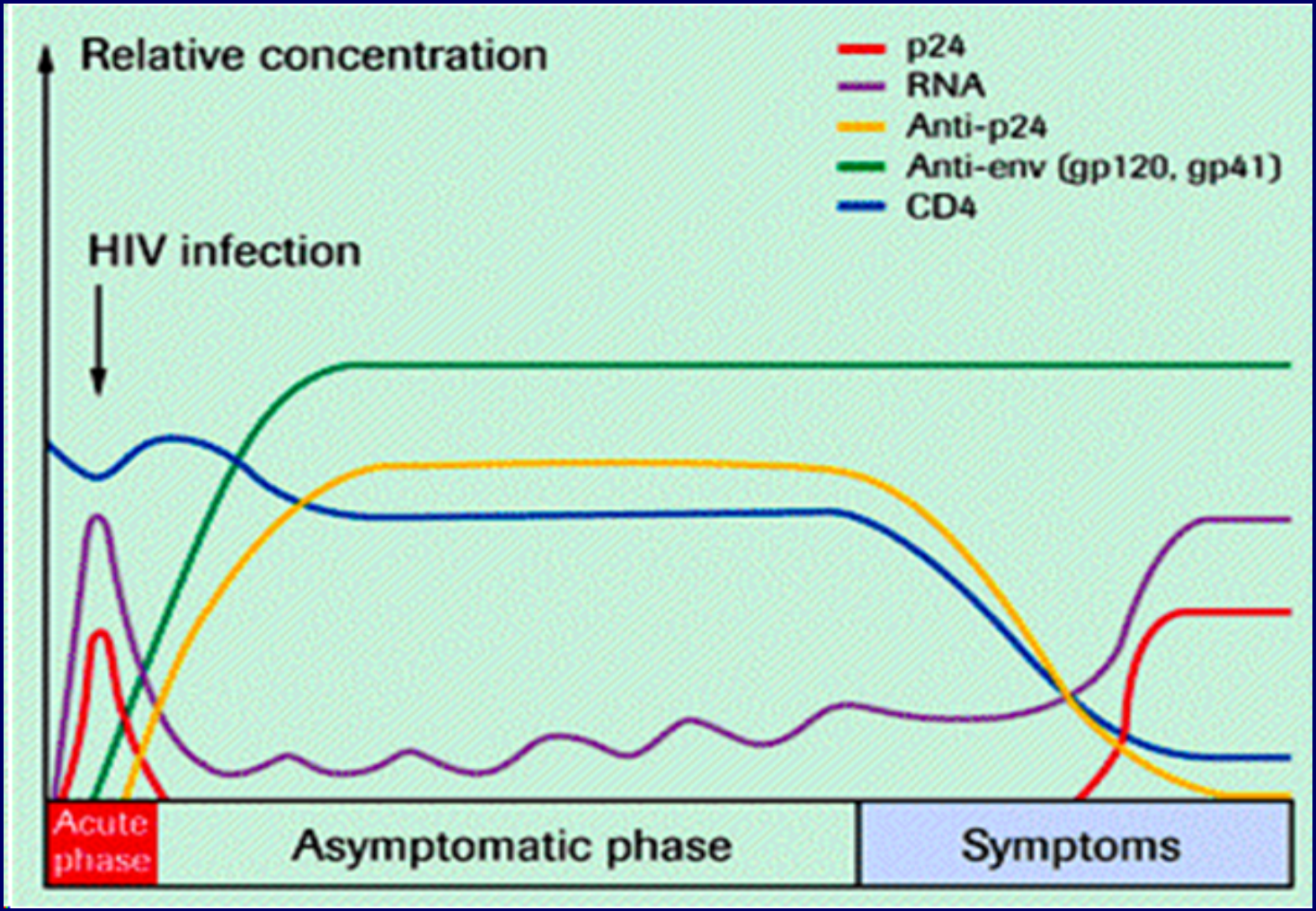
Blood markers in AIDS stage:

- 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/mm^3).

HIV RNA copies *VS* CD4+ T cell counts



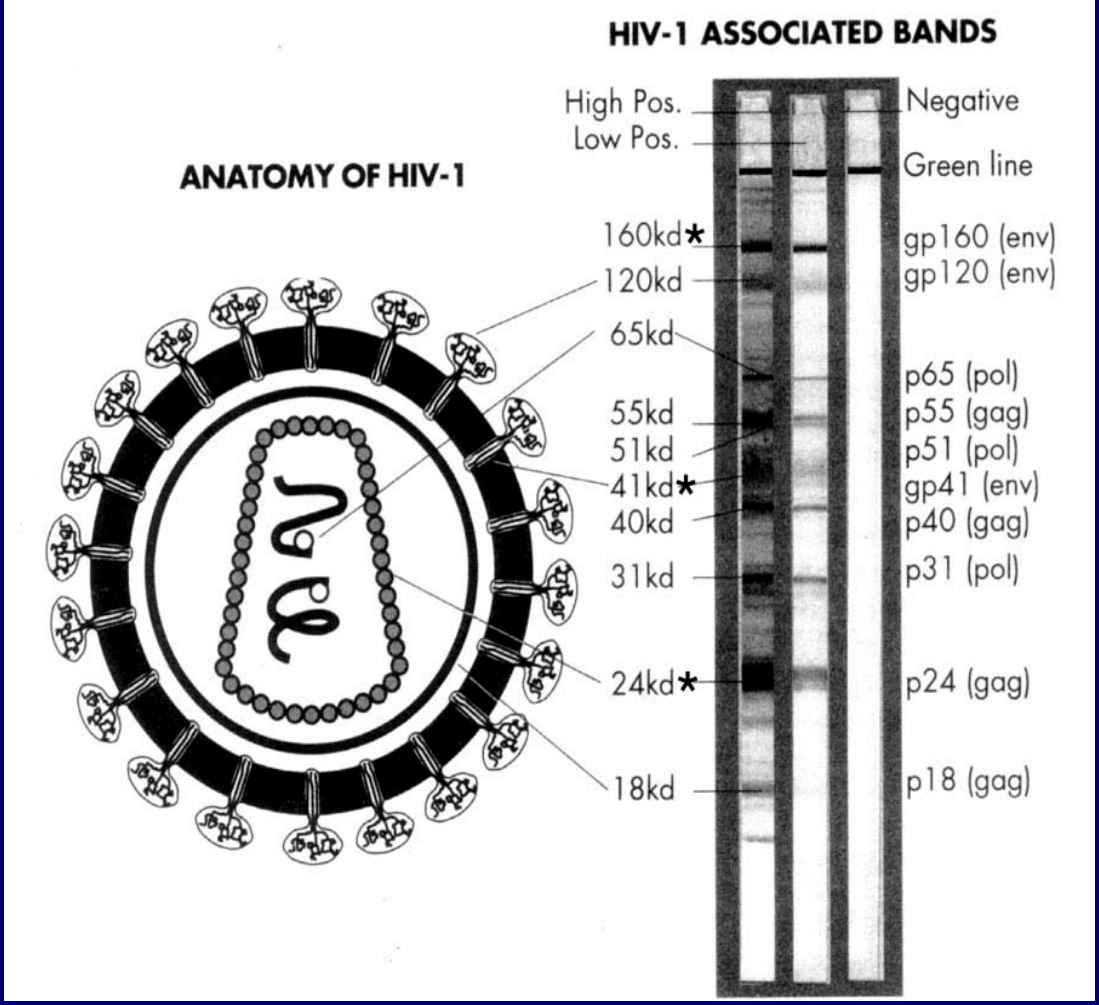
Serological profile of HIV infection



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 (does not 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

Notes on Medical Microbiology

By; Katherine N. Ward, A. Christine McCartney, and Bishan Thakker.
(2009)

Human Virology

By; Leslie Collier and John Oxford.
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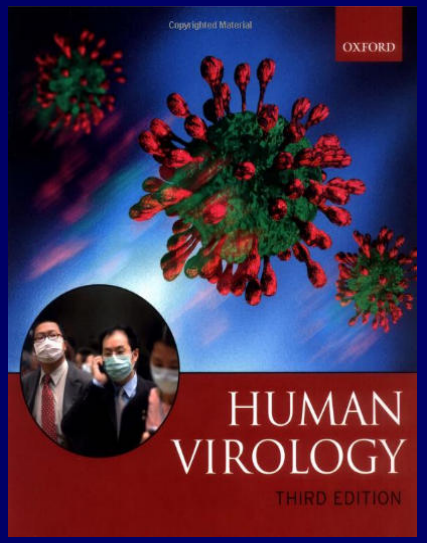

Thank you for your attention !

Questions ?