

HIV and AIDS

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HIV and AIDS

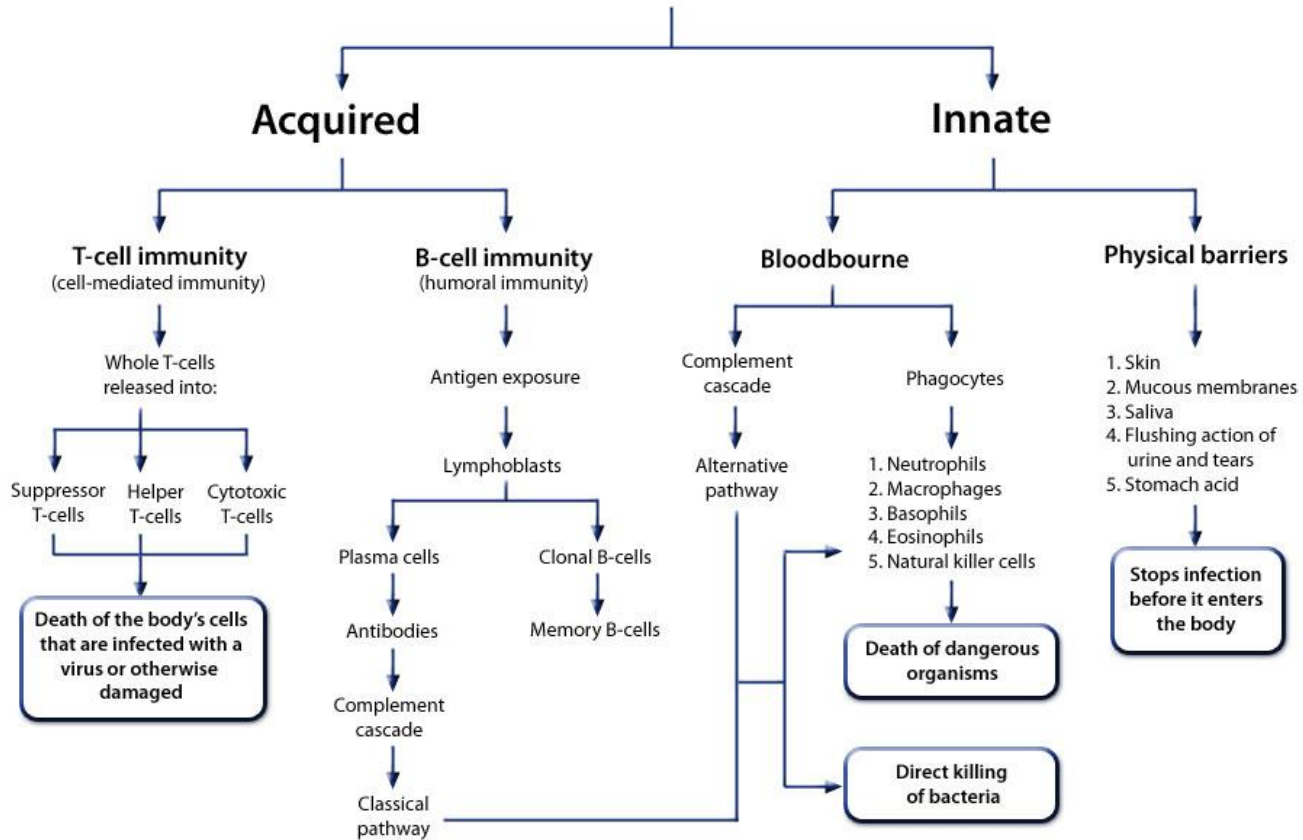
❖ Definition: HIV

**Infection with Human immunodeficiency Virus
which typically begins with :**

1] A brief acute retroviral syndrome

2] Transitions to a multi-year chronic illness that progressively depletes CD4 T- lymphocytes critical for maintenance of effective immune functionends up with life-threatening immunodeficiency

Immune system



HIV AND AIDS

- HIV:

It is an **RNA Lentivirus virus** belong to retrovirus family . It is called " **Retrovirus** " :

Retrovirus:

Information in the form of RNA is transcribed into DNA in the host cell .

- Transcription is the first step in gene expression. It involves copying a gene's DNA sequence to make an RNA molecule.
 - Transcription is performed by enzymes called RNA polymerase.
 - Translation: mRNA to Protein
-
- DNA to mRNA to Protein

HIV AND AIDS

There are two viruses

HIV1 and HIV2.

HIV1 : Predominate world wide

❖ HIV2 : closely resemble HIV-1 BUT is a much slower progression to AIDS. It Predominate in western africa.

It causes diseases by **disrupting the immune system function** as measured by CD4 cell depletion called :

AIDS

Acquired Immune Deficiency Syndrome.

- The hallmark of HIV Disease:
- Infection and viral replication within T-lymphocyte expressing the CD4 antigen resulting in :

Progressive depletion in CD4 cell counts .

This effect on CD4 (helper-inducer lymphocyte) will increase the risk of:

- 1) Opportunistic infections such as Pneumocystis Jiroveci
- 2) Neoplasm such as Lymphoma and Kaposi sarcoma

History

- **1st recognised in USA 1981**

CDC reported the occurrence of :

- 1) **Unexplained occurrence of pneumocystis pneumonia** in **5 healthy homosexual** in LA
- 2) **Kaposi sarcoma in 25 healthy homosexual** men in NY and LA.....later on ;
- 3) The disease became recognised in both male and female with (IUDs) as well as
- 4) Recipients of blood transfusion and haemophiles..
- **https://youtu.be/Ex8O_7fw-6U**

HISTORY

- 1983 :
- HIV was isolated from patient with lymphadenopathy
- 1984 :
- HIV was demonstrated to be the causative agent of AIDS
- 1985 :
- ELISA test was developed.

Epidemiology

❖ Asia

- 4.9 million people living with HIV
- National HIV prevalence is highest in southeast Asia 4.0 million
- Epidemic is expanding in Eastern Europe and central asia : 1.6 million

EPIDEMIOLOGY ..2016

36.7 million people globally were living with HIV in

- 1.8 million people became newly infected with HIV
- 3.5 million are children (less than 15)
- More than 2/3rd of all people with HIV live in **sub-saharan africa**
- 76.1 million people have become infected with HIV since the start of the epidemic.
- 35.0 million people have died from AIDS-related illnesses since the start of the epidemic.

- HIV is a fragile virus .It cannot live for very long outside the body
- HIV is primerly found in the blood,semen,or vaginal fluid of an infected person , so it is transmitted through :

HIV and AIDS

Transmission

❖ **Sexual** (heterosexual ,msm ,others)

Heterosexual is the most common mode of transmission worldwide.

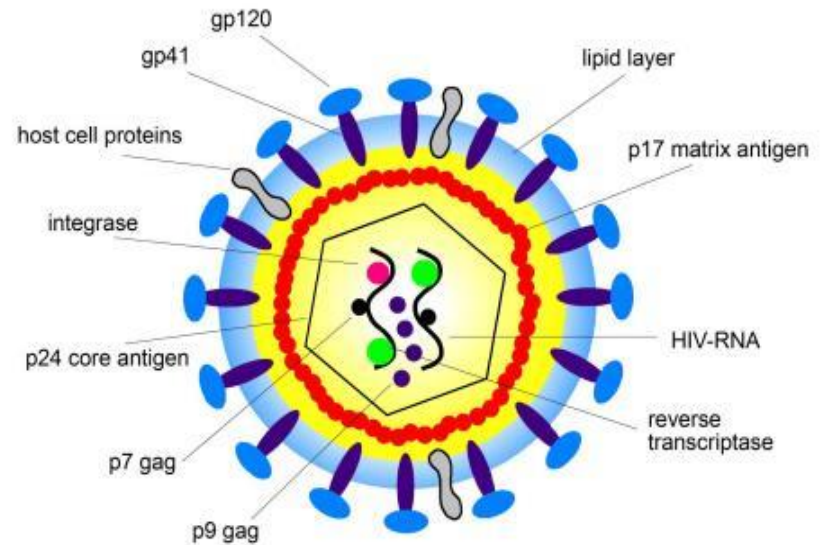
❖ **Vertical transmission** from pregnant woman to the newborn (MTCT) is the main mode of infection in children.

❖ **Blood and body fluid.**

❖ **IVDU.**

No evidence of spread by : casual contact .

Structure of the virus



❖ It is an **RNA virus**

❖ It is an icosahedral متعدد السطوح structure of :

1) **Lipid Envelope** (env) derived from infected cell, containing numerous external spikes formed by two major envelope proteins :

a) **The external gp 120**

b) **The trans membrane gp 41**

2) **Nucleocapsid (gag)** with P24 major core protein .

The core contains two single strands of RNA.

3) **Polymearse** (pol)

HIV life cycle & replication

- 1) Binding of Viral gp120 protein to CD4 receptor containing cells

T cell, Macrophages, and Microglial cells :

\

then ...

gp 120 and gp41 bind to the chemokines :

CCR5 and **CXCR4**

- 2) Fusion between cell membrane and the virion.

HIV life cycle & replication

3) Penetration

4) Upcoating

5) Reverse transcription

Formation of cDNA

6) Integration

7) Transcription of proviral DNA

A) formation of genomic RNA

b) formation of structural mRNA

HIV life cycle & replication

8) Translation of structural m RNA

- a) Formation of viral structural protien
- b) Packaging of genomic RNA of strucrural protien

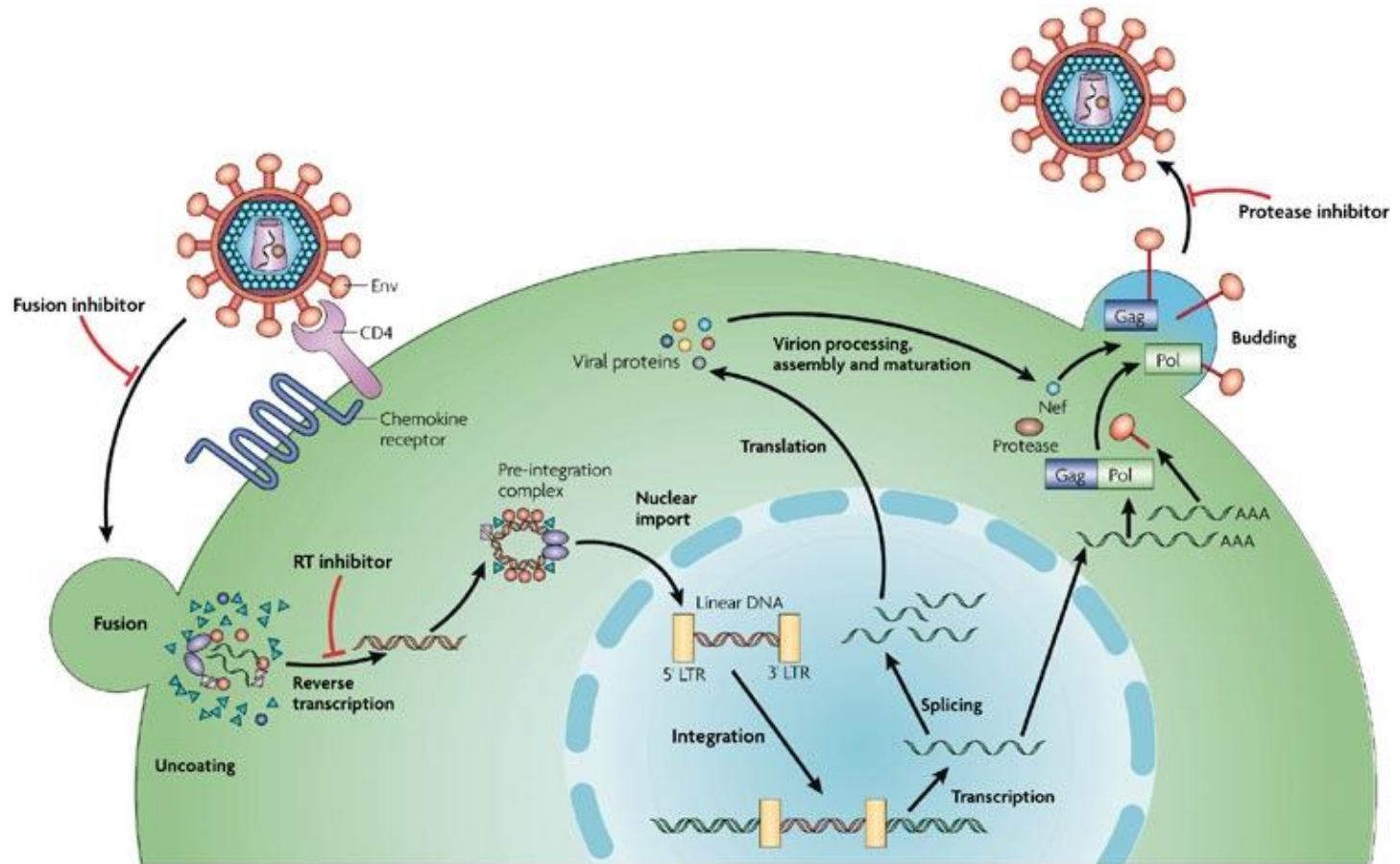
9) Final assembly

- a) insertion of viral specific glycoprotein into plasma membrane
- b) Budding
- c) Release of mature virions

10) Final maturation

BY cleavage of gag and pol by polymerase enzyme

HIV life cycle & replication



pathophysiology

- Early stage:
- Massive replication of the virus in the lymphatic tissues
.subsequently
- Permanent viral reservoirs containing proviral DNA are established in the latent T cell or macrophages.

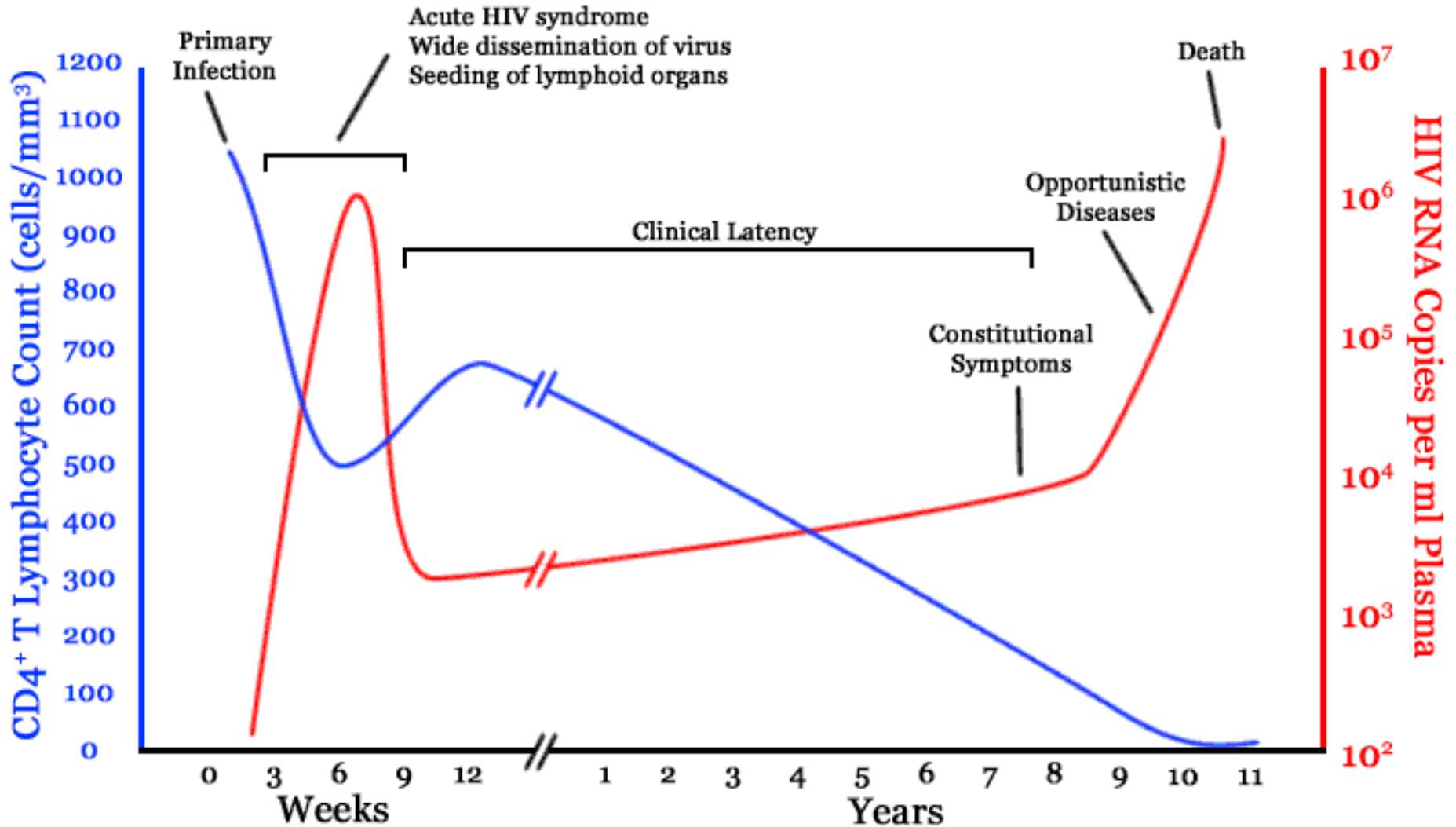
Acute infection

- Acute HIV infection: (exposure to symptoms: 2-4 wks)
- 50%–90% of persons develop symptoms within the first few weeks after they become infected with HIV It resemble infectious mononucleosis with :
- **Fever, malaise, lymphadenopathy, and skin rash..**
- **THEN.....**
- HIV RNA level falls and the symptoms resolve.
- CD4 cell count rebounds but remains below the baseline

Chronic HIV infection

- **Asymptomatic chronic phase:**
- Active viral replication is ongoing and progressive.
- Patient with high HIV RNA may progress to symptomatic disease than those with low HIV RNA level.
- Chronic immune activation lead to increase in various inflammatory markers.
- This increase the risk of Non-AIDS related comorbidities: CVD, Renal dysfunction and cancer

HIV Progression



HIV and AIDS

- **Immunological staging:**

CD4 positive T lymphocytes level is the main method of assessing the immune status of the HIV positive patient.

1. >500 cells/mm³ normal immunity.
2. 350-500 cells/mm³ mild deficiency.
3. 200-350 cells/mm³ moderate immune deficiency.
4. <200 cells/mm³ severe immune deficiency

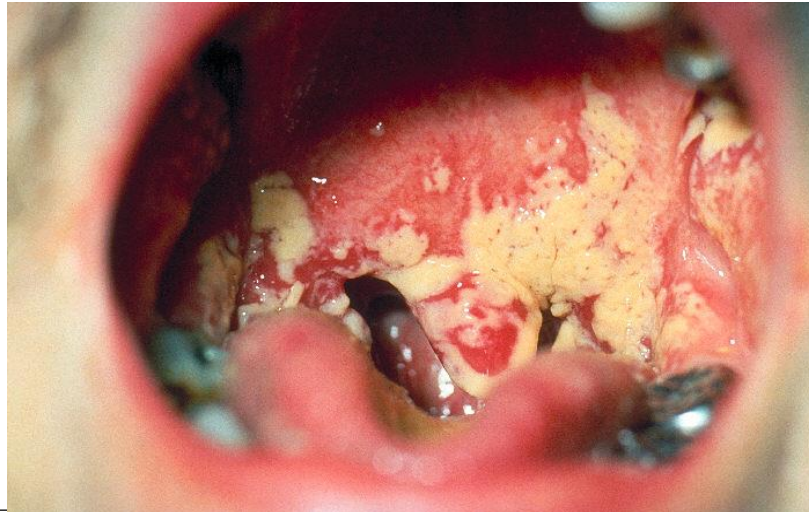
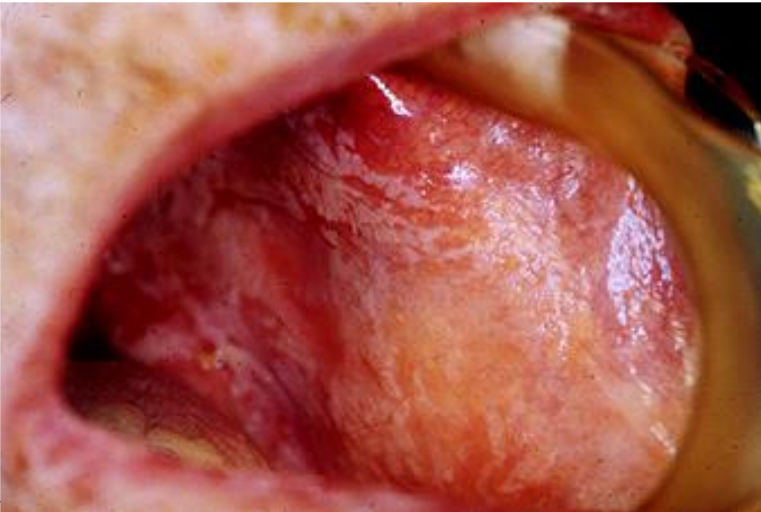
Clinical manifestation

Physical examination:

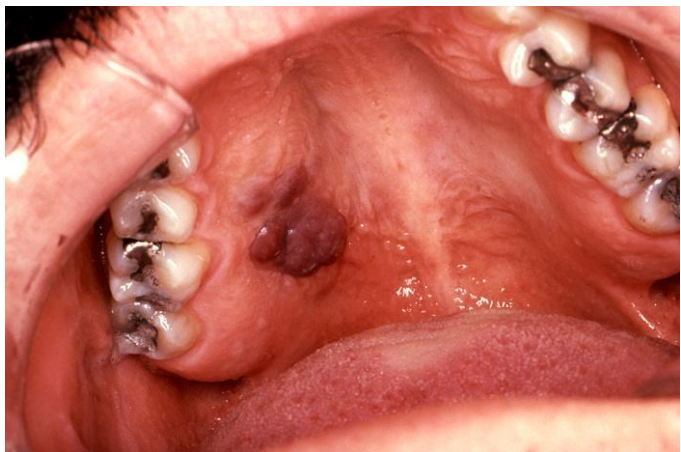
- **Skin:** condition associated with HIV
seborrheic dermatitis,
- **Oropharynx:**
 - 1) oral thrush
 - 2) hairy leukoplakia
 - 3) mucosal kaposi sarcoma
- **Lymph node:**
Generalized lymphadenopathy (TB , Lymphoma).
- **Eyes:**
Fundoscopy : CMV retinitis . (CD4 less than 50).
- **Genital exam:** ulcers, condylomatous lesions ..



ORAL TRUSH



KAPOSI SARCOMA



Condyloma acuminatum

Genital wart: 90% are caused by

HPV types 6 or 11

- Transmitted through sexual contact ..



A pointed papilloma typically found on the skin or mucous membranes of the anus and external genitalia.

Diagnosis by :visual inspection. confirmed by biopsy

HIV and AIDS

- ▶ Natural history :
- ▶ The **average time** from HIV to an AIDS- is **about 10 yrs**...then survival averages **1-2 yrs**.....**BUT**
- ▶ There is tremendous individual variability in these time intervals:
- ▶ Patients progress from acute HIV infection to death within 1-2 yrs.....and others
- ▶ Not manifesting HIV- related immunosuppression for 20 yrs

Stages of HIV infections

□ Stages of HIV infections:

A] **Viral Transmission :**

The mode of transmission does not affect the natural history of HIV disease .

B] **Acute HIV infection :**

Acute HIV occurs 1-4 wks after transmission .

Most patient manifest a symptomatic mononucleosis like-syndrom which is usually overlooked.

Stages of HIV infections

C] Seroconversion :

Development of a positive HIV antibody test within 4 wks and always by 6 months.

D] Asymptomatic HIV infection

It lasts variable amount of time

average 8-10 yrs and is accompanied by a gradual decline in CD4 counts..

COMPLICATION OF HIV/AIDS

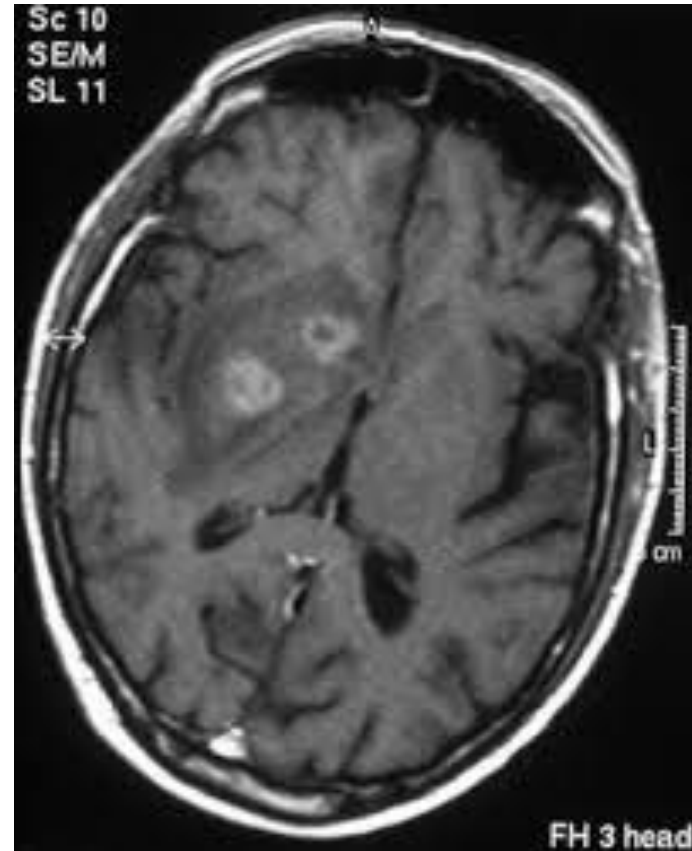
- **Candidiasis.** It causes inflammation and a thick, white coating on the mucous membranes of the mouth, tongue, esophagus or vagina

Tuberculosis: TB is the most common opportunistic infection and a leading cause of death .



COMPLICATION OF HIV/AIDS

- **Toxoplasmosis.** This potentially deadly infection is caused by *Toxoplasma gondii*, a parasite spread primarily by cats. It causes meningoencephalitis.
- DX: Serology and MRI.
- **Treatment:**
- **Combination of:**
- pyrimethamine plus sulfadiazine
- **Respond very well.**



Complication OF HIV/AIDS

- **Cancers common to HIV/AIDS**
- **A] Kaposi's sarcoma.** A tumor of the blood vessel walls, common in HIV-positive patients. Rare in none.

Kaposi's sarcoma usually appears as pink, red or purple lesions on the skin and mouth and can also affect the internal organs, including the digestive tract and lungs.

- **B] Lymphomas.** NHL.

HIV Screening and Diagnosis

- Indication and benefit:
- HIV-infected persons aware of their status.
- **Benefit:**
- Early HIV care and adherence to antiretroviral therapy (ART) prolong life
- Decrease the chances of HIV transmission ..
- 16% of the estimated 1.2 million persons with HIV infection in the United States are unaware of their infection .

Screening.

- DC recommends HIV screening for patients aged 13–64 years in all health-care settings.
- Persons should be notified that testing will be performed, but retain the option to decline or defer testing.

A separate consent form for HIV testing is not recommended.

HIV screening is recommended for all persons with STD.
syphilis, gonorrhea, and chlamydia.

Diagnosis:

- ❖ ELISA: is the screening test ,used to screen blood products and patients.
- ❖ Combo test : will detect HIV1 and HIV2 and P24 antigen.
Sensitivity of more than 99.5%

Home-testing kits only detect HIV antibodies and therefore will not. detect acute HIV infection.

Diagnosis:

- **Confirmation :**
- The INNO-LIA™ (HIV I/II) Score is a Line Immune Assay (LIA®), to confirm : antibodies against the human (HIV-1) and (HIV-2)
- Also differentiates between HIV-1 and HIV-2
- Sensitivity 100% ... specificity : 96%

Diagnosis

❖ **PCR: (polymerase chain reaction)** for quantitative RNA assay and used as :

- 1) Confirmatory test for undetermined cases.
- 2) To assess the viral load .
- 3) Babies born to HIV-positive mothers, because their blood contains their mother's HIV antibodies for several months.
- 4) Blood supplies

Not for routine testing:

- a) Decreased sensitivity at lower viral load
- b) Significant cost.

Counseling for Persons with HIV Infection

- Health-care providers should :
- assess the need for immediate medical care and psychosocial support.
- substance abuse counseling and treatment
- treatment for mental health disorders emotional distress,
- reproductive counseling,
- risk-reduction counseling, and case management
- determine whether any partners should be notified concerning possible exposure to HIV

Early management

- Reduces risk for HIV transmission,
- Decreases individual morbidity and mortality risk,
- Provides the opportunity to modify risk behaviors

- **Special Considerations:**
- All pregnant women should be tested for HIV infection during the first prenatal visit TO:
 - maintain the health of the woman,
 - enables receipt of interventions that can substantially reduce the risk for perinatal transmission of HIV.

Goals of Antiretroviral Therapy (ART)

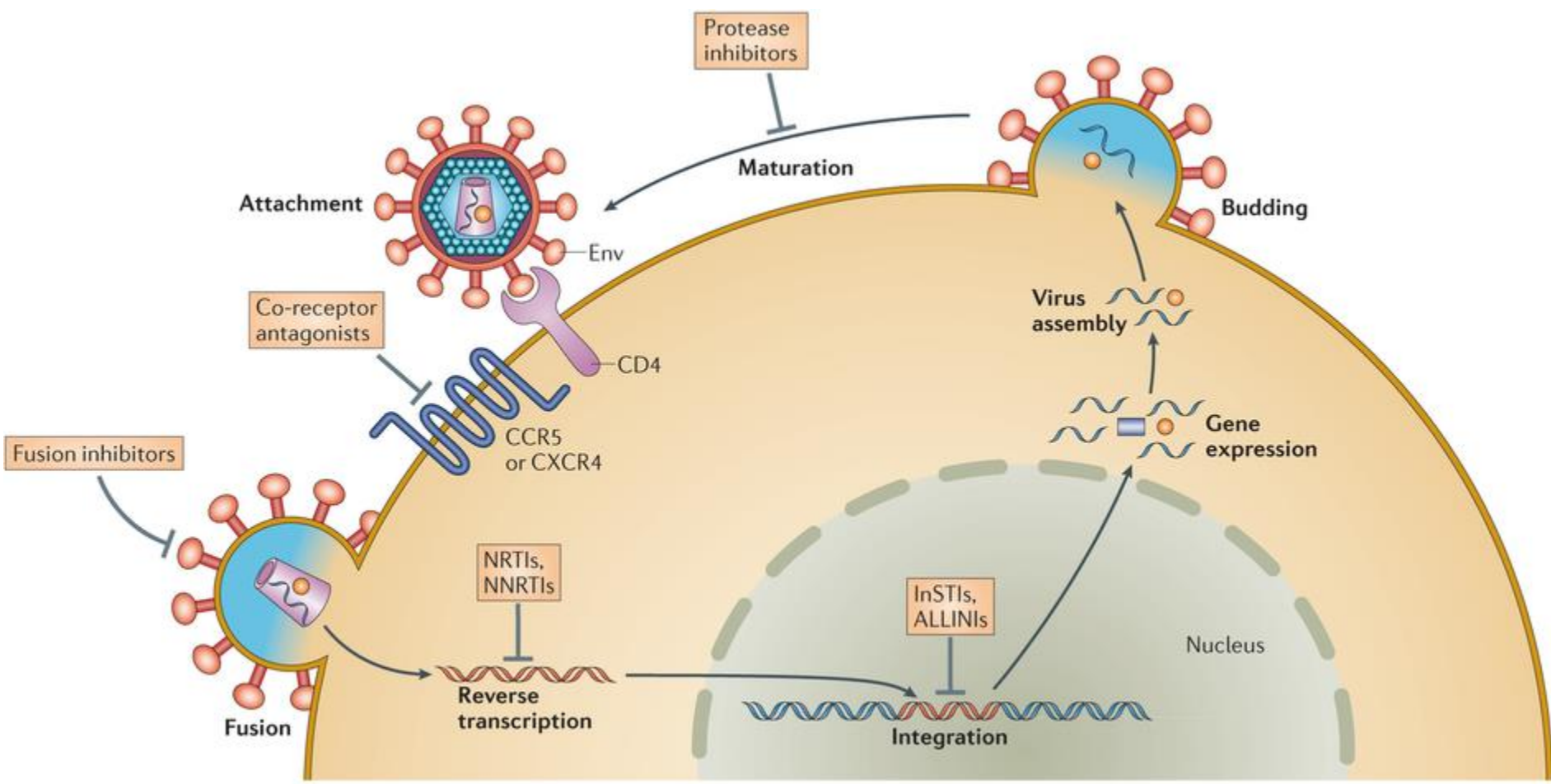
Eradication of HIV?

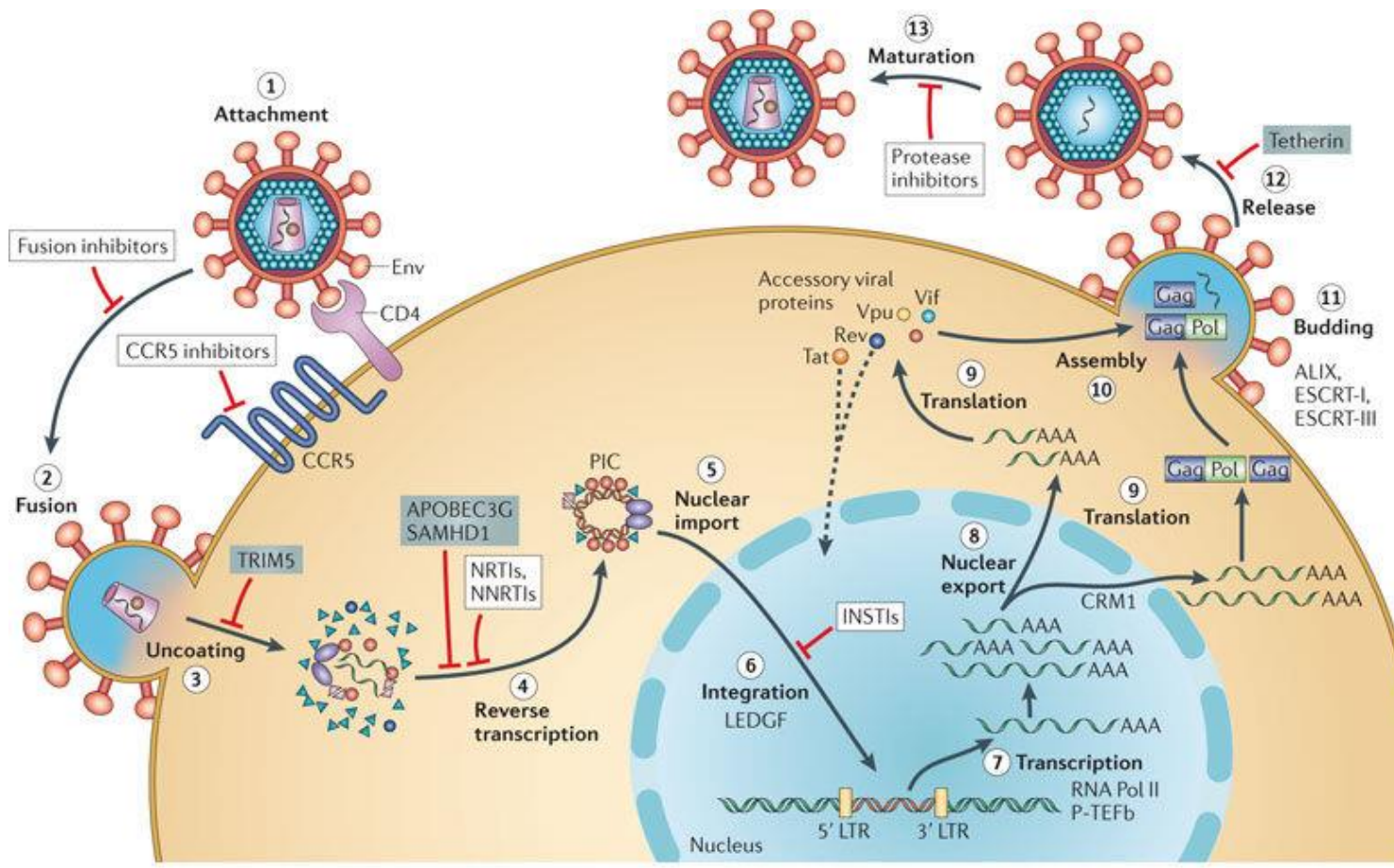
Not possible with currently available antiretroviral medications.

- **Improvement of quality of life**
- **Reduction of HIV-related morbidity and mortality**
- **Restoration and/or preservation of immunologic function**
- **Maximal and durable suppression of viral load**

Antiretroviral (ARV)

- Antiretroviral (ARV) regimen for a treatment-naive patient generally consists of:
- two nucleoside reverse transcriptase inhibitors (NRTIs) administered in combination with:
- a third active ARV drug from one of three drug classes:
- an integrase strand transfer inhibitor (INSTI),
- a non-nucleoside reverse transcriptase inhibitor (NNRTI), or a protease inhibitor (PI)

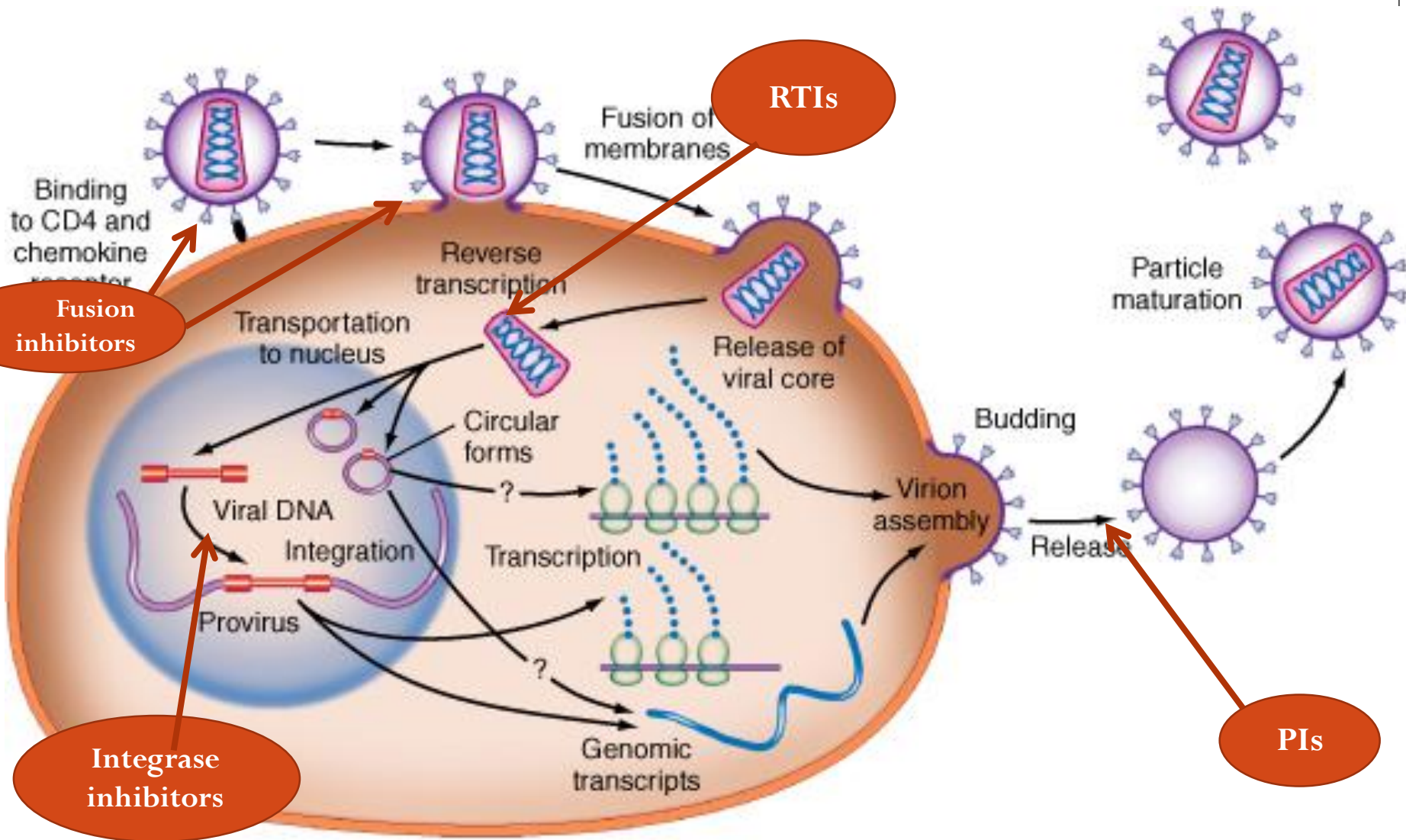




Treatment:

- Prophylaxis:
- If CD4 is below 200 :
- Patient at high risk to develop :
 - 1) *Pneumocystis jirovecii*: *Causing Pneumonia*
Prophylaxis: co-trimoxazole 1 ds OD
 - 2) *Mycobacterium Avium-Intracellulare*: CD4 count less than 50 cells/mm³
Prophylaxis: clarithromycin 500 mg orally twice a day.

HIV life cycle



Treatment

- Indication of initiation of antiretroviral drugs
 - ❖ A symptomatic disease with
 - 1) CD4 count less than 350
 - 2) Pregnancy
 - ❖ **Chronic infection**
 - a) Symptomatic disease .
 - ❖ **Post exposure prophylaxis.Prevention**

Prevention

- ▶ The only absolute way to Prevent sexual transmission of HIV infection is ::
اتباع قول الله تعالى

{ وَلَا تَقْرَبُوا الزَّيْنَى إِنَّهُ كَانَ فَاحِشَةً وَسَاءَ سَبِيلًا }

- ❖ **Abstinence from sexual relation completely**
- ▶ **Safer sexual contact :**
Use of condom...10% failure rate .
- ▶ **Circumcision** : results in **50% reduction of HIV acquisition**
- ▶ **Stop using IDUs**
- ▶ **Screen all blood** and blood products



Prevention

- The corner stone of an HIV prevention strategy is :
 - ❖ **Education**
 - ❖ **Counseling**
 - ❖ **Behaviour modification**
- ❖ If more than 25% of infected patient does not know . What to do ?
 - ..Routine testing between 13 and 64 ys..(CDC recommendations without written consent)

Pregnancy and HIV infection

Pregnant women infected with HIV infection carries risk to infect her baby by:

- 1) **In utero ...25-40%**
- 2) **Intrapartum ...60-75%**
- 3) **Breast feeding :**
 - 1) Established infection 14%
 - 2) Primary infection 29%

Current evidence suggests **most transmission** occur during the **intrapartum period** .

Overall risk for mother to child transmission (MTCT) is **16- 25 %**
(without antiretroviral Rx)

Perinatal hiv transmission

- Today the risk of perinatal transmission is :

Less than 2% with :

- ✓ **Effective antiretroviral therapy (ART)**
- ✓ **Elective caesarean section when appropriate**
- ✓ **Formula feeding**

Thank you

Any Q