

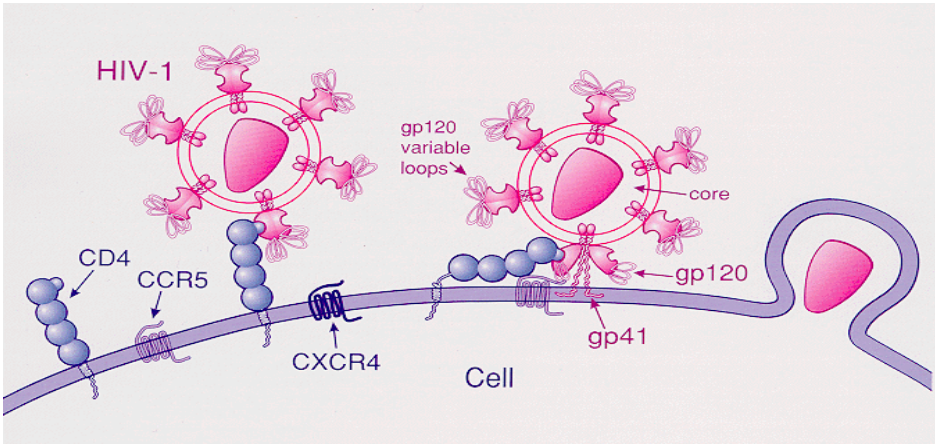
# Human Immunodeficiency Virus (HIV) & Acquired Immune Deficiency Syndrome (AIDS)



# SUMMARY



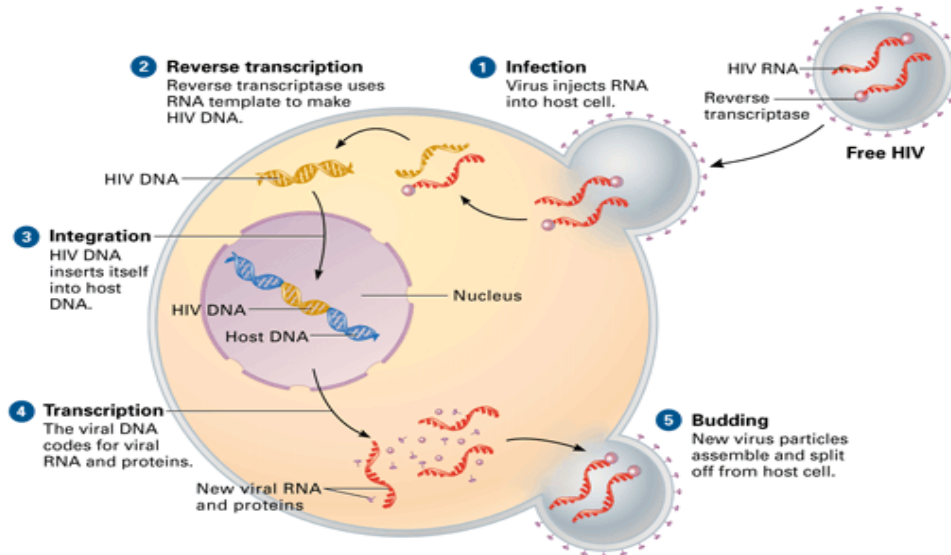
# How HIV Enters Cells?



gp120 env protein binds to CD4 molecule  
(CD4 found on T-cells macrophages, and microglial cells)

gp120 env protein binds to co-receptor  
Chemokine receptors: (CCR5 and CXCR4 receptors)

Binding of virus to cell surface results in fusion of viral envelope with cell membrane  
Viral core is released into cell cytoplasm.

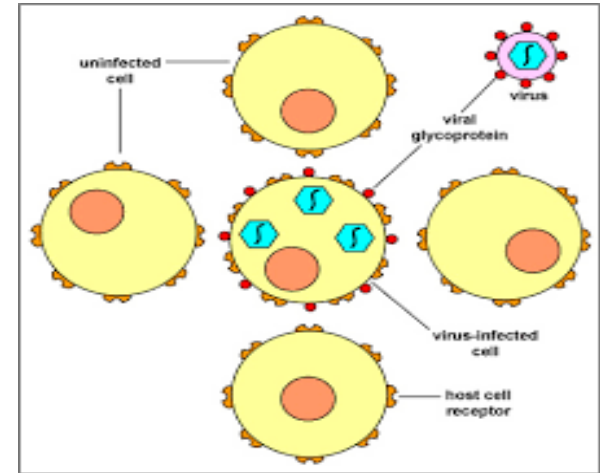


# HIV Infection Stages

Acute HIV Infection	Chronic HIV Infection (Clinical Latency)	AIDS
2 to 4 weeks	8-10 years w/o treatment	10 to 12 years w/o treatment
Flu-like symptoms	Asymptomatic	opportunistic infections ( e.g.: TB and candida) and cancer.
HIV multiplies <b>rapidly</b> and spreads throughout the body.	HIV continues to multiply in the body but at <b>very low levels</b> .	- HIV gradually disrupts the immune system the body can't fight off
<ul style="list-style-type: none"> <li>- <b>Peak</b> in HIV RNA copies</li> <li>- Steep <b>decline</b> in CD4 (300-400)</li> </ul>	<ul style="list-style-type: none"> <li>- HIV RNA copy number in the plasma <b>declines</b>.</li> <li>- CD4 cell in the peripheral blood <b>increases</b> again.</li> </ul>	<ul style="list-style-type: none"> <li>- Rapid <b>increase</b> in HIV RNA</li> <li>- CD4 count of <b>less than 200</b> cells/mm<sup>3</sup></li> </ul>
<ul style="list-style-type: none"> <li><b>1- Viremic</b>, with a high viral load and a negative HIV antibody test. (4-8 weeks)</li> <li><b>2- Sero-cversion</b> HIV antibody test becomes positive. (after 8 week)</li> <li><b>3- Asymptomatic Phase:</b> fall of CD4 count by about 50-150 cells per.</li> </ul>	<p style="text-align: center;"><b>Viral set-point</b></p> <p>HIV RNA copy number in the plasma declines again, and the stabilized plasma concentration after the peak of the primary infection.</p>	-
All mucosal CD4 T lymphocytes are lost, especially in GIT → Increased circulating lipopolysaccharide (LPS) levels → chronic immune activation → higher susceptibility to HIV.	Usually advances to AIDS in 10 to 12 years.	-

## ✧ Mechanisms of CD4 Depletion and Dysfunction:

- **Direct:**
  - ✓ Elimination of HIV-infected cells by virus-specific immune responses
  - ✓ Loss of plasma membrane integrity because of viral budding
- **Indirect:**
  - **Syncytium formation:**
    - ✓ Observed in HIV infection, most commonly in the brain
    - ✓ Uninfected cells may then bind to infected cells due to viral gp120
    - ✓ This results in fusion of the cell membranes and subsequent syncytium formation.
    - ✓ These syncytia are highly unstable and die quickly
  - **Apoptosis**
  - **Autoimmunity**



## ✧ Role of Cellular Activation in Pathogenesis of HIV:

- **HIV induces immune activation**
  - ✓ Which may seem paradoxical because HIV ultimately results in severe immunosuppression
- **Activated T-cells support HIV replication**
  - ✓ Inter-current infections are associated with transient increases in viremia
  - ✓ Accounts for why TB worsens underlying HIV disease

## ✧ Role of Cytokine Dys-regulation in Pathogenesis of HIV:

- **HIV is associated with increased expression of pro-inflammatory cytokines**
  - ✓ TNF-alpha, IL-1, IL-6, IL-10, IFN-gamma
- **HIV results in disruption and loss of immuno-regulatory cytokines**
  - ✓ IL-2, IL-12
  - ✓ Necessary for modulating effective cell-mediated immune responses (CTLs and NK cells)

# Multiple Choice Questions

1. HIV target major cells in human body known as:

- A. C-lymphocytes
- B. B-lymphocytes
- C. T-lymphocytes

2. Increased circulating lipopolysaccharide (LPS) levels, increases susceptibility to :

- A. HIV
- B. HSV
- C. Syphilis

3. In acute stage of HIV infection negative HIV antibody test result means:

- A. High viral load
- B. Fall of CD4 count by about 50-150 cells per
- C. None

4. Syncytium formation is related to:

- A. Direct mechanisms of CD4 depletion and dysfunction
- B. Indirect mechanisms of CD4 depletion and dysfunction
- C. Both

5. HIV is associated with increased expression of which of the following pro-inflammatory cytokines

- A. IL-1
- B. IL-6
- C. Both

6. Mechanisms of HIV entering the cells starts with:

- A. gp120 env protein binds to CD4
- B. gp1 env protein binds to CD4
- C. Only chemokine receptors:

7. Flu-like symptoms are present in which stage of HIV infection:

- A. Acute
- B. Chronic
- C. AIDS

8. CD4 count of less than 200 cells/mm<sup>3</sup> means:

- A. AIDS
- B. HIV infection in chronic phase
- C. Asymptomatic

9. Sero-cversion in acute phase on HIV infection indicates which one of the following:

- A. HIV antibody test becomes positive.
- B. HIV antibody test becomes negative.
- C. High high viral load

10. Role of cellular activation in pathogenesis of HIV:

- A. HIV induces immune activation
- B. HIV reduces immune activation
- C. None