

HIV & AIDS

Dr. Abdulkarim Alhetheel

Assistant Professor in Microbiology Unit

College of Medicine & KKUH

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)

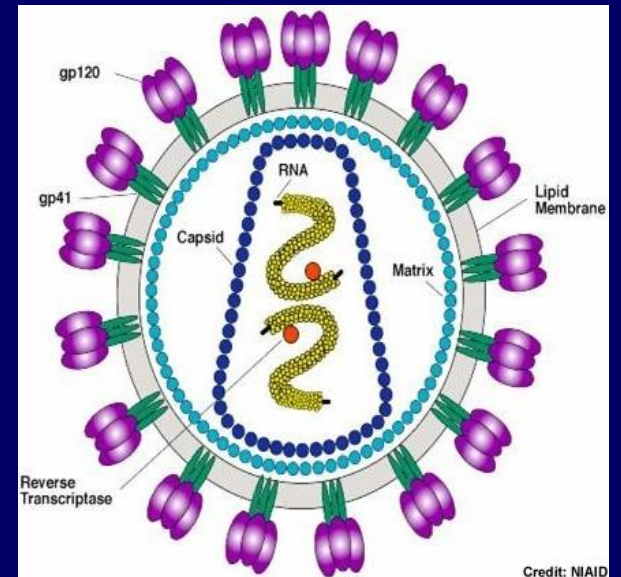
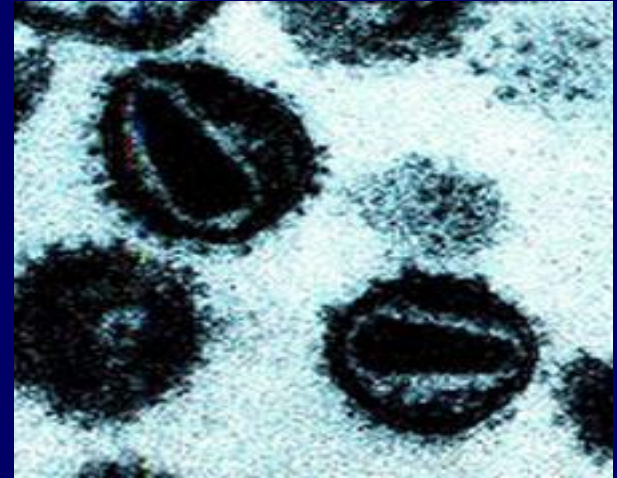
- Is the end stage of the disease that is associated with CD4+ T cell depletion, multiple or recurrent opportunistic infections, and unusual cancer (Kaposi sarcoma).

Characteristics of HIV

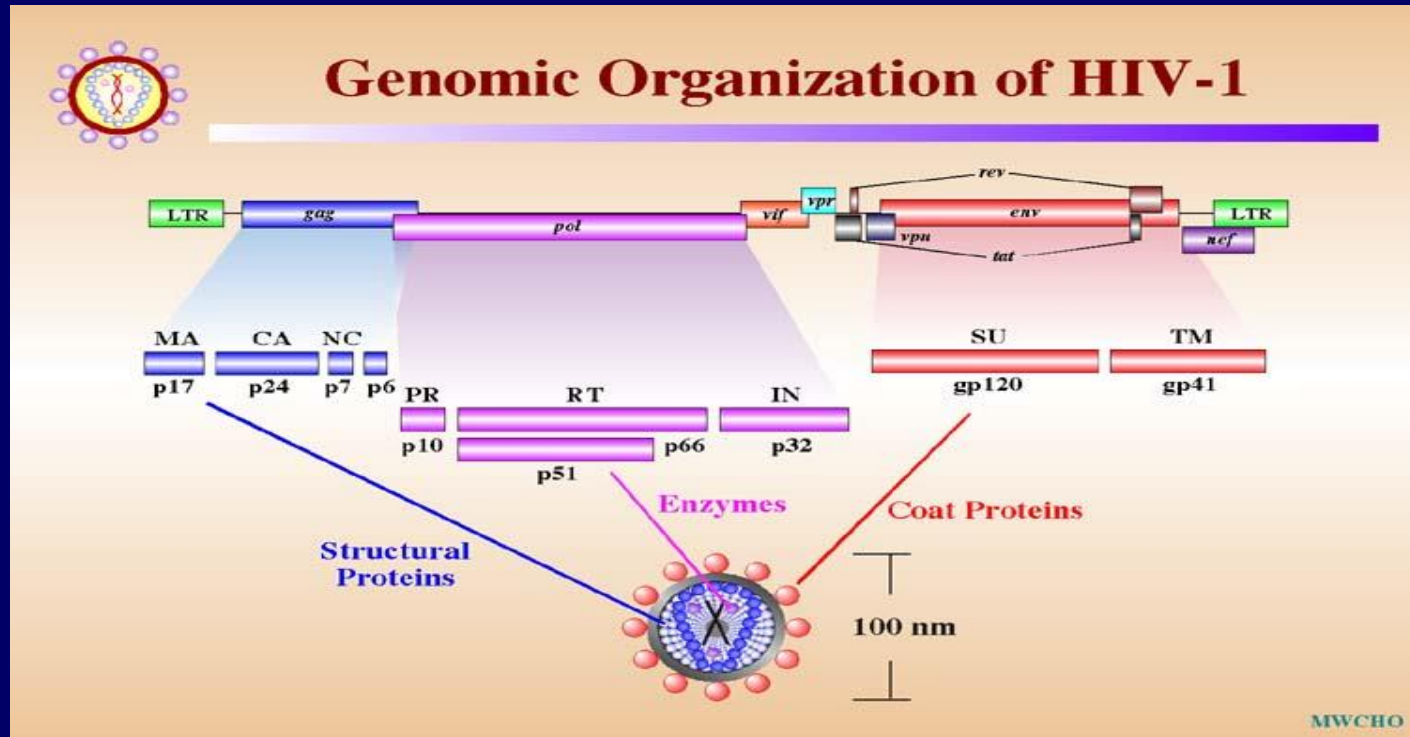
- Family of *Retroviridae*.

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.



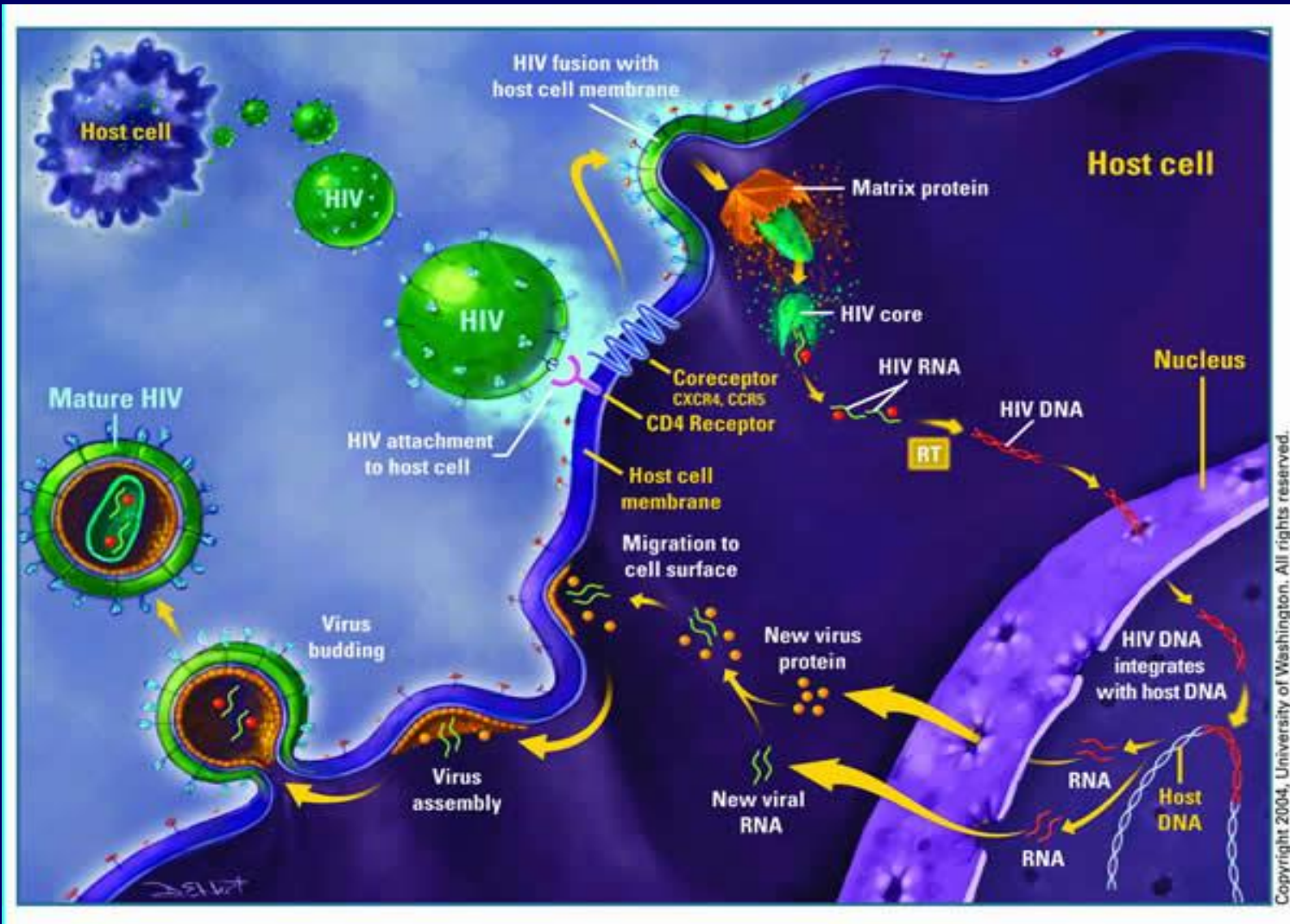
HIV genome



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.

Continued..

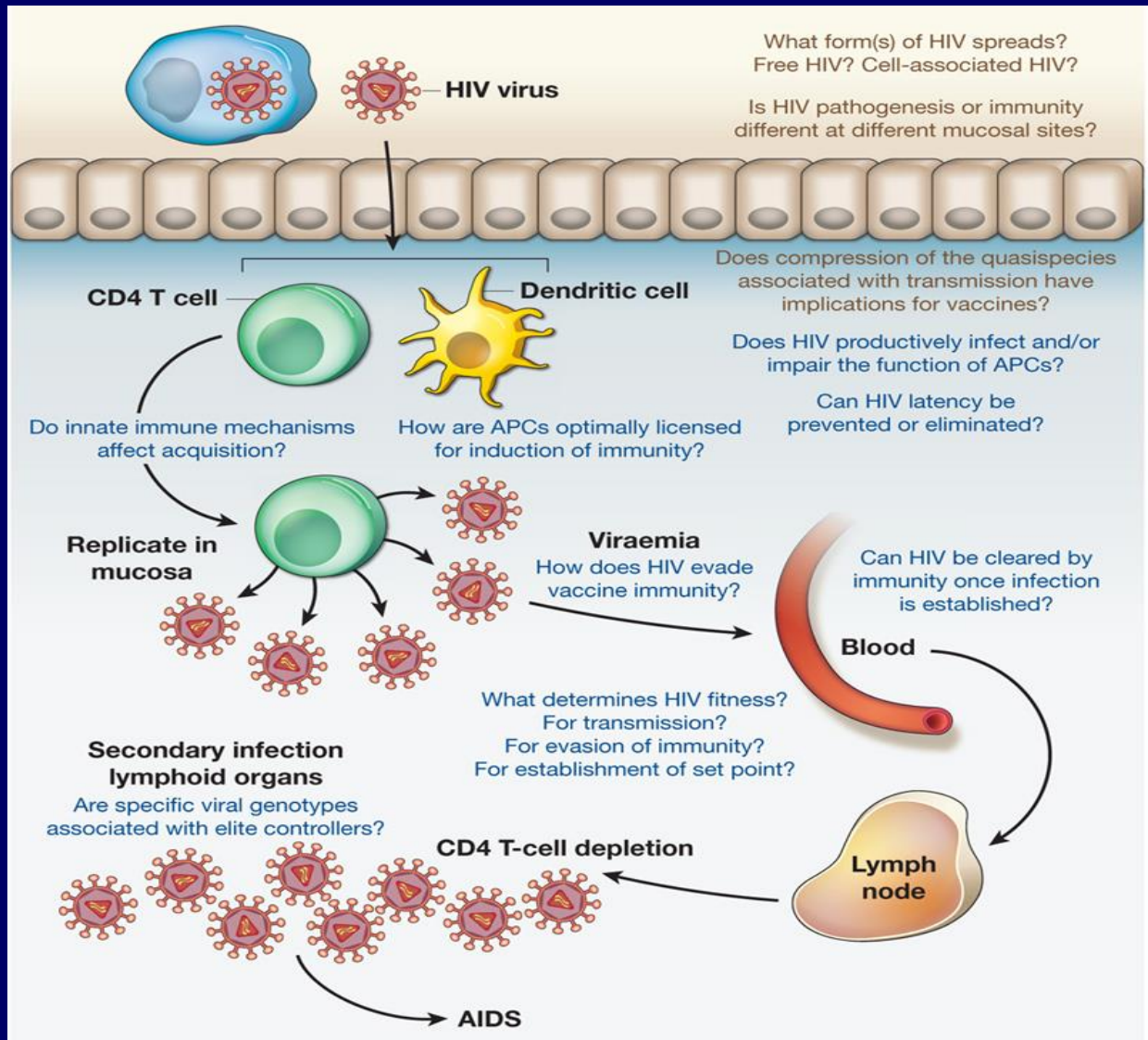
3- Perinatally (from mother to baby):

- 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

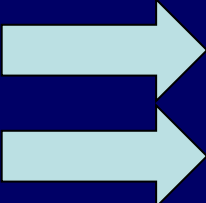
- HIV is **easily** inactivated by treatment for 10 min at 37°C with any of the following:
 - 10% House hold bleach, Sodium hypochlorite
 - 50% Ethanol
 - 35% Isopropanol
 - 0.5% Paraformaldehyde
 - 0.3% Hydrogen peroxide

HIV pathogenesis



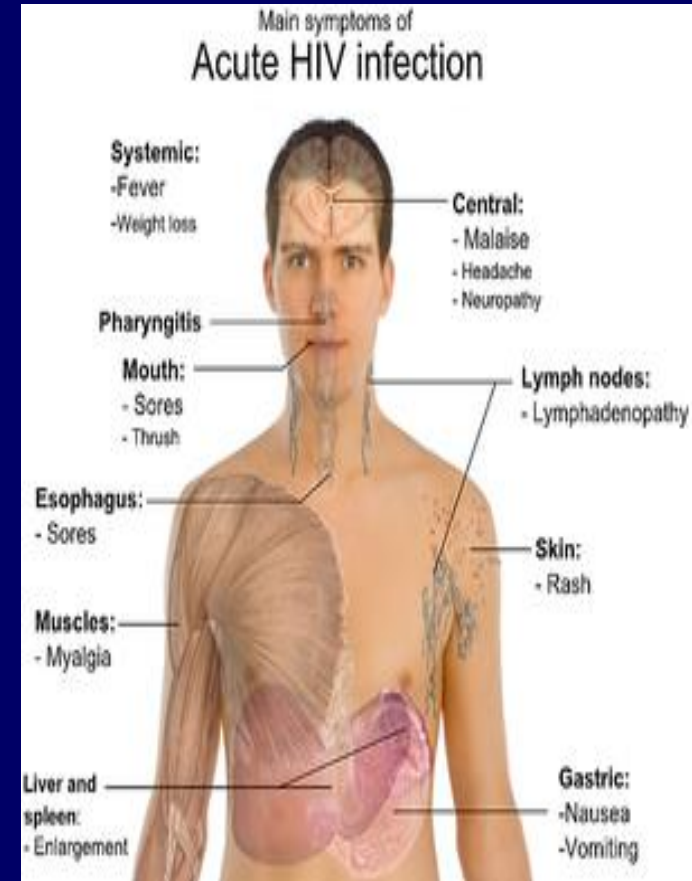
Stages of HIV infection

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:

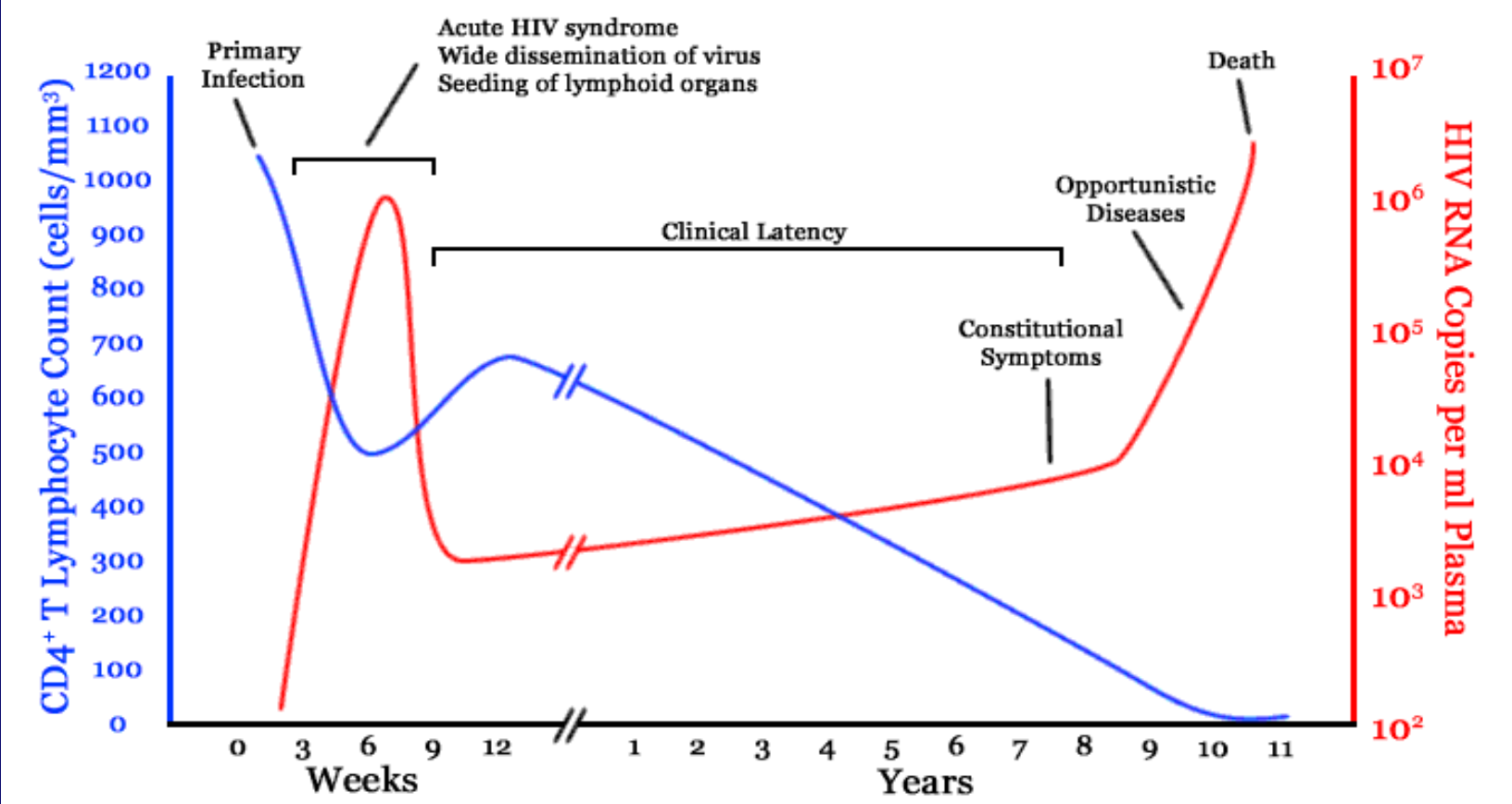
- Incubation period 2 weeks and lasts for about 12 weeks.
- Mostly asymptomatic, but in about 25-65% of the cases, patients may develop symptoms resemble infectious mononucleosis or Flu (fever, headache, anorexia, fatigue, lymphadenopathy, skin rash) which resolved in 2 weeks.
- Rapid viral replication (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 > 500 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.

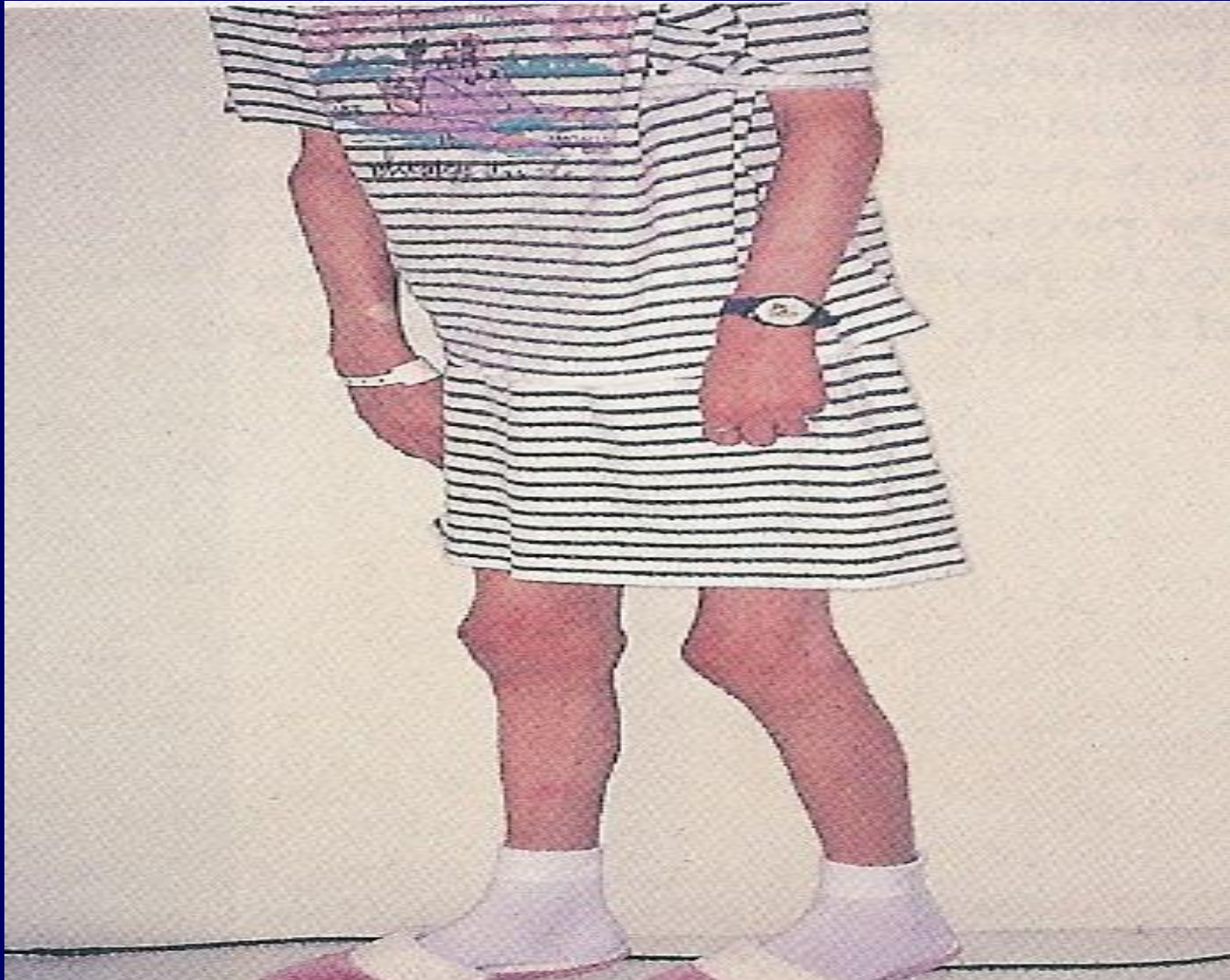


AIDS-related complex (ARC)

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.

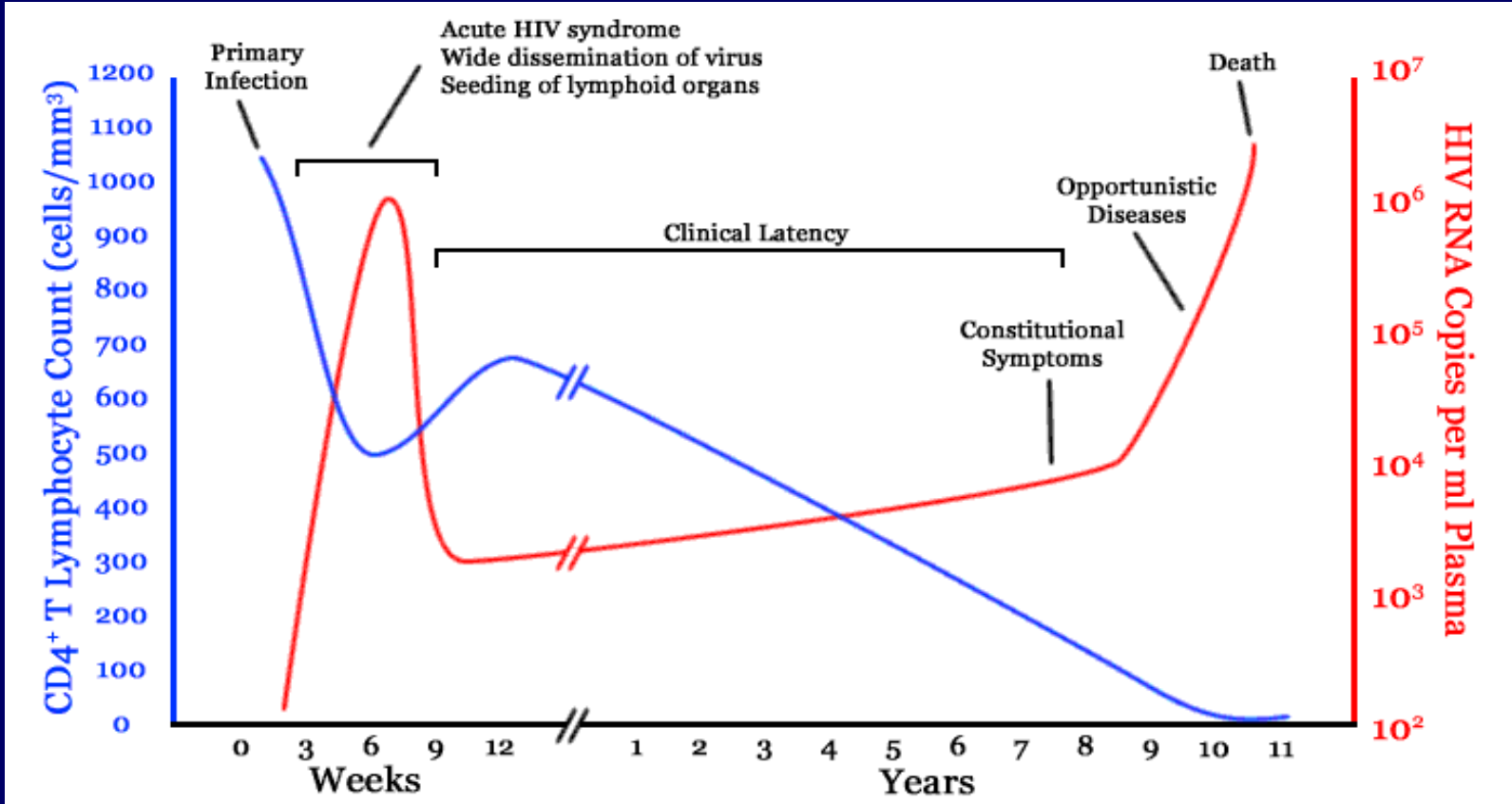
Slim disease



Blood markers in the chronic stage:

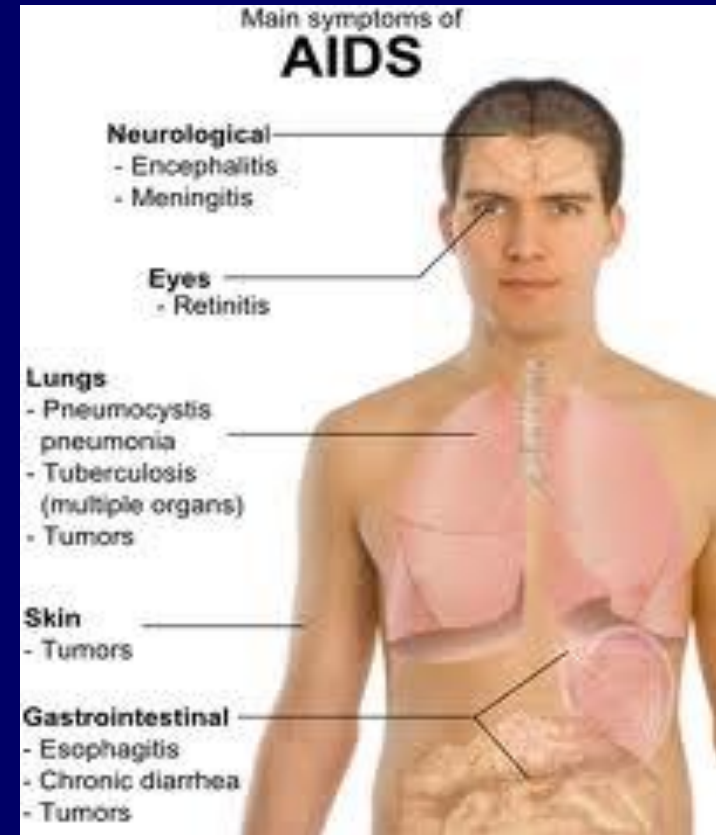
- Viral load (**HIV RNA**) increases gradually, but **HIV core antigen (p24)** may not appear in blood.
- Anti-envelop (**Anti-gp120**) & Anti-core (**Anti-p24**) are positive.
- **CD4+ T cell** count **gradually decreased** but still more than 200 cells/mm³

HIV RNA copies VS CD4+ T cell counts



AIDS phase:

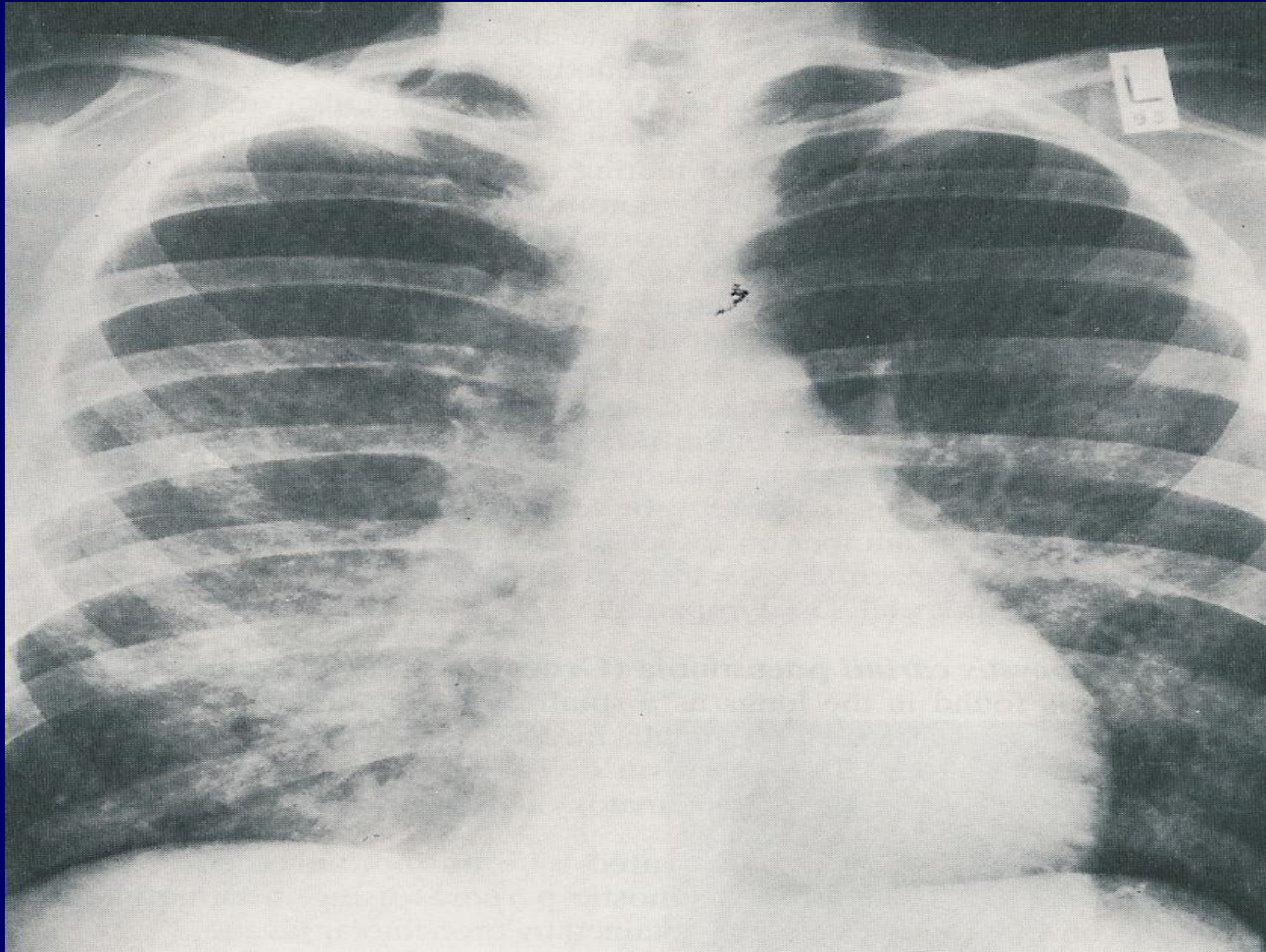
- The end stage of the disease.
- Continuous viral replication (high viral load).
- Marked decrease in CD4+ T cell count < 200 cell/mm³.
- Defects in cellular immunity.
- Persistent or frequent multiple opportunistic infections.
- Unusual cancer (Kaposi sarcoma).



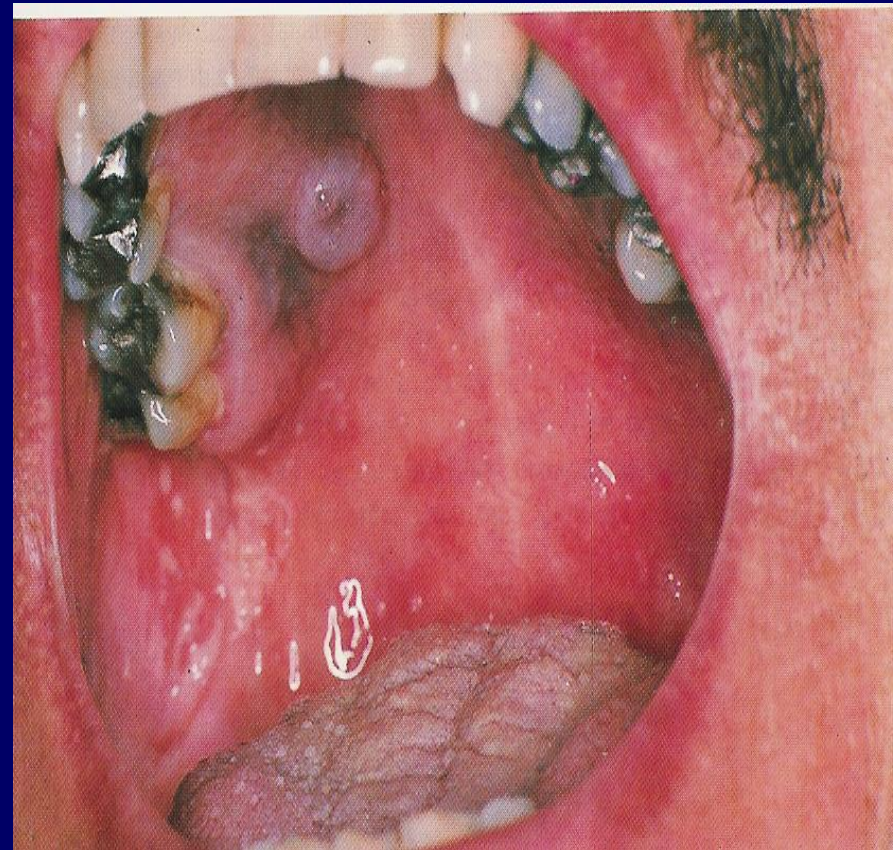
Continued..

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. <i>Mycoplasm</i> a <i>avium</i> , <i>M. tuberculosis</i> – disseminated, extrapulmonary) <i>Salmonella</i> (recurrent, disseminated) septicemia
protozoa	<i>Toxoplasma gondii</i> (disseminated, including CNS) <i>Cryptosporidium</i> (chronic diarrhea) <i>Isospora</i> (with diarrhea, persisting more than one month)
fungi	<i>Pneumocystis jiroveci</i> (pneumonia) <i>Candida albicans</i> (esophagitis, lung infection) <i>Cryptococcus neoformans</i> (CNS) histoplasmosis (disseminated, extrapulmonary) <i>Coccidioides</i> (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. <i>Haemophilus</i> , <i>Streptococcus</i> , <i>Pneumococcus</i>) 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



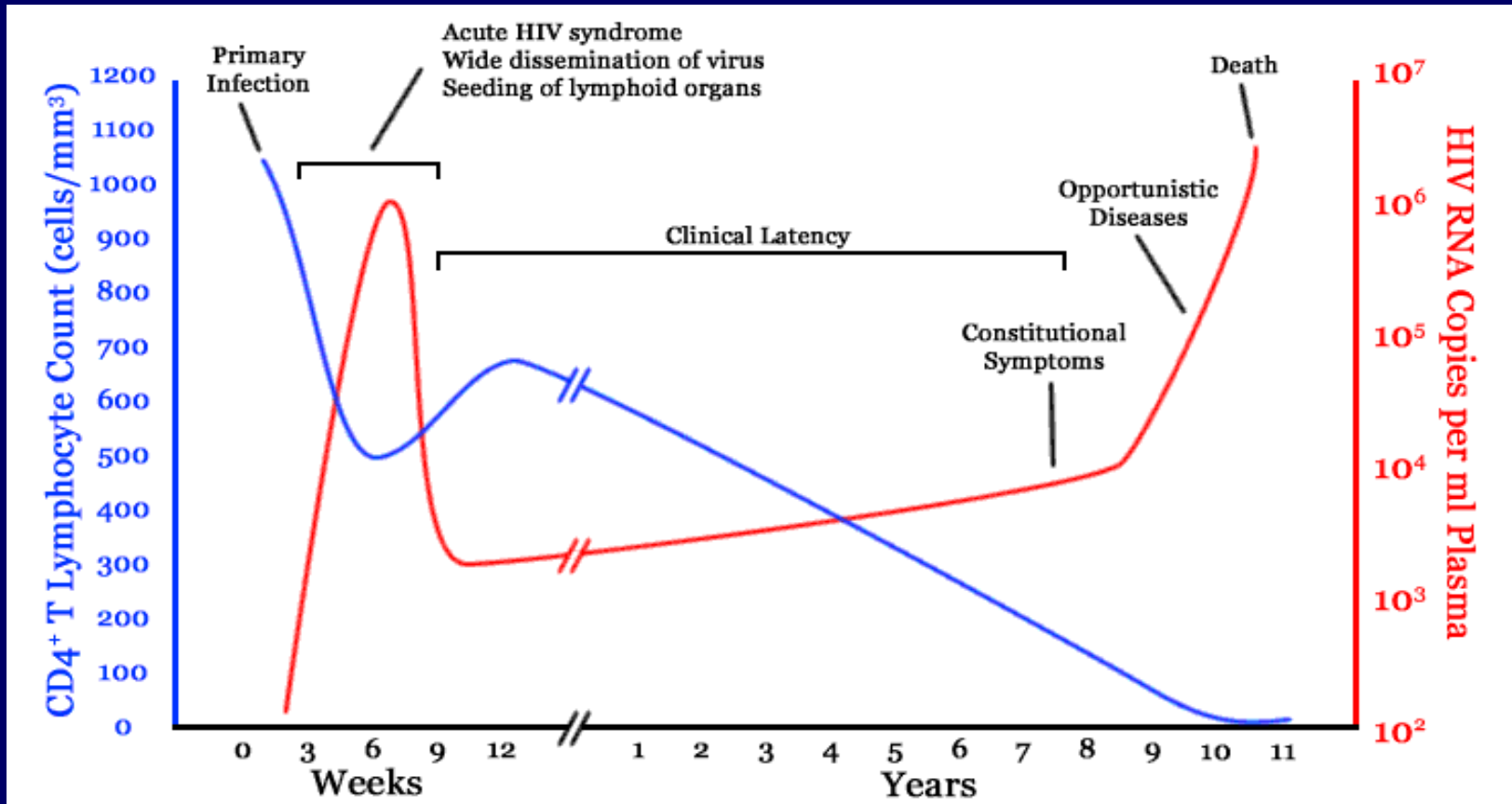
Kaposi sarcoma / Candida infection



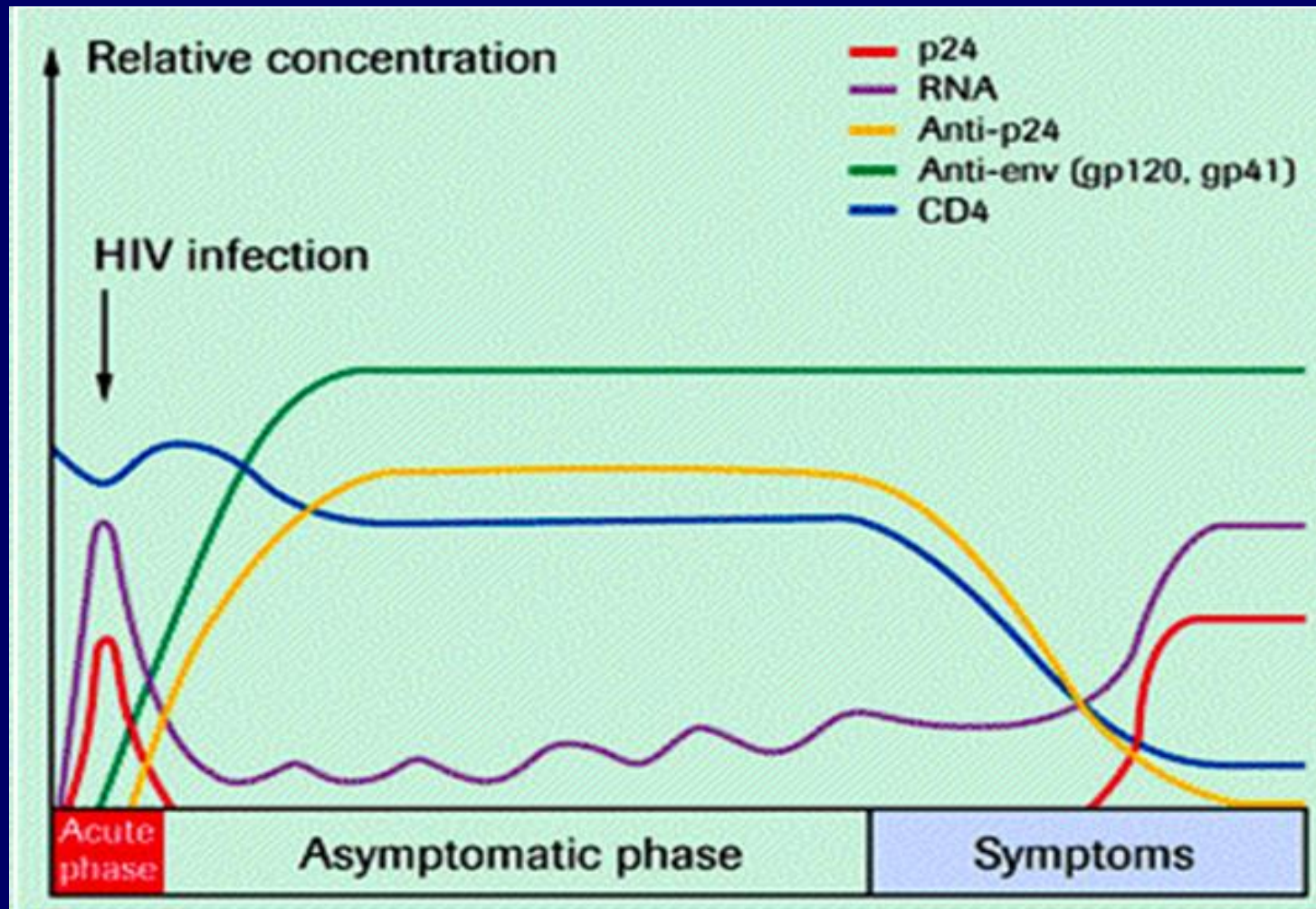
Blood markers in AIDS stage:

- 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/mm³).

HIV RNA copies VS CD4+ T cell counts



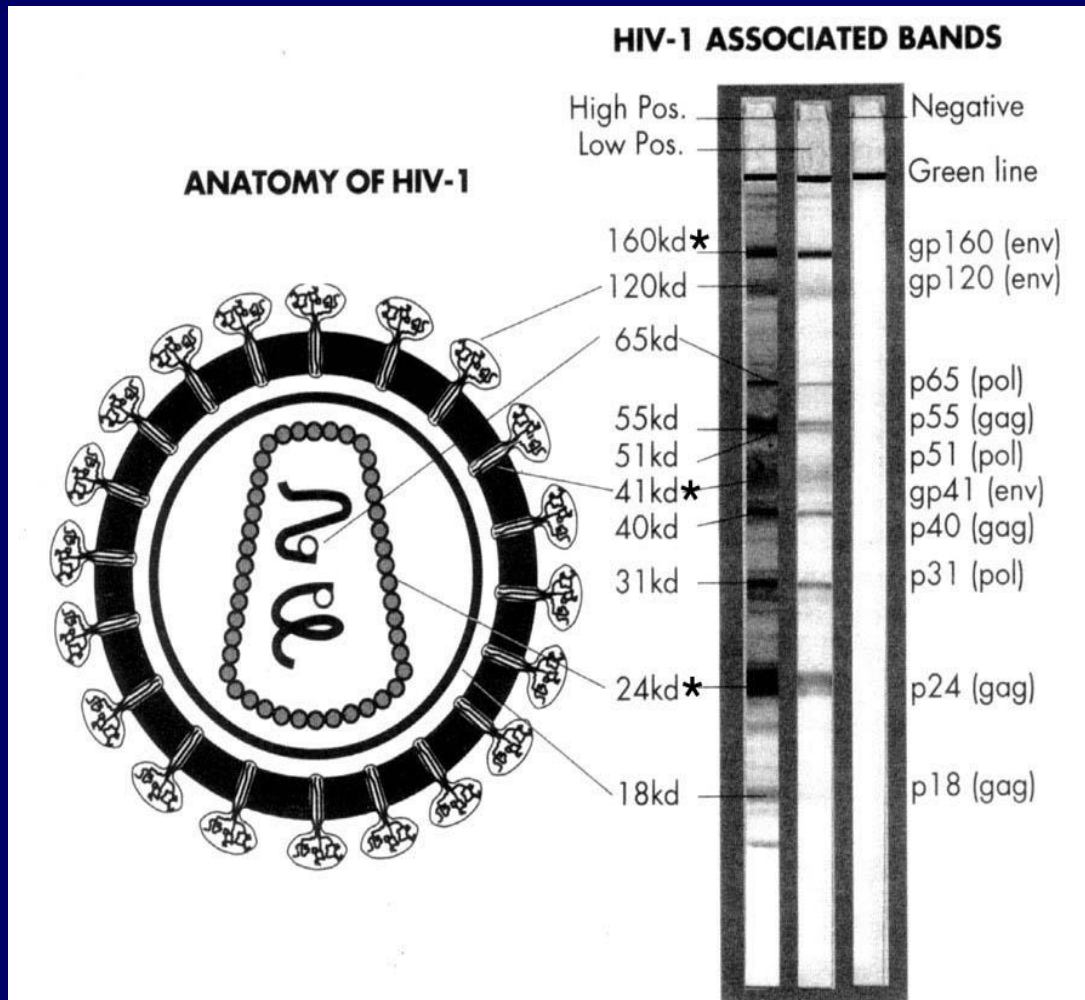
Serological profile of HIV infection



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.

Continued..

- 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

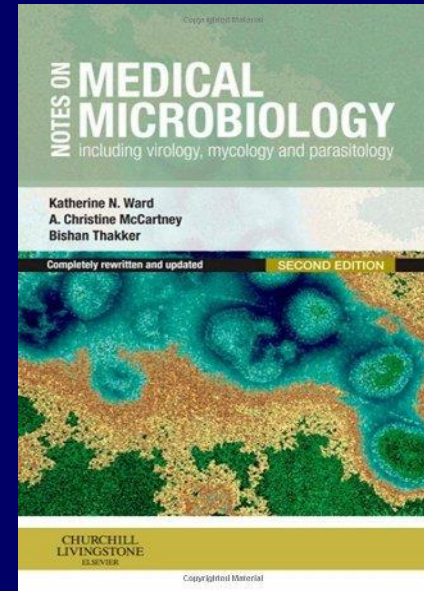
Goals of HIV treatment

- 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

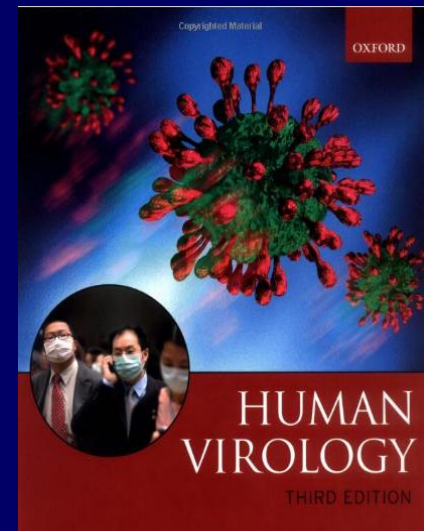
Notes on Medical Microbiology

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



Human Virology

By; Leslie Collier and John Oxford.
(2006)



Thank you for your attention !

Questions ?