

Human Immunodeficiency Virus (HIV)

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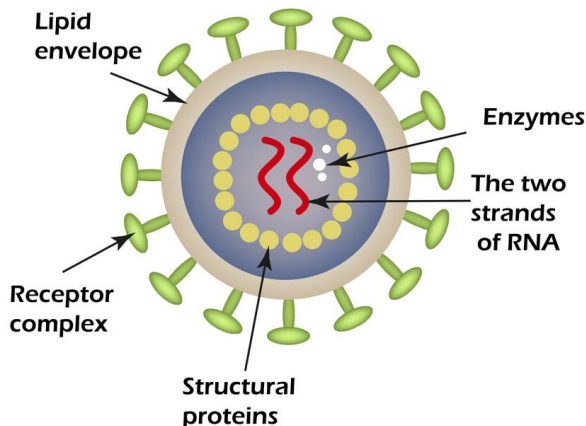
Introduction

- HIV is a viral infection that destroy helper T cells of the immune system
- Produce multi-organ diseases
- Characterized by long incubation periods and persistent infection

Morphology

- Retroviruses transcribe RNA to DNA
- Two viral strands of RNA found in core surrounded by protein outer coat.
- Enveloped virus
- These knob-like structures responsible for binding to target cell.

The structure of the HIV virus



Types of HIV

❖ Two species of HIV infect humans:

1. HIV-1

- More virulent, relatively easy to transmit
- Majority of HIV infections globally
- 3 types of HIV-1: (based on alterations in *env* gene)

2. HIV-2

- Less transmittable
- Largely confined to West Africa

Origins of HIV

HIV-1 likely descended
from SIV_{cpz}



chimpanzee

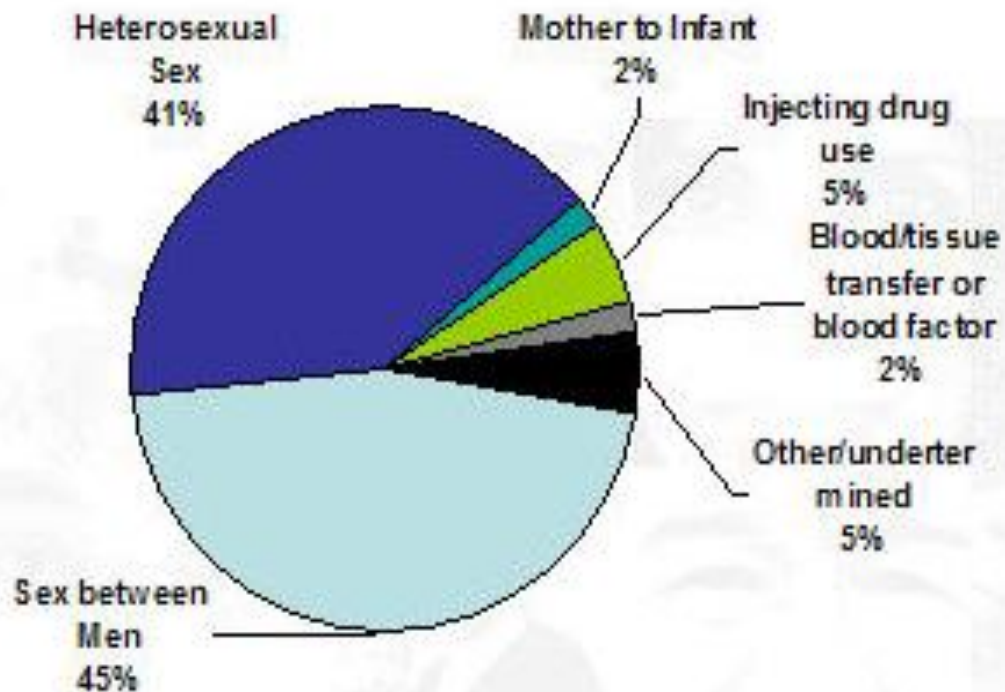
HIV-2 likely descended
from SIV_{sm}



Transmission

- Sharing of infected drug injection needles/syringes
- Accidental needle stick (healthcare professionals)
- Unprotected sex with infected individual
- Blood transfusions/Organ transplants
- Transmission from infected mother-to-fetus during pregnancy or delivery
- Transmission from breast milk of infected mother to her baby

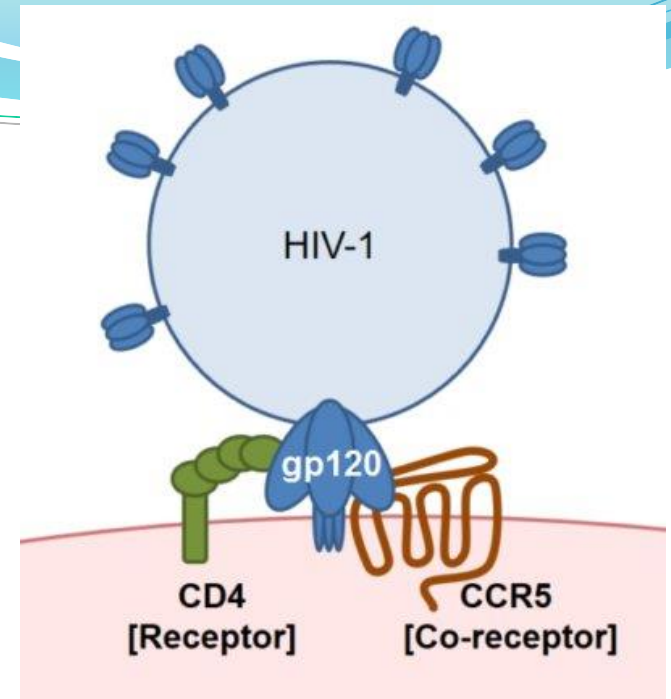
Route of Transmission of HIV Infection, infections before 2006



Pathogenesis and Virulence Factors

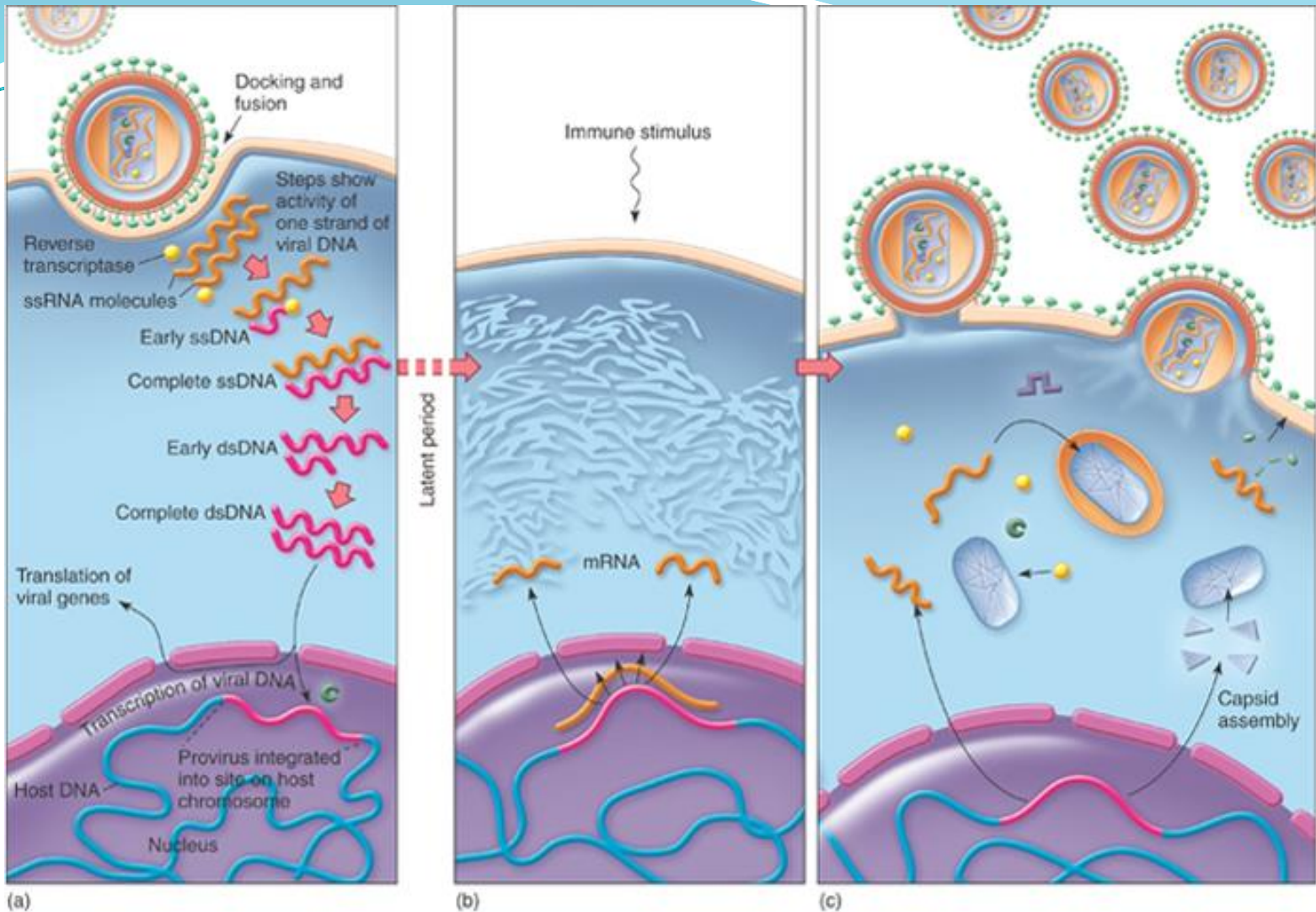
- HIV enters through mucous membrane or skin and travels to dendritic phagocytes beneath the epithelium, multiplies and is shed.
- HIV attaches to **CD4 molecules** and **co-receptor**; HIV fuses with cell membrane.

- HIV target **CD₄+ cells**
 - Th cell
 - Dendritic cells
 - Macrophages
- HIV use **gp120** to attached to CD₄ and co-receptors to get inside the cells
- Co-recptros
 - CXCR₄ on T cells
 - CCR₅ on T cell, macrophage, monocytes and dendritic cells



Pathogenesis and Virulence Factors

- **Reverse transcriptase** makes a DNA copy of RNA.
- Viral DNA is integrated into host chromosome



(a)

The virus is adsorbed and endocytosed, and the twin RNAs are uncoated. Reverse transcriptase catalyzes the synthesis of a single complementary strand of DNA (ssDNA). This single strand serves as a template for synthesis of a double strand (ds) of DNA. In latency, dsDNA is inserted into the host chromosome as a provirus.

(b)

After a latent period, various immune activators stimulate the infected cell, causing reactivation of the provirus genes and production of viral mRNA.

(c)

HIV mRNA is translated by the cell's synthetic machinery into virus components (capsid, reverse transcriptase, spikes), and the viruses are assembled. Budding of mature viruses lyses the infected cell.

Primary effects of HIV infection:

- extreme leukopenia – lymphocytes in particular
- formation of giant T cells allowing the virus to spread directly from cell to cell
- Infected macrophages release the virus in central nervous system, with toxic effect, inflammation.

Secondary effects of HIV:

- Destruction on CD4 lymphocytes allows for opportunistic infections and malignancies.

Clinical Manifestations

- Human Immunodeficiency Virus (HIV) has an incubation period of about 10 years and eventually leads to Acquired Immunodeficiency Syndrome (AIDS), resulting in the impairment of the immune system.
- This can lead to death from infections, secondary diseases from opportunistic bacteria and/or viruses that are usually harmless to people, or many different types of cancers.
- Common diseases associated with HIV infection:
 - Kaposi's sarcoma (KS)
 - Pneumocystis carinii pneumonia (PCP)
 - Mycobacterium avium complex (MAC)



- Early Symptoms:

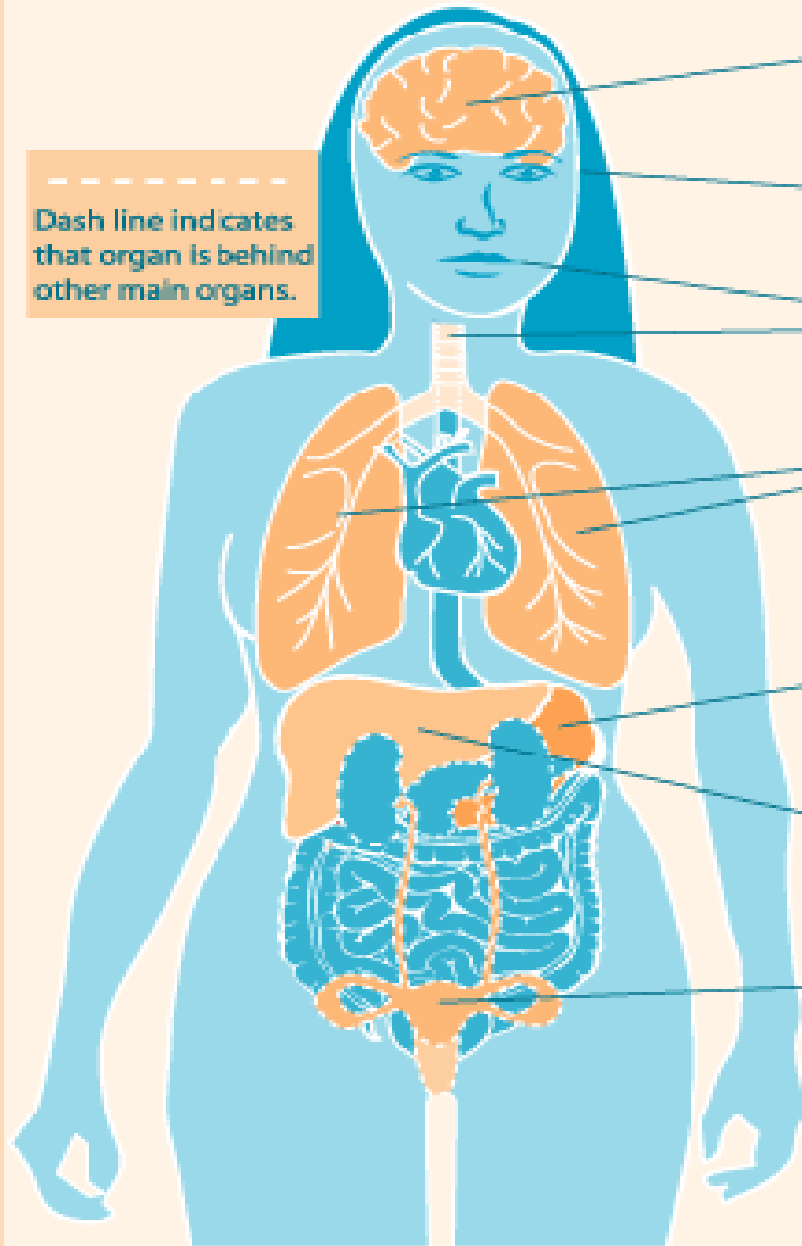
- Most don't exhibit symptoms when first infected
- However, may have flu-like symptoms (fever, headache, tired, enlarged lymph nodes) 1-2 months after exposure
- Very infectious during this period

- Later Symptoms:

- More severe symptoms may not appear until after 10yrs, however this varies with each individual
- Decline in number of CD4 + T cells
- The most advanced stage of AIDS is classified as having < 200 CD4+ T cells/cubic millimeter of blood (in healthy adults CD4+ T-cell counts = 1,000+)

Opportunistic Infections

Dash line indicates that organ is behind other main organs.



Brain

Toxo (toxoplasmosis)
Cryptococcal meningitis

Eyes

CMV (cytomegalovirus)

Mouth and Throat

Candidiasis (thrush)★

Lungs

PCP (pneumocystis carinii pneumonia)★
Histoplasmosis
TB (tuberculosis)

Stomach

MAC (mycobacterium avium complex)
Crypto (cryptosporidiosis)
CMV (cytomegalovirus)

Liver

HCV (hepatitis C virus)

Reproductive System

HPV (human papillomavirus) and Cervical cancer
Menstrual problems
Vaginal candidiasis (yeast infection)
PID (pelvic inflammatory disease)
UTI (urinary tract infections)
Genital ulcers

- The treatment for HIV is called **antiretroviral therapy** (ART). ART involves taking a combination of HIV medicines (called an HIV treatment regimen) every day.
- ART is recommended for everyone who has HIV. People with HIV should start taking HIV medicines **as soon as possible**. ART can't cure HIV, but HIV medicines help people with HIV live longer, healthier lives. ART also reduces the risk of HIV transmission.
- A main goal of HIV treatment is to reduce a person's viral load to an undetectable level.

Treatment

- Anti-viral agents
 - AZT (Zidovudine) azidothymidine
 - Viramune (Nevirapine)
 - Norvir (Ritonavir)

Vaccine

- Currently, no vaccines approved for use by the FDA