

429 PATHOLOGY TEAM



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*** HUMAN IMMUNODEFICIENCY VIRUS; HIV INFECTION ***

★ or **Highlighted** ; Very important note

★ or **Highlighted** ; an MCQ

Highlighted ; Understand only

About the Virus:

Retrovirus (of the **Lentivirus** family) **contains only RNA** (can't replicate on its own)

It is the **Human Immunodeficiency Virus (HIV)** → causes **Acquired Immune Deficiency Syndrome (AIDS)**

[*AIDS is a late stage of HIV*]

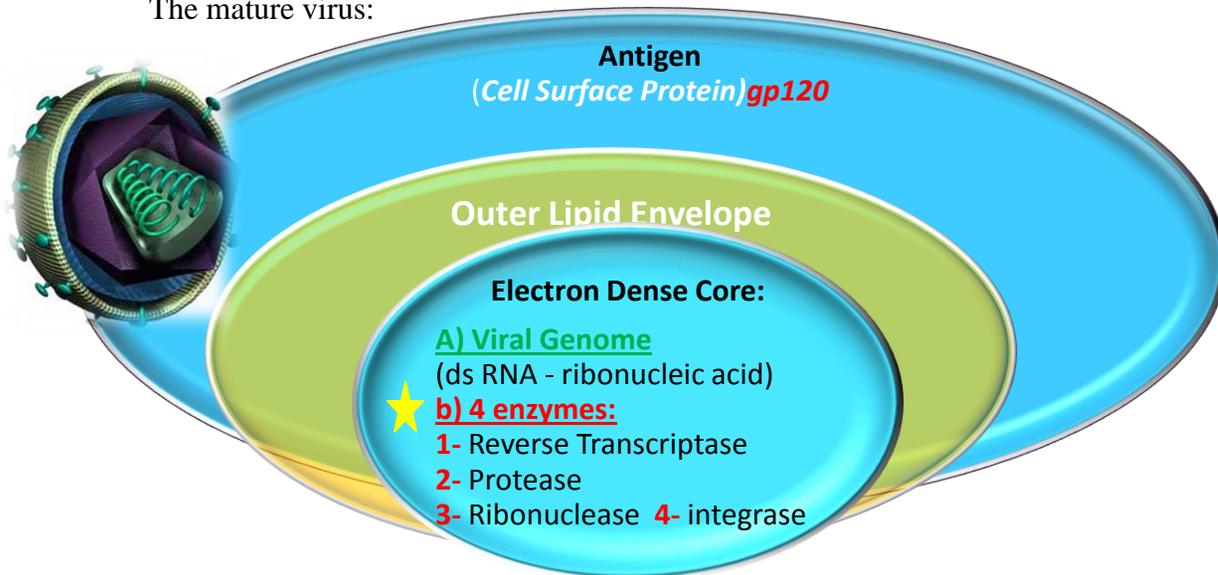
- **The result of HIV infection** is the **destruction of the immune system**.
- **Types:**
 - **HIV-1** (most common type and is the type that has led to the worldwide AIDS epidemic).
 - HIV-2 (much less common).

- **HIV infection risks:**

Death from development of *Opportunistic Infections*, *Tumors* and *the Inevitable Manifestations Of AIDS*.

Structure and Function

The mature virus:



Functions of **gp120**:

Aids in binding of the virus to **Target Cells (HOW?)**

Target cells have **CD4 receptors** on their surface, **gp120 is responsible in tropism/attraction** to these CD4 receptors

→ helps in entry of HIV into host cell

→ **binding to 2 co-receptors:**

CXCR4 and **CCR5** on the host cell surface.

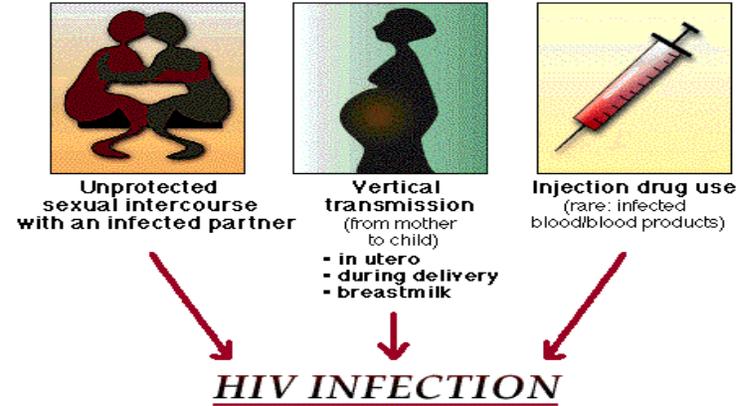
The probability of infection depends on:

A -The **number of infective HIV** virions in the body fluid, which contacts the host.

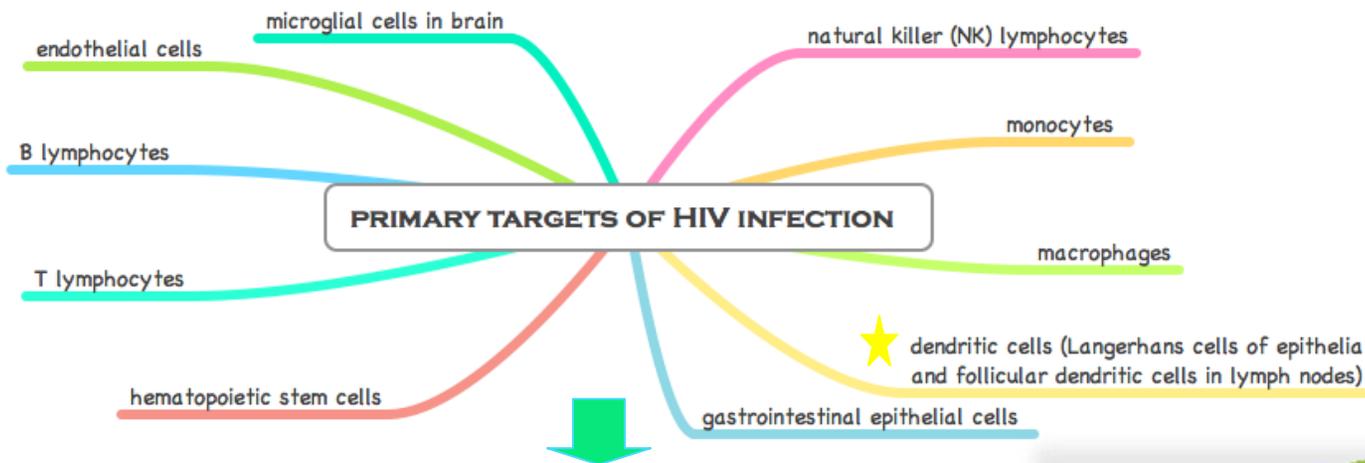
B -the **number of cells with CD4 receptors** available at the site of contact.

Establishment of the infection:

1) Virus enters the body by one of the Various modes of **transmission**:



2) Viral particle is **attracted** to a cell with a **CD4 receptor** (cells of *Mononuclear Phagocyte System*; in the graph below) and then **enters it** by its gp120 (mentioned earlier).



★ **Macrophages & Langerhans cells are both important as:**

Reservoirs and **vectors** for the spread of HIV in the body.

They both can be HIV-infected but are not destroyed themselves.

HIV can then be carried *elsewhere* in the body.

★ **3) The virus **replicate** by using the host cell's DNA (it has only RNA)**

How??

- It **transcribe (reverse transcription)** its **RNA** to the host cell's **DNA** → forms **Proviral DNA** ((by its **Reverse Transcriptase** enzyme)).
- It **inserts** its **Proviral DNA** formed; into **host cell genomic DNA** ((by its **Integrase** enzyme)).

→ Proviral DNA is within the infected cell's genome

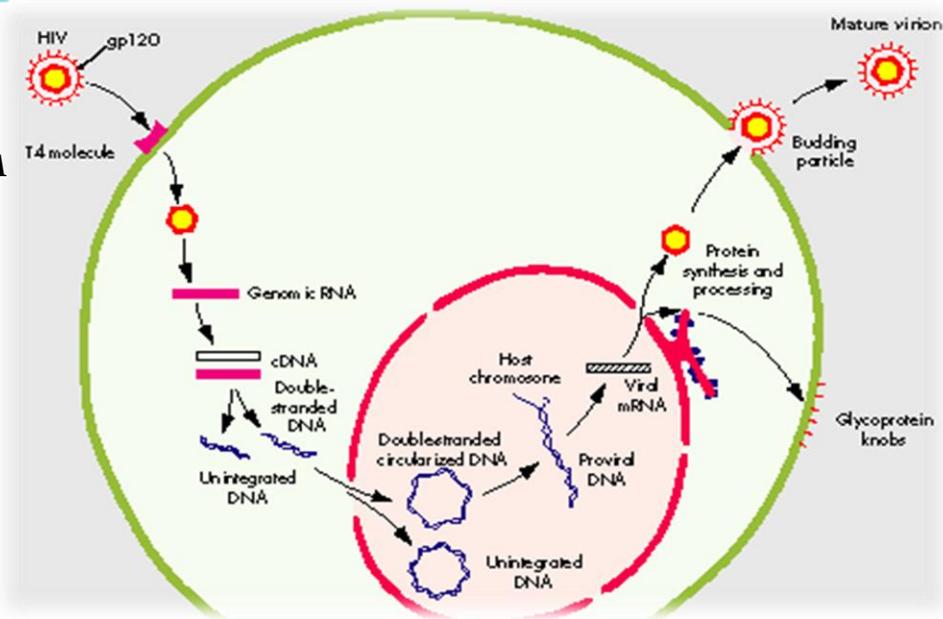
→ HIV provirus is replicated by host cell

→ produced additional HIV virions

c) Those new cells are **released by surface budding**

d) *Infected cells* undergo lysis with this release.

→ infect additional cells (continuous cycle)



↓

4) When the infection **extends** to the Lymph Nodes:

The HIV virions are **trapped** in the processes of **follicular dendritic cells (FDCs)**, which become infected, but are not destroyed. They provide a reservoir → infect CD4+ T lymphocytes that are passing through the lymph node.

↓

- ★5) HIV has the ability to **mutate** easily → this leads to the emergence of **HIV variants** within the infected person's cells → cells become more toxic and can resist drug therapy. Over time, different tissues of the body may harbor differing HIV variants depending on the way it **mutate**.

The major modes of transmission of HIV (the high risk population)

Primary as a **Sexually Transmitted Disease** or **Parenteral route**

HIV can be present in a variety of body fluids and secretions of the *infected person*. They include:

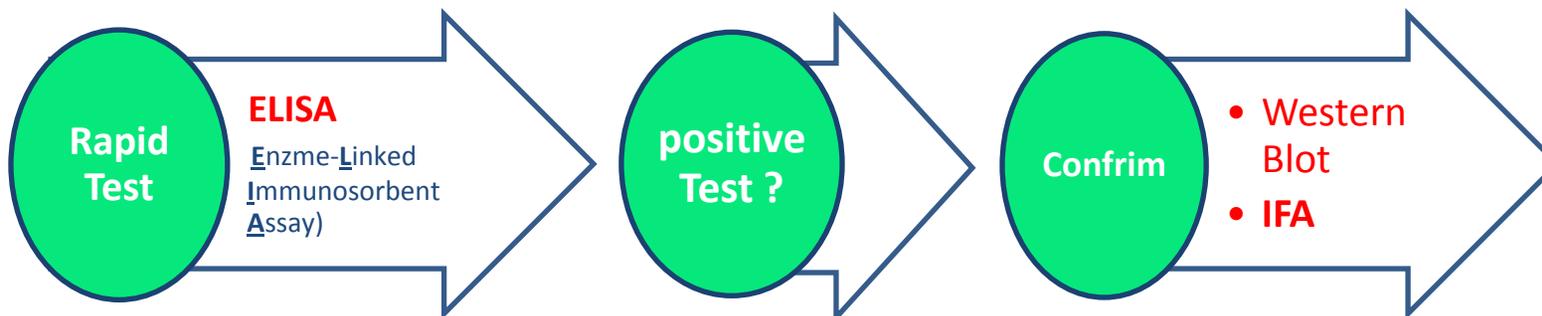
- Genital secretions
- Blood
- Breast milk.
- Genital secretions

NOTE:

- Saliva, urine, tears, and sweat is of no major clinical importance (transmission of HIV through these fluids does not routinely occur due to low concentration of HIV in them).
- HIV infection is not spread by casual contact in public places, households, or in the workplace.
- HIV is not spread by insect vectors.
- There is no vaccine to prevent HIV infection



Diagnosis of HIV:



Average HIV infected person may take up to **several weeks** to become **seropositive**, and then may live **up to 8-10 years**, on average, before development of the clinical signs and symptoms of **AIDS**.

Primary HIV Infection and Acquired Immunodeficiency Syndrome (Clinical AIDS)

	Primary HIV infection	Clinical AIDS
Initial Appearance	<p>One of the following might occur:</p> <ol style="list-style-type: none"> 1. Infection may go unnoticed in at least half of cases 2. Produce a mild disease which quickly subsides 3. Produce acute HIV infection, followed by a long clinical "latent" period lasting years 	<p>The stage of clinical AIDS is reached in years after initial infection and is marked by :</p> <p>the development of one or more of the typical opportunistic infections or neoplasms common to AIDS.</p>
Clinically	<p>Acute infection: may include:</p> <ul style="list-style-type: none"> ✓ Fever ✓ generalized lymphadenopathy ✓ pharyngitis ✓ rash ✓ arthralgia ✓ diarrhea. <p>These symptoms diminish over 1 to 2 months.</p> <p>Latent infection: may appear for years</p> <p>Where there is an <i>ongoing immune system destruction</i> but still, enough of the immune system remains intact to provide immunity and prevent most infections</p>	<p>The progression to clinical AIDS is also marked by:</p> <p>★ Syncytia-forming (SI) variants of HIV:</p> <ul style="list-style-type: none"> • Appears in about half of HIV infected patients • Have greater attraction to CD4 cells • Are associated with more rapid CD4+ cell decline
Development of Signs / Symptoms	<p>Primarily targets the immune system.</p> <ul style="list-style-type: none"> ➤ When a significant number of CD4 lymphocytes have been destroyed. ➤ When production of new CD4 cells cannot match destruction. <p>Result: failure of the immune system, leads to the appearance of clinical AIDS</p>	<p>★ Laboratory testing for CD4 lymphocytes:</p> <p>When the CD4 lymphocyte count drops below 200/microliter, then the stage of clinical AIDS has been reached.</p> <p>This is the point at which the characteristic opportunistic infections and neoplasms of AIDS appear.</p>

Common Complications seen with AIDS:

We consider them as markers for AIDS stage

Cytomegalovirus

Causes:

Pneumonia

Serious disease in the brain and gastrointestinal tract

Common cause for retinitis and blindness

Mycobacterial Infections

Organisms:

Myco-bacterium tuberculosis.

Myco-bacterium avium complex (MAC) infection

Definitive diagnosis:

★ by culture and PCR.

Pneumocystis jiroveci

Formerly known as *Pneumocystis carinii*
The most frequent opportunistic infection seen with AIDS.

It commonly produces a pulmonary infection.

Diagnosis: either by

1. Histologically by finding the organisms in cytologic (bronchoalveolar lavage)
2. Biopsy (transbronchial biopsy) material from lung.

Fungal Infections

- ★ 1. **Candidiasis** of the esophagus, trachea, bronchi, or lungs.
- ★ 2. ***Cryptococcus neoformans*** (produces pneumonia and meningitis)
- ★ 3. ***Histoplasma Capsulatum***
- ★ 4. ***Coccidioides Immitis***

Others

- ★ 1. **Toxoplasmosis** caused by *Toxoplasma gondii* is a protozoan parasite that leads to infection of the brain with AIDS.
- ★ 2. **Herpes simplex infection**
- ★ 3. **Crypto-sporidium and Micro-sporidium** produce voluminous watery diarrhea in patients with AIDS.

Malignant Neoplasms

- ★ 1. **Kaposi's Sarcoma**
Produces reddish purple patches or nodules over the skin
Can be diagnosed with skin biopsy.
Visceral organ can also be involved
2. **Malignant lymphomas**
Commonly it is B-cell NonHodgkin's Lymphoma. ★
They are typically of a high grade
Often in the brain
Very aggressive
Responds poorly to therapy

Must know:

- Names of the complications
- Cells infected
- Types of organisms causing infection

Miscellaneous

- ★ **Lymphoid interstitial pneumonitis (LIP)**

A condition involving the lung that can be seen in
★ **AIDS in children**