

# Lecture 4



## HIV & AIDS

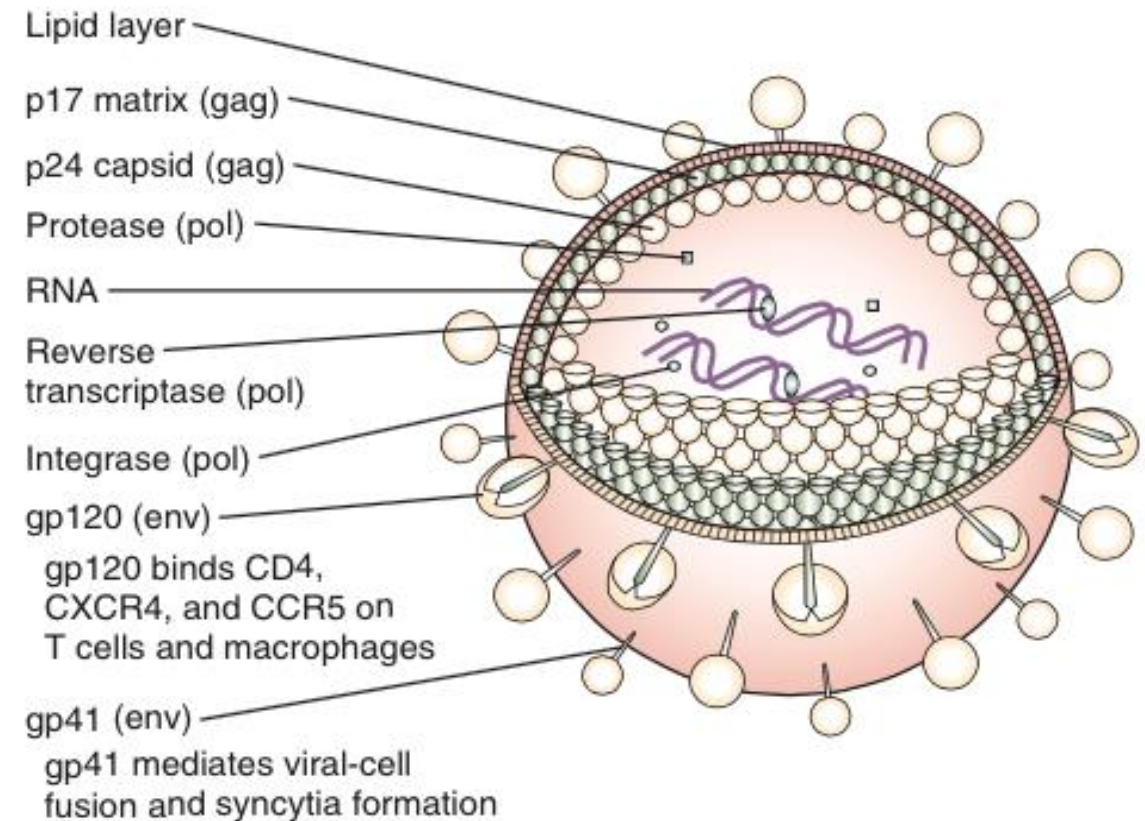
- Additional Notes
- Important
- Explanation
- Examples

# Introduction

- Human immunodeficiency virus (HIV) Is a retrovirus that causes human AIDS.
- HIV infects mainly **CD4+ T cells**, macrophages, and dendritic cells which express the surface receptor CD4.
- Destroying CD4+ T cells leads to opportunistic infection.
- 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**).
- HIV patient is different from an AIDS patient. AIDS is an end stage of HIV virus.
- **HIV-1: most common cause of AIDS**
  - ✓ 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.

# Characteristics of HIV

- Virion consist of:
  - ✓ Glycoprotein envelope (gp120, gp41).
  - ✓ Matrix layer (p17).
  - ✓ Capsid (p24).
  - ✓ Two copies of ss-RNA.
  - ✓ Enzymes:
    - Reverse transcriptase
    - Integrase,
    - Protease
- The genome consists of 9 genes:
  - ✓ 3 structural genes (gag, pol, env)
  - ✓ 6 non-structural genes (tat, nef, rev, vif, vpr, vpu)



ANIMATED VIDEO ABOUT HIV:

<https://www.youtube.com/watch?v=hdgNnXLY8LU>

# Transmission of HIV

- Sexually (unprotected sex):
  - ✓ Mainly in homosexual.
  - ✓ 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).
  - ✓ Using contaminated or not adequately sterilized tools in surgical or cosmetic practice (dental, tattooing, body piercing).
  - ✓ Sharing contaminated needles, razors, or tooth brushes.
- 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%).

# 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 number 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.
- **Antibody tests may give false negative (no antibodies were detected despite the presence of HIV) results during the window period, an interval of three weeks to six months between the time of HIV infection and the production of measurable antibodies to HIV seroconversion.**

# Chronic phase:

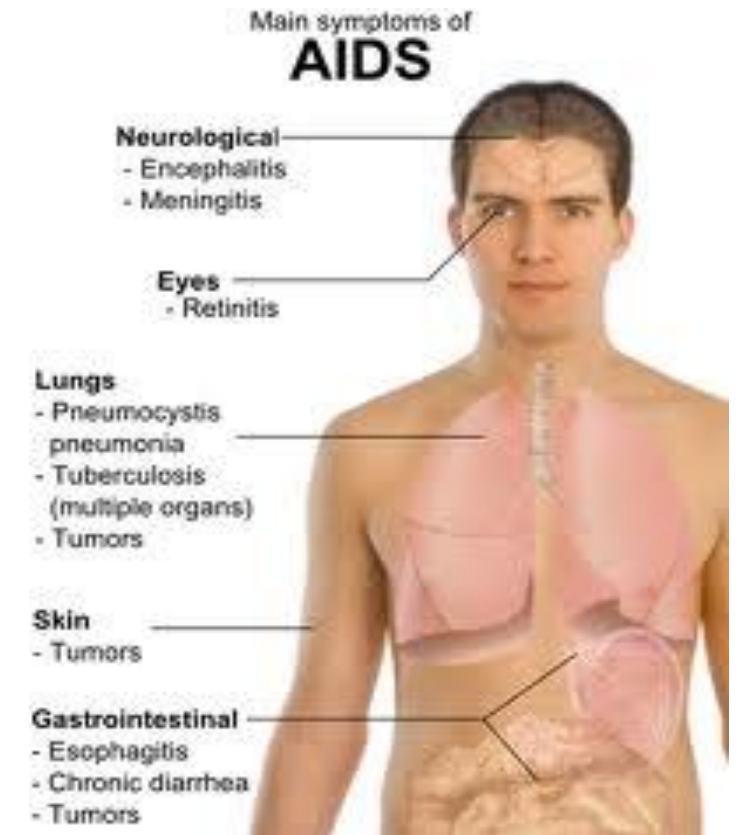
- Lasts for about 10 years in adults, and 5 years in children.
- **Totally asymptomatic but the patients is still contagious.**
- Relatively low viral load ( $<10^4$  copies/mL).
- **CD4+ T cell count  $> 500$  cells/mm<sup>3</sup>.**
- At the end of this stage, two syndromes appear:
  1. Persistent generalized lymphadenopathy (PGL).
  2. AIDS-related complex (ARC).
- Blood markers in the chronic stage:
  - ✓ Viral load (**HIV RNA**) increases gradually, and **HIV core antigen (p24)** in blood.
  - ✓ **Anti-envelop (Anti-gp120) & Anti-core (Anti-p24)** are positive.
  - ✓ **CD4+ T cell** count **gradually decreased**

- 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.

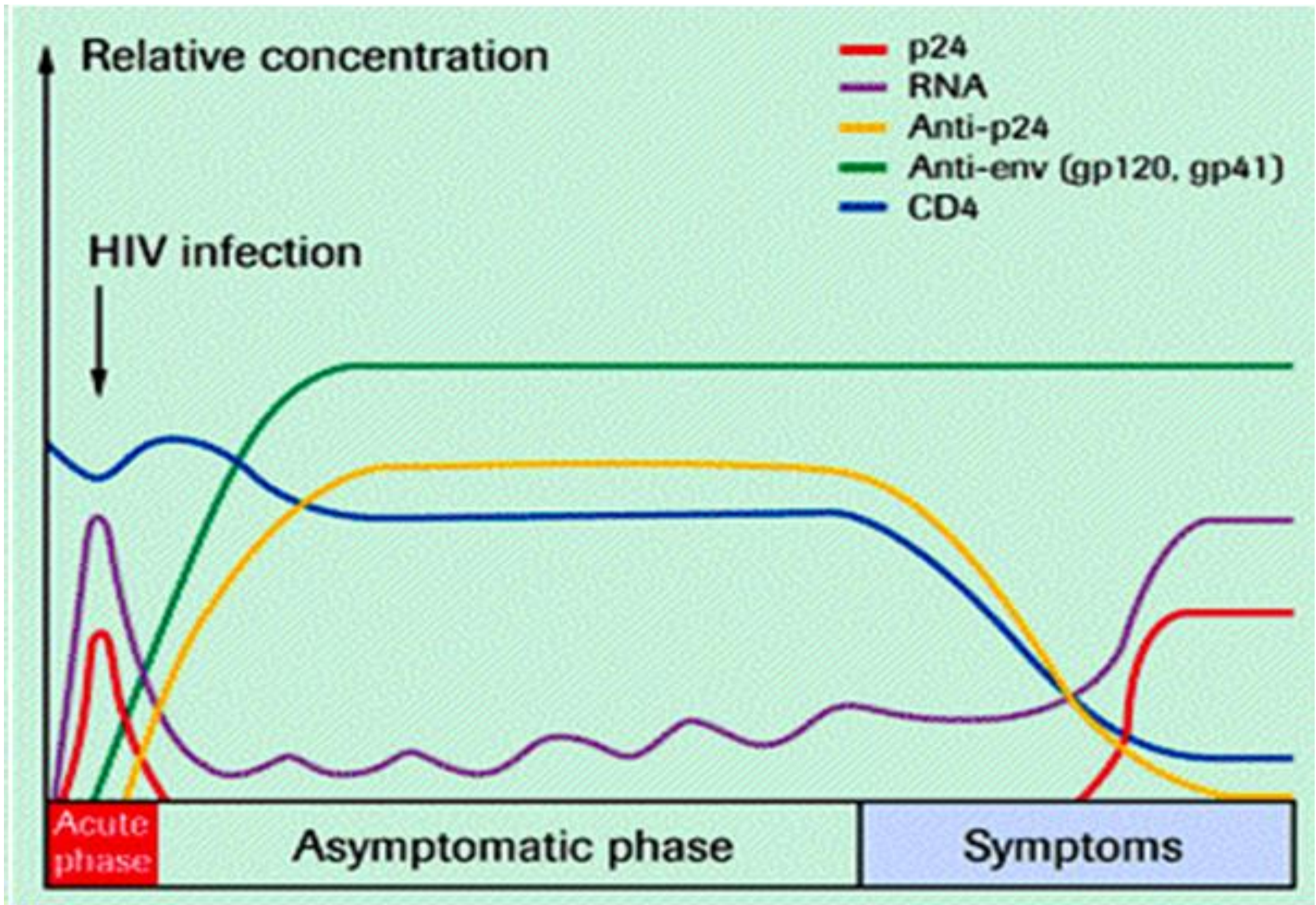


# AIDS phase:

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

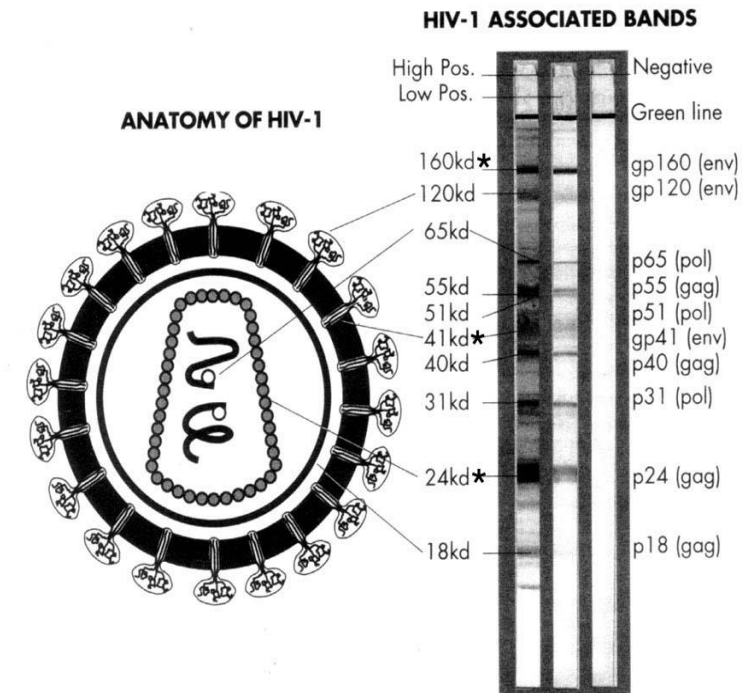






# Diagnosis

- 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.
- The western blot is an antibody detection test. The viral proteins are separated first and immobilized. In subsequent steps, the binding of serum antibodies to specific HIV proteins is visualized.



# Management

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

- 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.

# Treatment

- Is a combined therapy known as **High Active Antiretroviral Therapy (HAART)**.
- HAART does not clear (eradicate) the virus from the body, and should be taken all life. But it prevents its duplication.
- 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.

| Reverse transcriptase  |   | Proteases inhibitors  |
|--|---|---|
| Nucleoside analog RT inhibitors for <b>HIV-1 &amp; HIV-2</b>   | Non-nucleoside analog RT inhibitors for <b>HIV-1 only</b>   | <ul style="list-style-type: none"><li>• Saquinavir</li><li>• Indinavir</li><li>• Nelfinavir</li><li>• Ritonavir</li></ul> |
| <ul style="list-style-type: none"><li>• <b>Zidovudine (AZT)</b></li><li>• Zalcitabine (ddC)</li><li>• Stavudine (d4T)</li><li>• Lamivudine (3TC)</li></ul> | <ul style="list-style-type: none"><li>• <b>Nevirapine</b></li><li>• Delavirdine</li><li>• Efavirenz</li></ul> |   |