HIV and AIDS

UGS-3ed year-Faculty of Medicine

Introduction

HIV

Human **I**mmunodeficiency **V**irus

H	**Infects only Human beings**
I	**Immunodeficiency virus weakens the immune system and increases the risk of infection**
V	**Virus that attacks the body**

Introduction

AIDS

Acquired **I**mmune **D**eficiency **S**yndrome

A	**A**cquired, not inherited
I	Weakens the **I**mmune system
D	Creates a **D**eficiency of CD4+ cells in the immune system
S	**S**yndrome, or a group of illnesses taking place at the same time

HIV has three main mechanisms by which it evades the immune system:

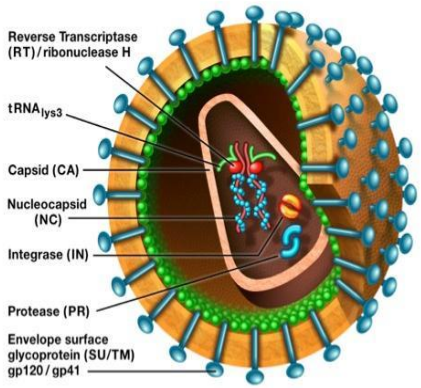
(1) Integration of viral DNA into host cell DNA

(2) High rate of mutation of the *env* gene

(3) Production of the Tat and Nef proteins that down-regulate class I MHC proteins

HIV general characteristics

- Enveloped virus of the lentivirus subfamily of ***retroviruses.***

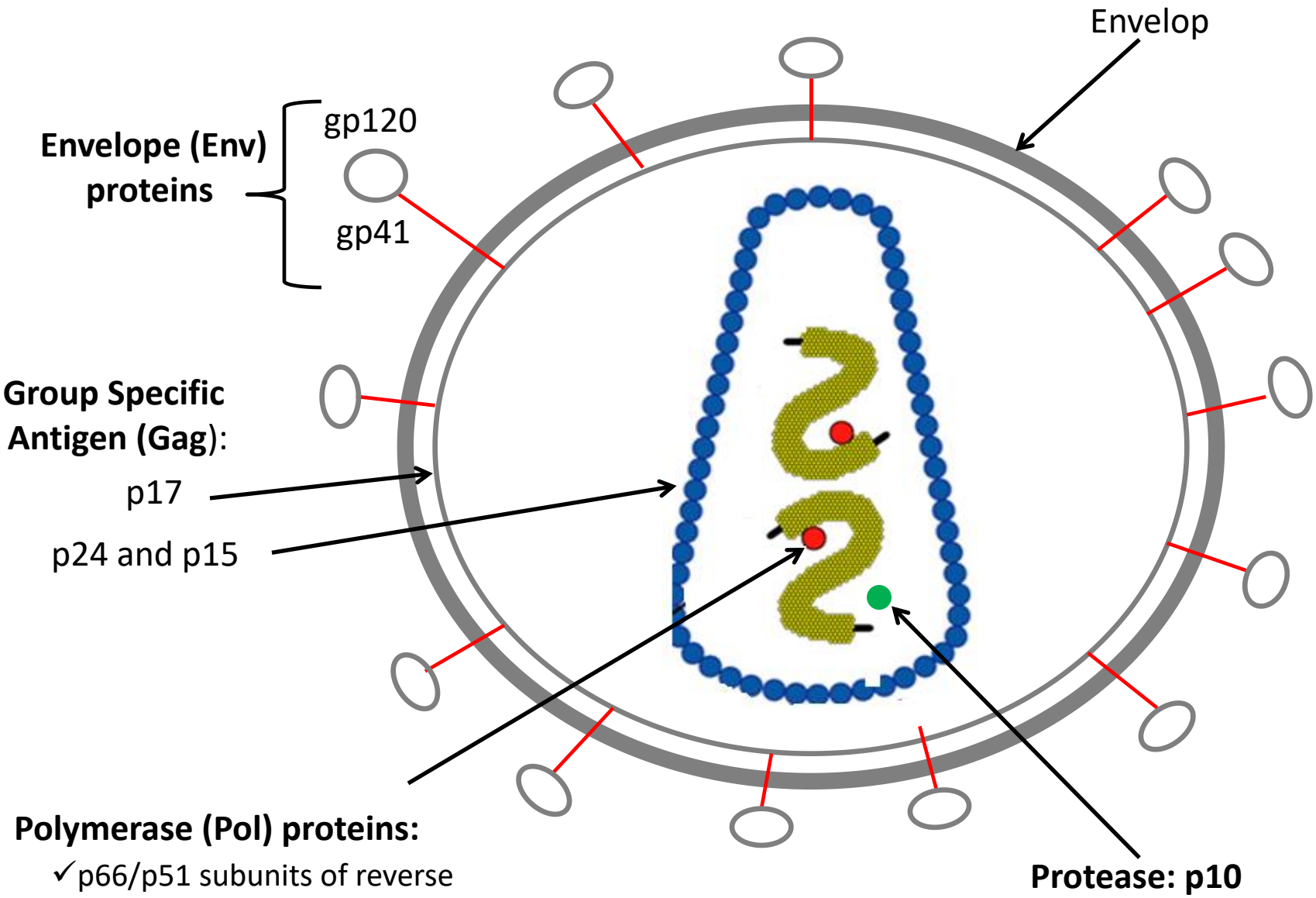


- Retroviruses transcribe RNA to DNA.

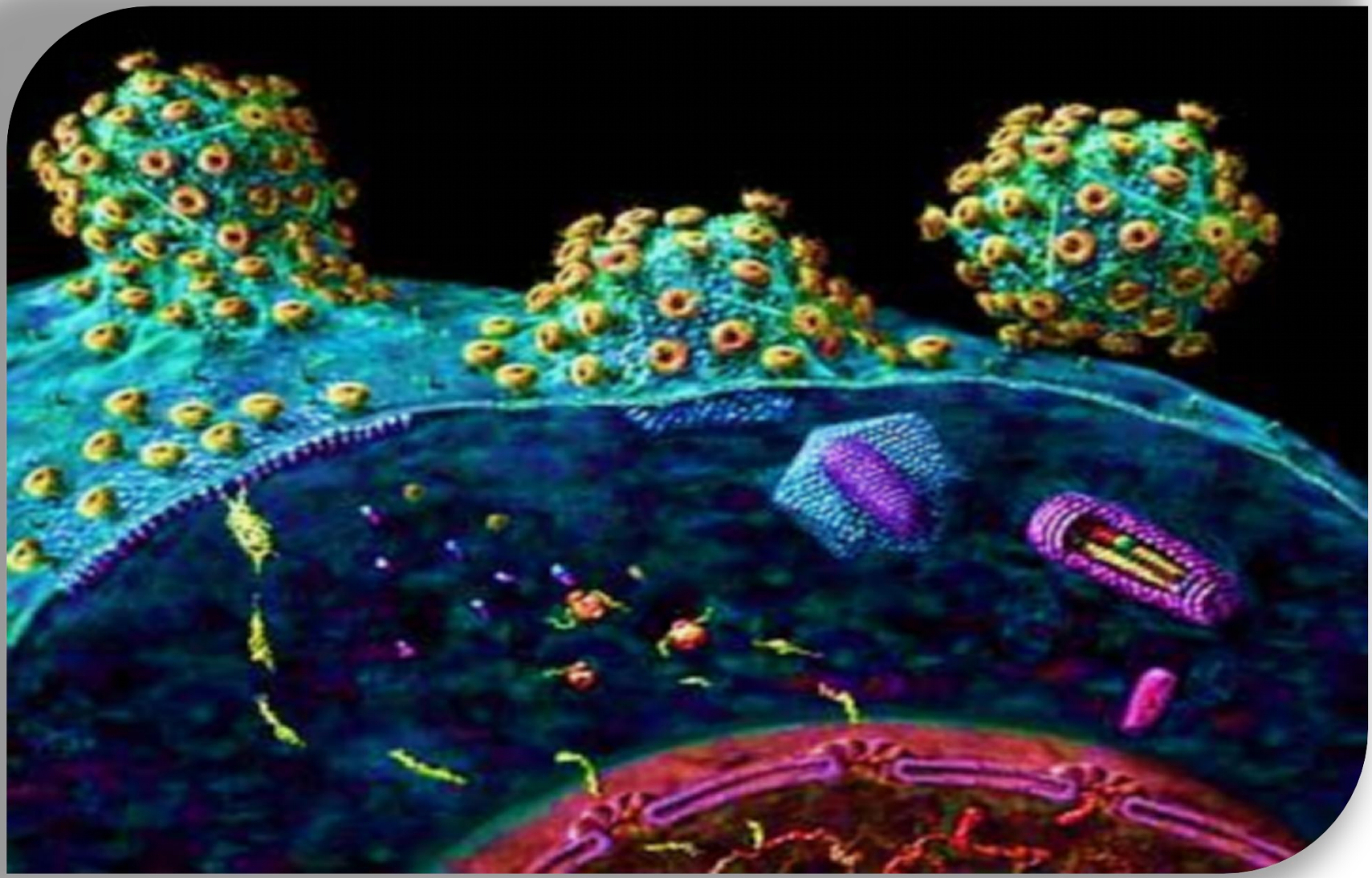
- Two viral strands of RNA found in core

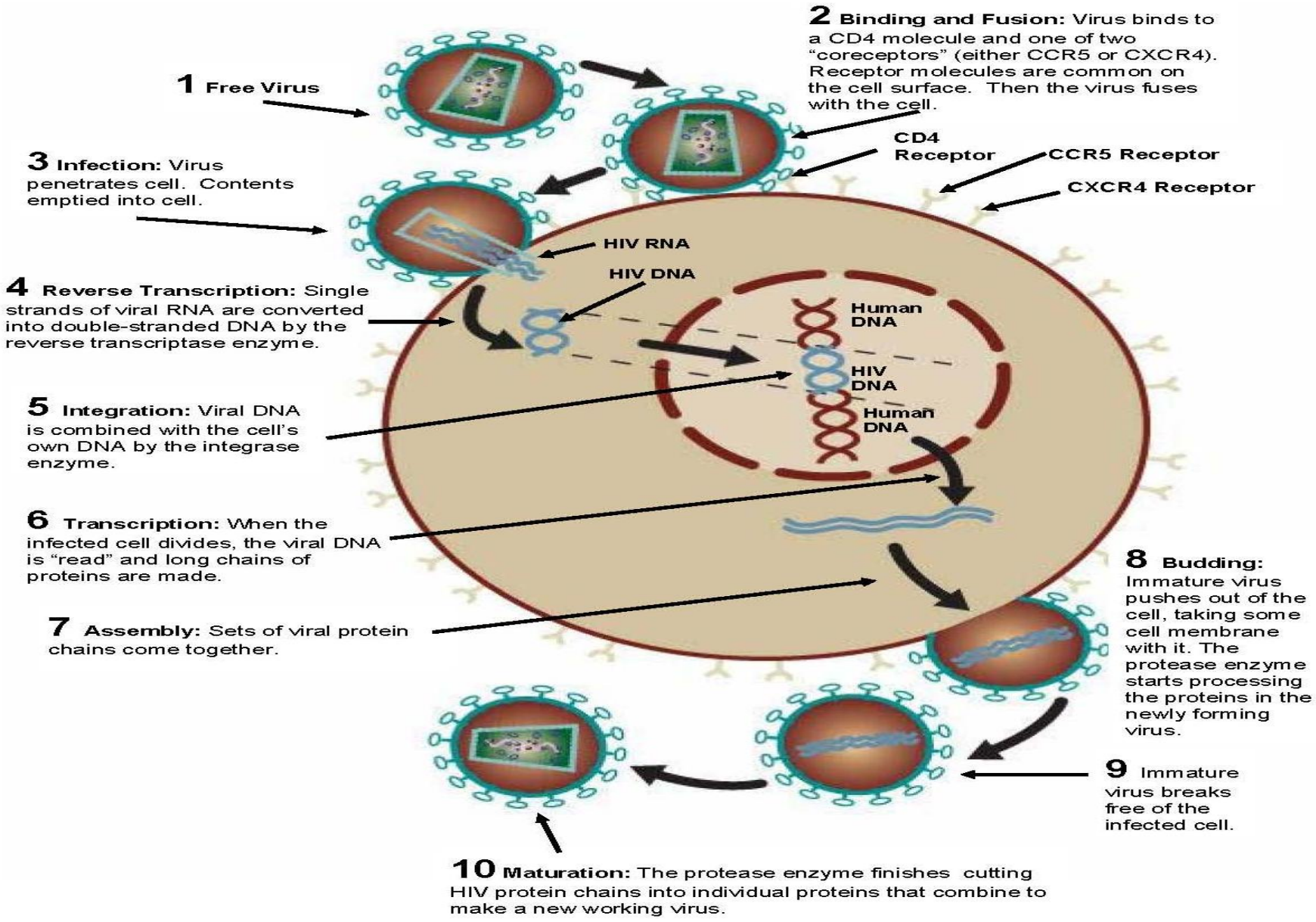
- Outer envelope contains a lipid matrix within which specific viral glycoproteins are imbedded and responsible for binding to target cell.

HIV structure



HIV Replication Cycle

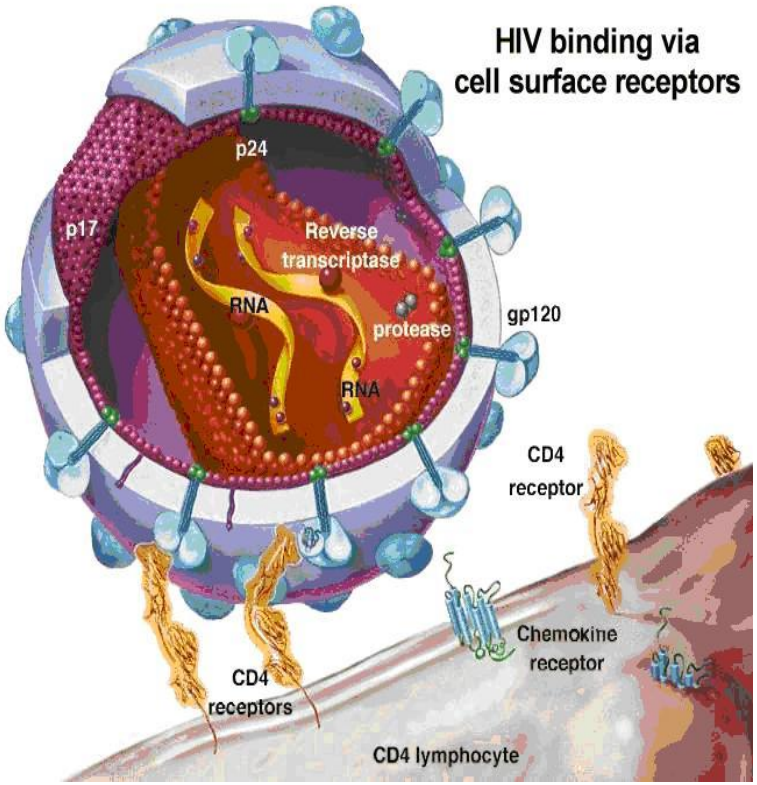



1 Free Virus
2 Binding and Fusion: Virus binds to a CD4 molecule and one of two "coreceptors" (either CCR5 or CXCR4). Receptor molecules are common on the cell surface. Then the virus fuses with the cell.
CD4 Receptor
CCR5 Receptor
CXCR4 Receptor
3 Infection: Virus penetrates cell. Contents emptied into cell.
HIV RNA
HIV DNA
4 Reverse Transcription: Single strands of viral RNA are converted into double-stranded DNA by the reverse transcriptase enzyme.
Human DNA
HIV DNA
Human DNA
5 Integration: Viral DNA is combined with the cell's own DNA by the integrase enzyme.
6 Transcription: When the infected cell divides, the viral DNA is "read" and long chains of proteins are made.
7 Assembly: Sets of viral protein chains come together.
8 Budding: Immature virus pushes out of the cell, taking some cell membrane with it. The protease enzyme starts processing the proteins in the newly forming virus.
9 Immature virus breaks free of the infected cell.
10 Maturation: The protease enzyme finishes cutting HIV protein chains into individual proteins that combine to make a new working virus.

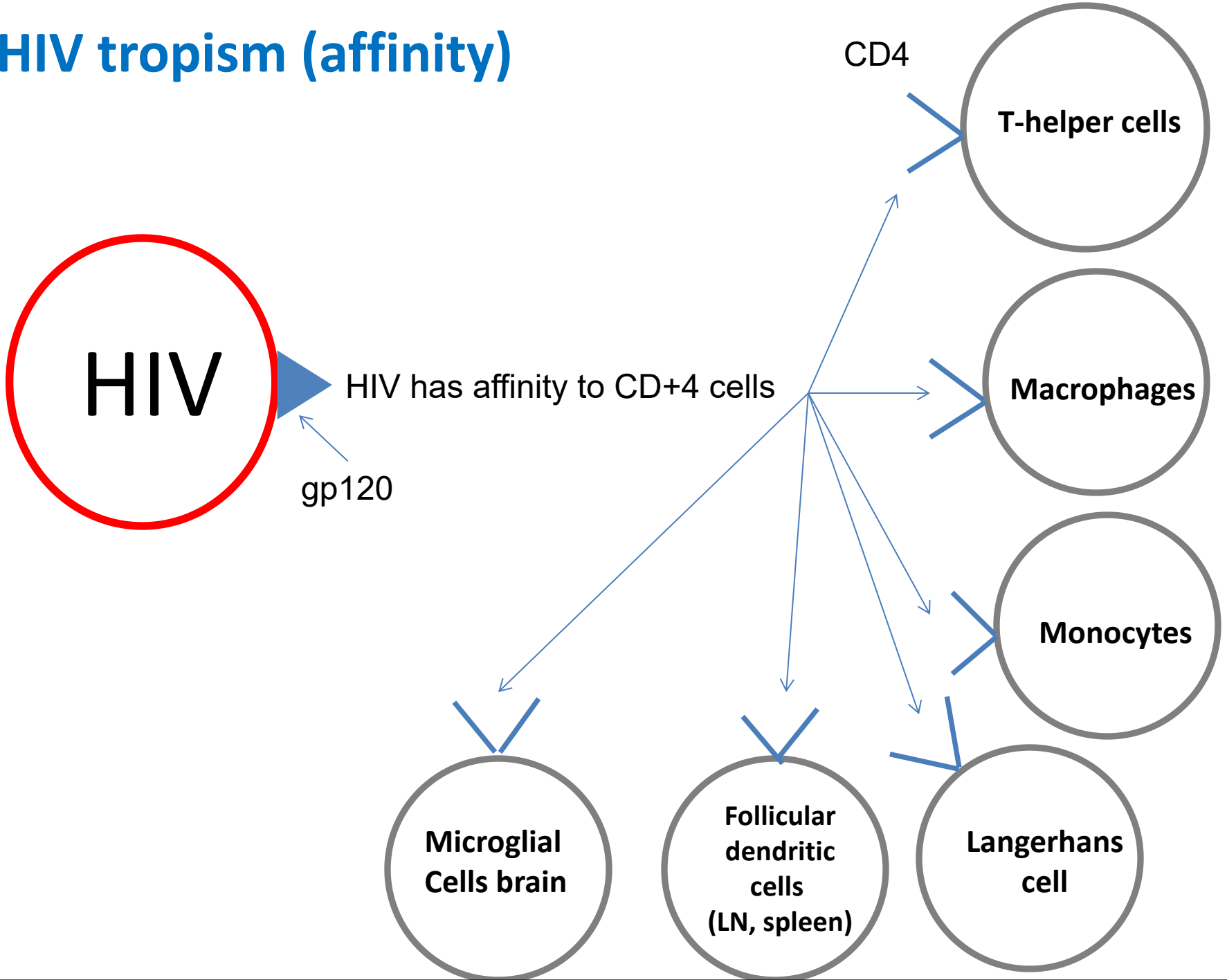
There are several important antigens of HIV:

(1) **gp120 and gp41** are the **type-specific envelope glycoproteins.**

- gp120 protrudes from the surface and interacts with the CD4 receptor .
- gp41 is embedded in the envelope and mediates the fusion of the viral envelope with the cell membrane at the time of infection.



HIV tropism (affinity)



Transmission of HIV

- Direct contact with **infected blood**
- **Sexual contact (85%)** : oral, anal, or vaginal
- Direct contact with **semen or vaginal and cervical secretions**
- **HIV-infected mothers to infants** during pregnancy, delivery, or breastfeeding

Transmission of HIV

HIV is not transmitted by

- Coughing, sneezing
- Touching, hugging
- Water, food
- Public baths
- Handshakes
- Work or school contact
- Using telephones
- Sharing cups, glasses, plates, or other utensils

Stages of HIV Disease

The HIV infection progresses through a clinical course which divides into

- Acute/Early infection
- Period of clinical latency
- Stage of AIDS

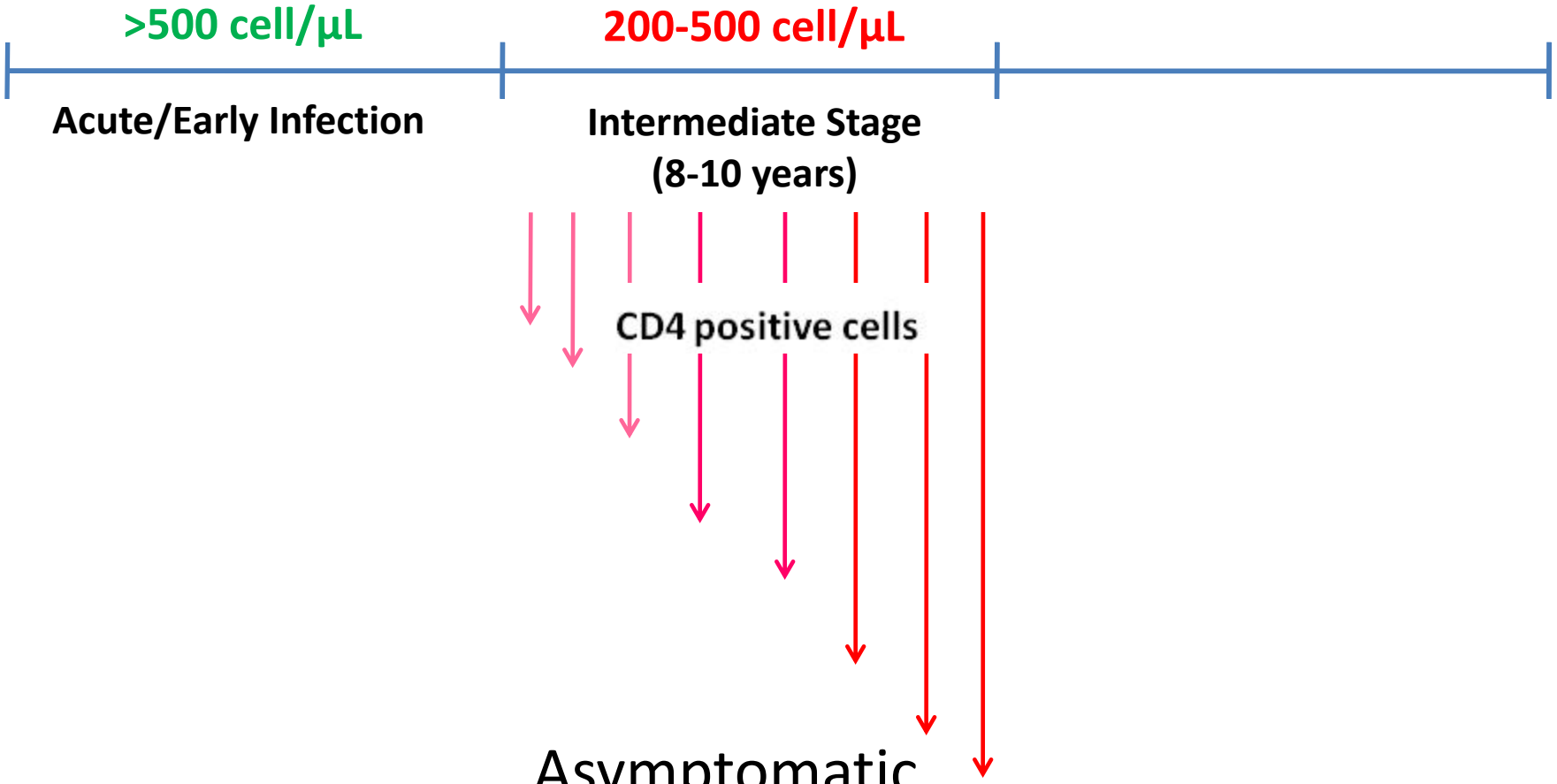
Stages of HIV Disease

Acute infection

Enters acute stage of infection

- 1-6 weeks: flu like illness
- lasts 1-3 weeks
- Infectious stage
- Extremely high levels of HIV in the blood (hallmark of this disease stage)

Stages of HIV Disease



The reference range is from 500 to 1300 cells/µL peripheral blood

Stages of HIV Disease

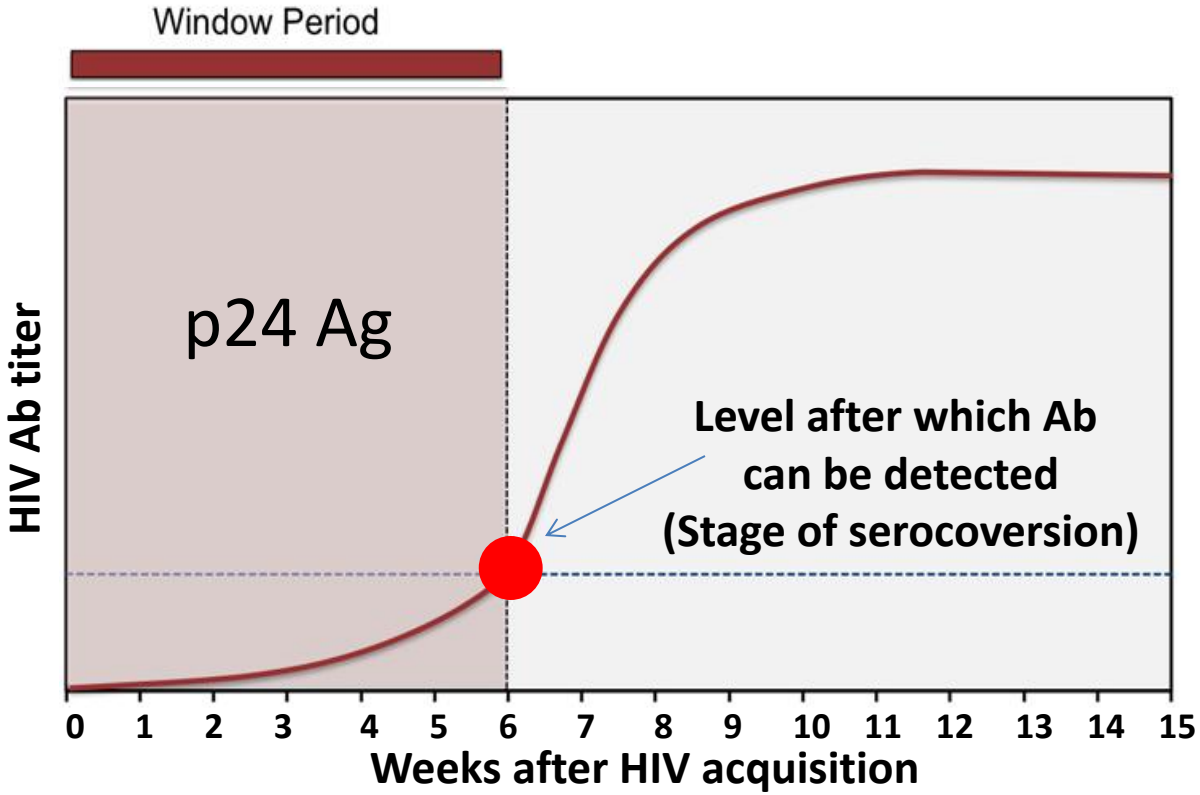
Acute/Early Infection:

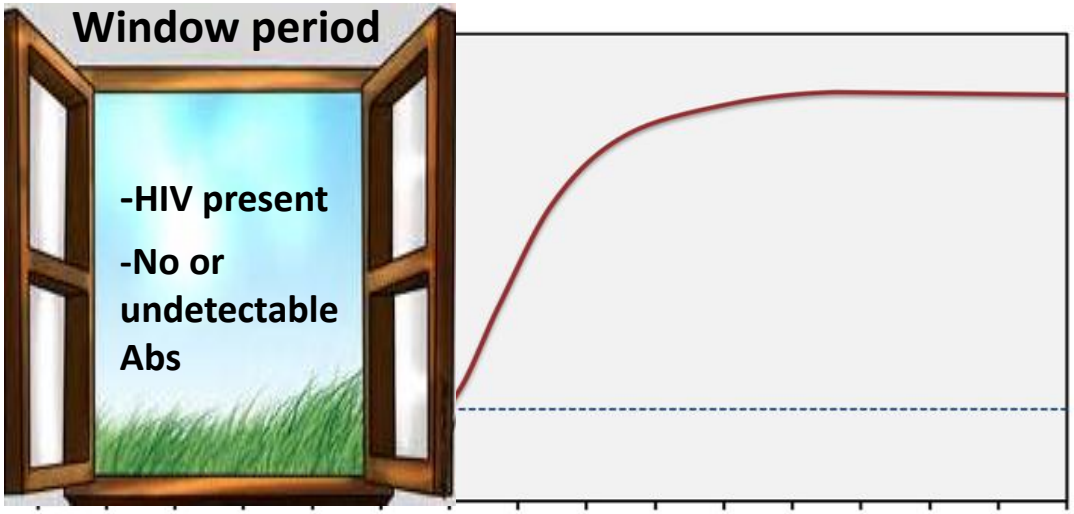
- Following HIV transmission, approximately 50% of individuals will develop a febrile, flu-like illness with some or all of the following conditions:

  - Swollen glands
  - Rash
  - Oral ulcers
  - Muscle aches
  - Sore throat
  - Headache
  - Diarrhea
  - Hepatospleenomegaly (small %)
  - Nausea or vomiting

- Onset of illness is generally 1-6 weeks following exposure and can last 1-3 weeks
- Within days, H**IV disseminates into** lymph nodes, central nervous system where it "hides out" and remains dormant.

Diagnosis of HIV infection during acute infection





Stages of HIV Disease

Acute/Early Infection (con't)

Diagnosis

- Testing for HIV antibody may be negative at this time.
- Diagnosis of HIV in general can made by obtaining a quantitative HIV RNA PCR (viral load test) or a pro viral cDNA test.
- A positive HIV antibody usually develops by 4-6 weeks following transmission and after 6 months to get accurate results on tests for **HIV** antibodies

Stages of HIV Disease

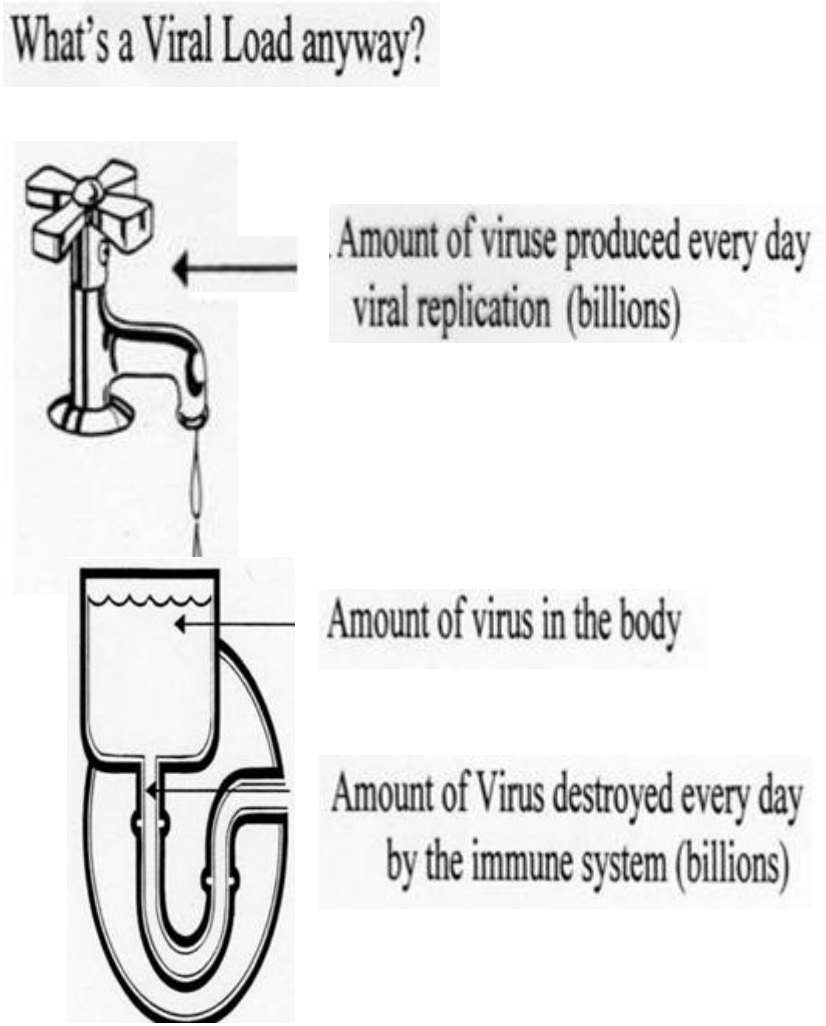
Intermediate Stage

- T cell destruction by HIV begins to weaken the immune system over time
- In general if untreated, there is an 8-10 year period during which an HIV+ individual undergoes a gradual **decline** in immune function (monitored by laboratory testing of CD4 count) and **increase** in HIV viral load (monitored by laboratory testing of viral load).
- Often no symptoms exhibited during the intermediate disease stage

Stages of HIV Disease

Viral Load

- Severity of illness is determined by amount of virus in the body (increasing viral load) and the degree of immune suppression (decreasing CD4+ counts)
- Higher the viral load, the sooner immune suppression occurs



Stages of HIV Disease

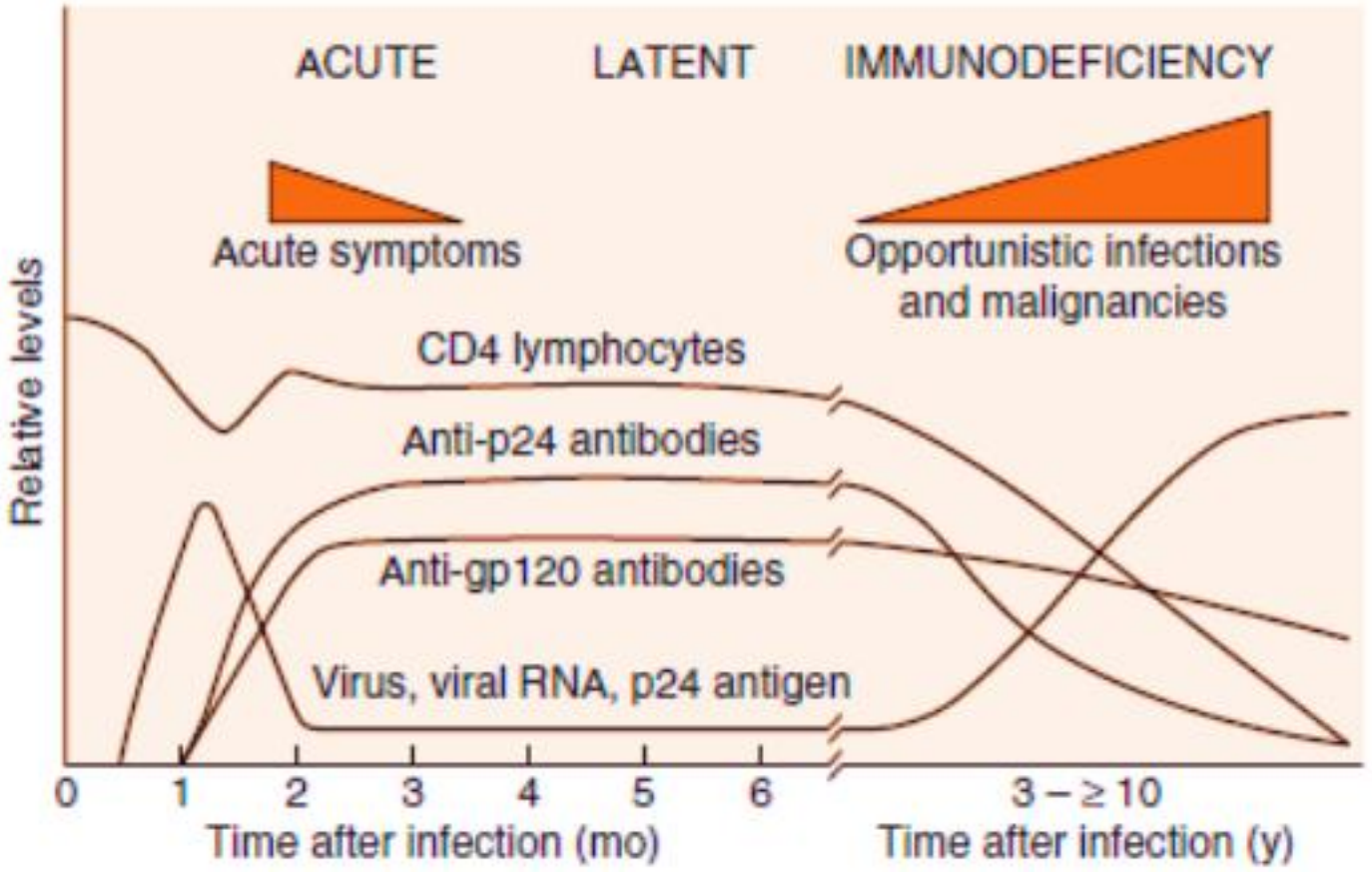
Stage of AIDS

- More than 50% of people do not know they are HIV-infected until they become symptomatic (an indicator of advanced disease).

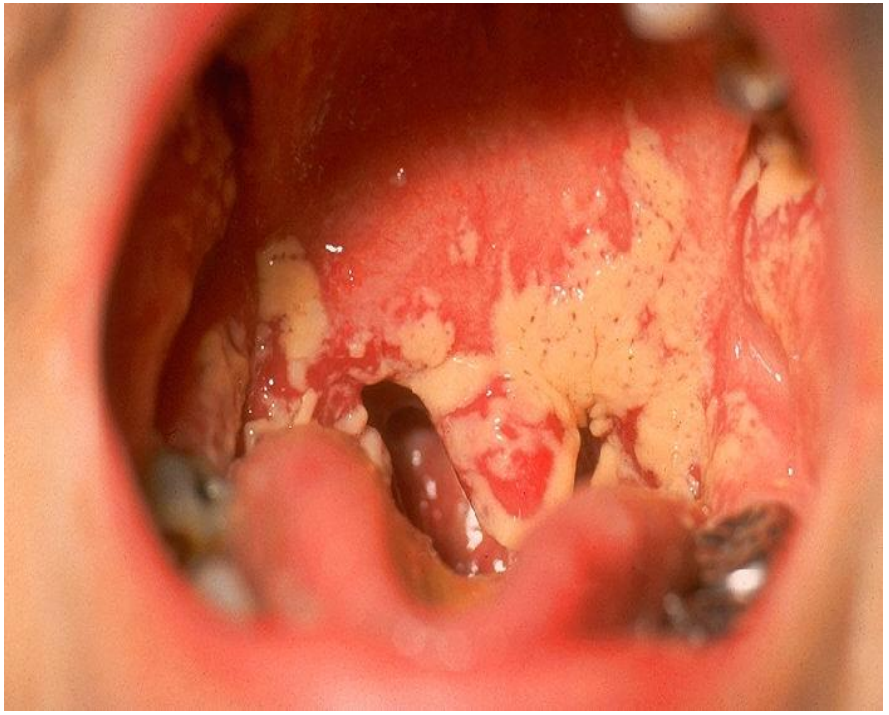
- Hallmarks of this stage of the disease include:
  - Opportunistic infections or malignancies
  - Rashes
  - Recurrent vaginal candidiasis
  - Herpes zoster
  - Thrush
  - Neuropathy
  - Diarrhea
  - Recurrent infections
  - Cancers
  - Anemia

>500 cell/µL	200-500 cell/µL	< 200 cell/µL
Acute/Early Infection	Intermediate Stage	Stage of AIDS

Time course of HIV infection



Oral Candidiasis (thrush)

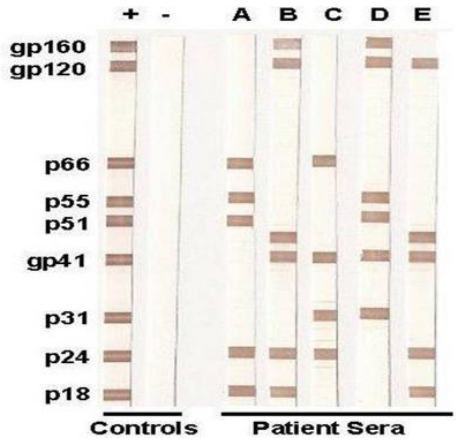


Oral Hairy Leukoplakia

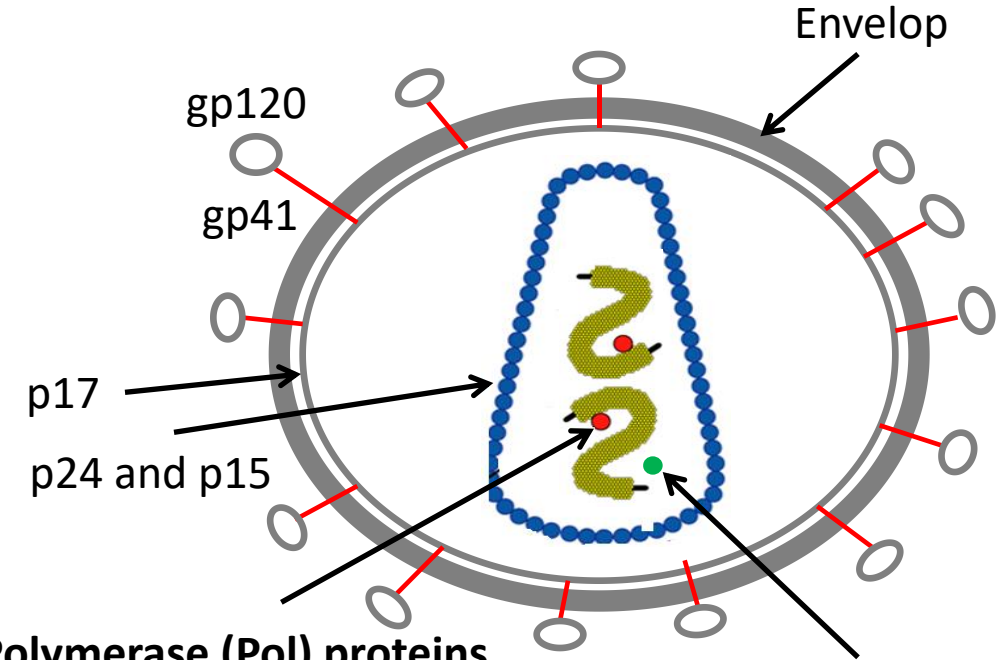
Due to the Epstein-Barr virus under immunosuppressed conditions

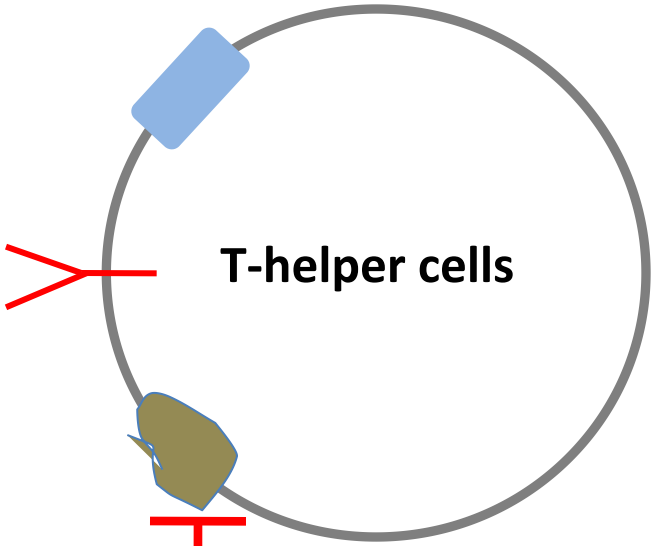
Laboratory Diagnosis:

- Detecting antibody with ELISA.
- Western blot as confirmatory test.
- Determine the “viral load” → PCR.
- OraQuick is a rapid screening immunoassay for HIV antibody
- p24 antigen test or viral culture.



Treatment





Polymerase (Pol) proteins

The nucleoside analogue reverse transcriptase inhibitors:

- Abacavir
- Tenofovir

Protease

Protease inhibitors:
Indinavir (IDV)
Ritonavir (RTV)

Coreceptor antagonists:
maraviroc (MVC)

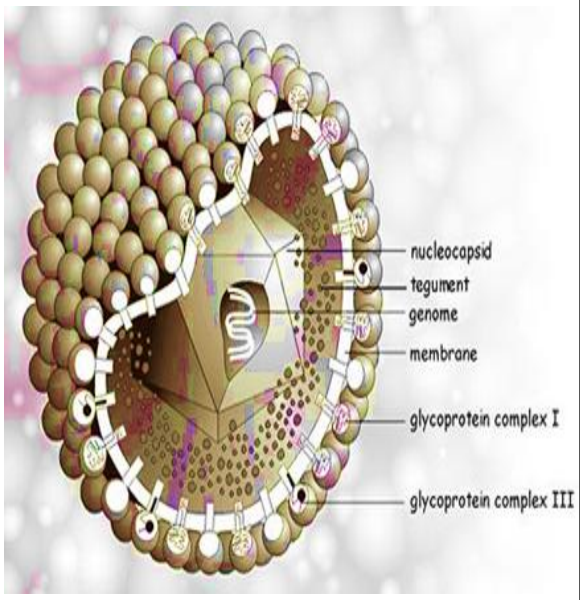
Integrase inhibitors:
raltegravir

HSV-2, HPV, Molluscum contagiosum virus & CMV

UGS Module

Herpes Simplex Virus-Type 2

- ***Diseases:*** **Herpes genitalis, aseptic meningitis, and neonatal infection.**
- ***Characteristics:*** **Enveloped, icosahedral nucleocapsid and linear dsDNA. One serotype.**
- ***Transmission:*** **Sexual contact** in adults and during **passage** through the **birth canal** in neonates. **Genital herpes** is caused by **HSV-1 and HSV2 (most common)**.



Pathogenesis:

- **Initial vesicular lesions** occur on **genitals**. The virus then travels up the axon → **latent in sensory** (**lumbar or sacral**) **ganglion** cells.

- **Recurrences** are less severe than **the primary infection**. **HSV-2 infections** in neonate can be life-threatening because of reduced CMI.

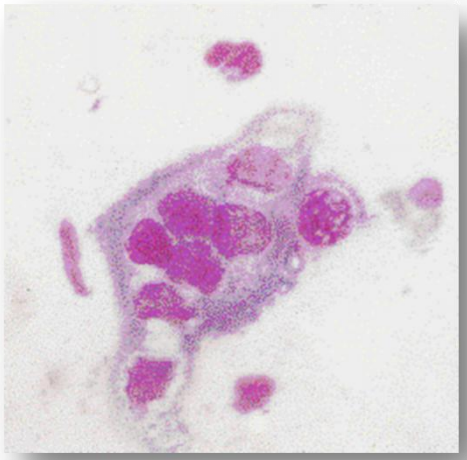
- Asymptomatic shedding of HSV-2 in the female genital tract →neonatal infections.

Genital herpes:

- **Before the blisters appear**, the person may feel the skin **tingling, burning, itching, or have pain** at the site where the blisters will appear

- **Small, painful blisters** filled with clear or straw-coloured fluid →**break** → shallow painful **ulcers** → **crust** → heal over 7 - 14 days or more.
  - **Enlarged and tender lymph nodes** in the groin
  - **Dysuria**
  - **Vaginal discharge.**
  - **Recurrence** → latency.

Laboratory Diagnosis



- **CPE in cell culture** → antibody neutralization or fluorescent antibody test.
- **Fluids** from blisters → microscope, PCR.

Treatment:

Acyclovir → primary and recurrent genital infections as well as neonatal infections.

Prevention

- Protection from exposure to vesicular lesions.
- Cesarean section
- No vaccine.

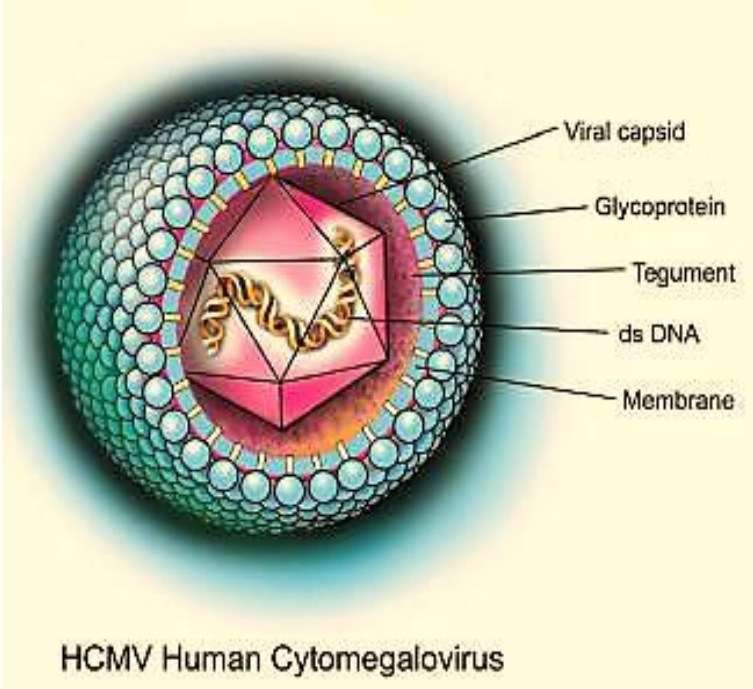
Cytomegalovirus

Diseases:

- Congenital abnormalities, Cytomegalic inclusion body disease in infants.
- Mononucleosis in transfusion recipients.
- Pneumonia and hepatitis in immuno- compromised patients.
- Retinitis and enteritis in AIDS patients.

Characteristics:

- **Enveloped** virus with **icosahedral** nucleocapsid and **linear dsDNA**.
- **No virion polymerase.**
- **One serotype.**

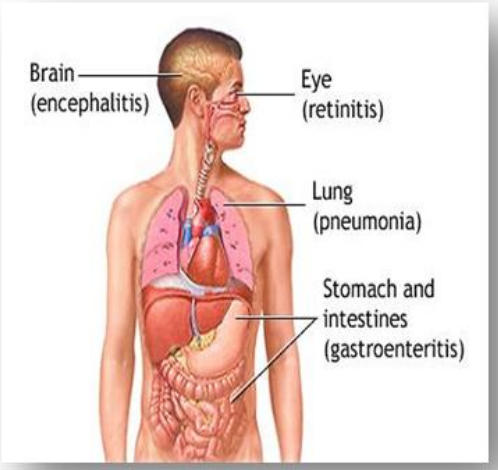


Transmission & Epidemiology:

- **Worldwide**, and more than **80% of adults have antibody** against this virus.
- Virus is found in **many human body fluids**, ex., **saliva, semen, cervical mucus etc.**
- It is transmitted via these fluids, across the placenta, or by organ transplantation.

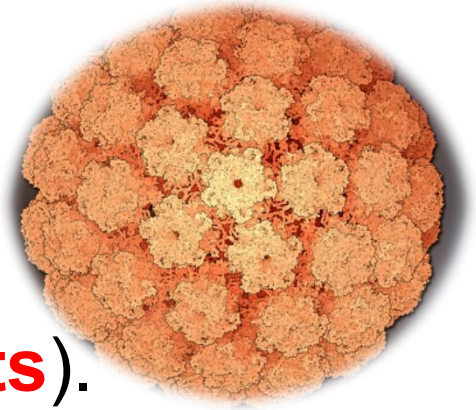
Pathogenesis :

- **The fetus: cytomegalic inclusion disease:** multinucleated giant cells with prominent intra-nuclear inclusions. the virus spreads to many organs (e.g., central nervous system and kidneys)→congenital abnormalities.



Human Papillomavirus

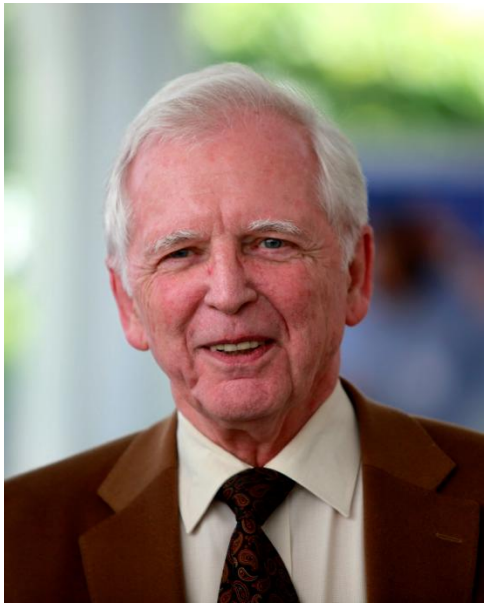
Diseases:

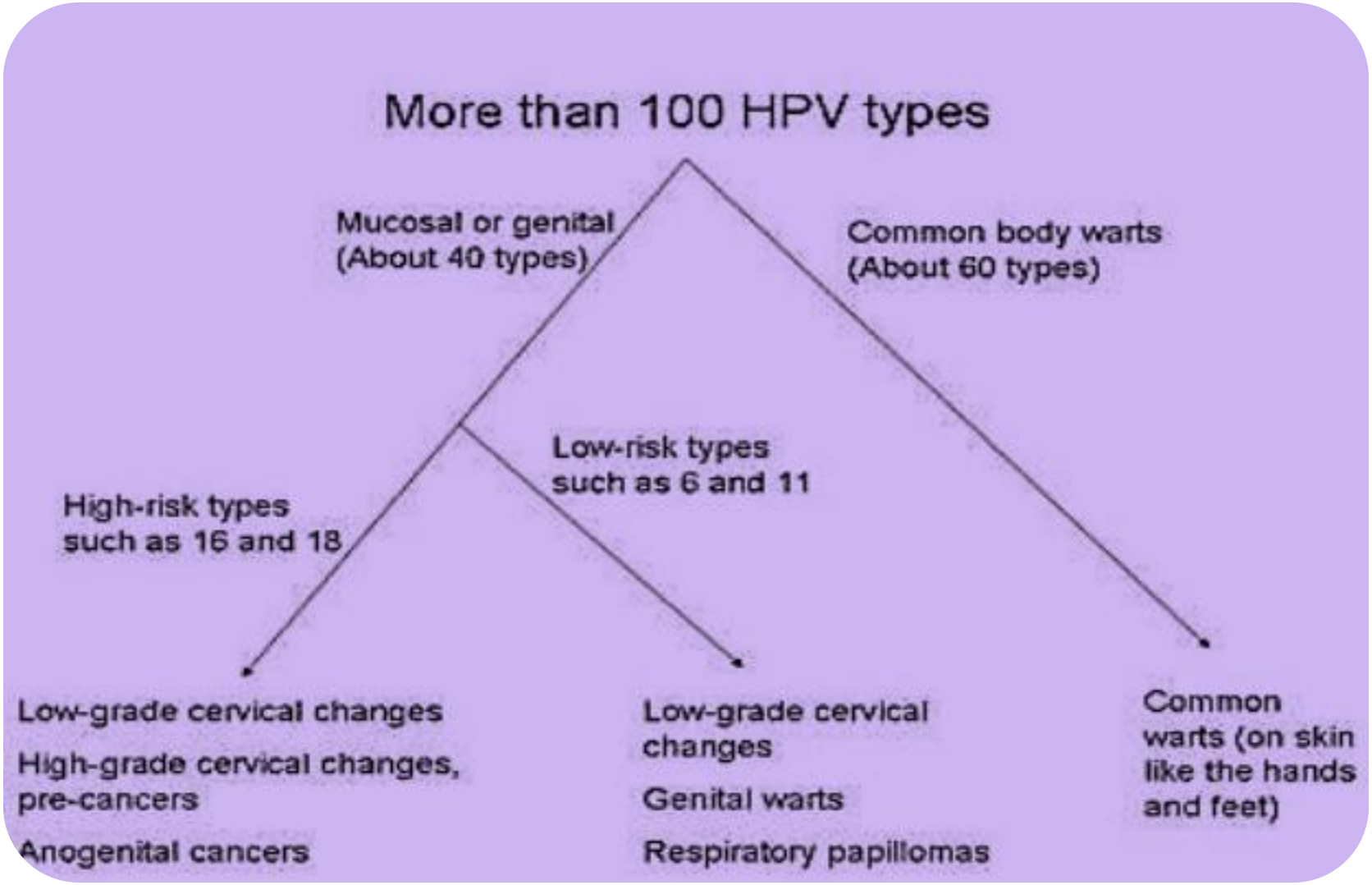


- Infects the **epidermis and mucous membranes** causing papillomas (**warts**).
- Several types of HPV, especially **types 16 and 18**, can lead to **cancers** of the cervix, vulva, vagina, and anus in women. In men, it can lead to cancers of the anus and penis.

History of discovering link between virus and cancer

- Dr. Harald zur Hausen of the German Cancer Research Centre, Heidelberg, Germany, was awarded 2008 Nobel Prize in Physiology or Medicine for his discovery of human papilloma viruses causing cervical cancer.

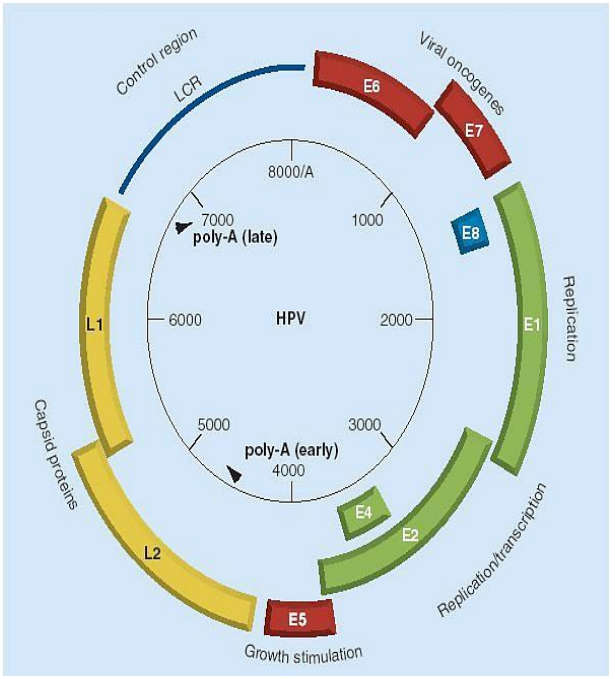



More than 100 HPV types
Mucosal or genital
(About 40 types)
Common body warts
(About 60 types)
Low-risk types
such as 6 and 11
High-risk types
such as 16 and 18
Low-grade cervical changes
High-grade cervical changes, pre-cancers
Anogenital cancers
Low-grade cervical changes
Genital warts
Respiratory papillomas
Common warts (on skin like the hands and feet)

Important Properties:

- **Non-enveloped** viruses with **ds circular DNA** and an **icosahedral** nucleocapsid.

- Two of the **early genes**, **E6** and **E7,** are implicated in carcinogenesis. They encode **proteins** that **inactivate** proteins encoded by **tumor suppressor genes**



Transmission:

- **Skin-to-skin contact** and by **genital contact.**
- **from infected mother to the neonate** during **childbirth**.

Pathogenesis & Immunity:

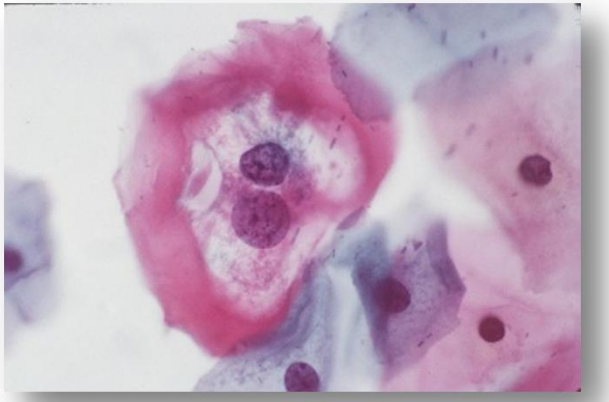
- Infect **squamous epithelial cells → cytoplasmic vacuole**. **Koilocytes → (hallmark)** of infection.
- Both **cell-mediated immunity and antibody → regression of warts**.
- **Immunosuppressed patients** have **more extensive** warts.

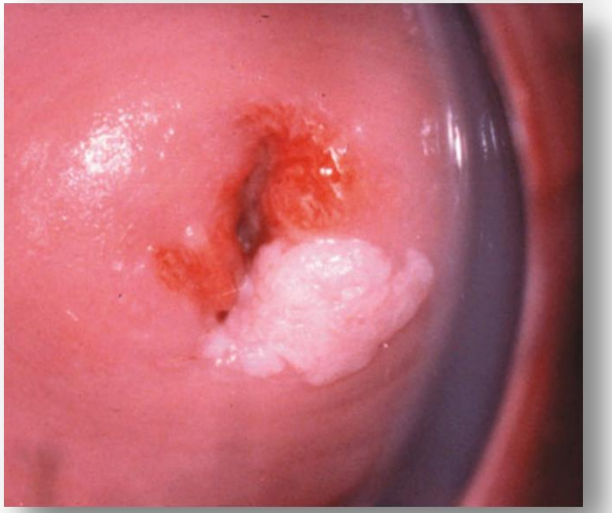
Clinical Findings:

- **Skin** and **plantar warts → HPV-1-4**
- Genital warts (**condylomata acuminata**), **respiratory tract papillomas→ HPV-6 and HPV-11**.
- **Carcinoma** of the **uterine cervix**, the **penis**, and the **anus**, as well as **premalignant lesions → HPV-16 and HPV-18.**
- **HPV-16 →oral cancers**.

Laboratory Diagnosis:

- **Cervical Papanicolaou (Pap) test:** **detect koilocytes** in the lesions.
- **DNA hybridization.**
- **PCR–based test :** 14 high-risk genotypes.
- **Occult premalignant lesions** of the cervix and penis can be revealed by applying **acetic acid to the tissue**.





Treatment:

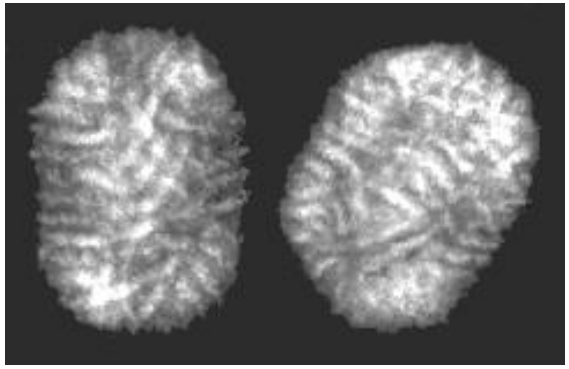
- **Genital warts** → alpha interferon → preventing recurrences.
- Liquid nitrogen → **skin lesions**, salicylic acid →**plantar lesions** or removed surgically .
- **Cidofovir** → **severe HPV infections.**

Prevention:

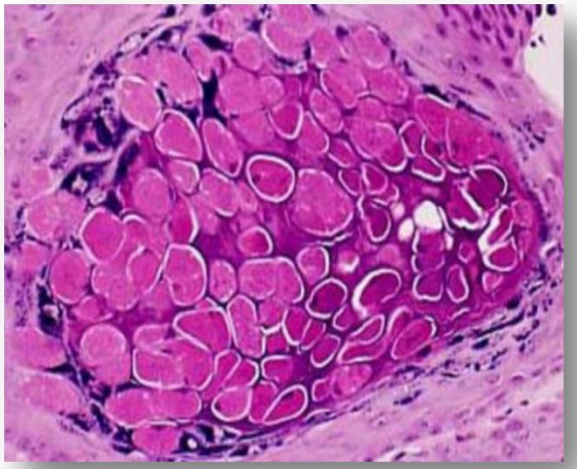
- **Condoms**.
- **Two vaccines against HPV: Gardasil,** a recombinant vaccine against four types of HPV (**6, 11, 16 and 18**), and **Cervarix** (**16 and 18**). **Both are delivered in three shots over six months.** HPV **immunizations have no effect** on existing papillomas.
- **Circumcision**

Molluscum Contagiosum Virus

- Member of the poxvirus family.
- MCV is transmitted by **close personal contact, including sexually.**
- Adults often have lesions in the genital area.



Diagnosis:



- Typically made **clinically**.
- **Skin biopsy** may be necessary in immunocompromised patients to exclude malignancy.
- Skin biopsy will reveal “Molluscum bodies” – eosinophilic inclusions in the epidermis.

Treatment:

- Curettage or liquid nitrogen or laser therapy.
- Topicals: Podophyllotoxin cream, salicylic acid, potassium hydroxide.
- Cidofovir: in extensive lesions. Antiretroviral therapy →resolve.
- There is no vaccine.

Thank you