HIV and AIDS

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HIV and AIDS

- Definition: HIV

Infection with Human immundefeciency Virus

which leads to :

Chronic and without treatment usually fatal infection characterized by :

A} **Progressive immundeficiency**

B } **Opportunistic infection**

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 Translation

DNA---------- RNA---------- PROTIEN

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 recogonised in USA 1981**

  CDC reported the occurance of :

- 1) Unexplained occurance of pneumocyctis pneumonia in 5 healthy homosexual in LA

- 2) Kaposi saarcoma in 25 healthy homosexual men in NY and LA…..later on ;

- 3) The disease became recogonised in both male and female with (IUDs) as well as
- 4) Recipients of blood transfusion and haemophilics

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

Summary of the global HIV epidemic (2018)

	People living with HIV in 2018	People newly infected with HIV in 2018	HIV-related deaths 2018
Total	37.9 million [32.7 million – 44.0 million]	1.7 million [1.4 million – 2.3 million]	770 000 [570 000 – 1.1 million]
Adults	36.2 million [31.3 million – 42.0 million]	1.6 million [1.2 million – 2.1 million]	670 000 [500 000 – 920 000]
Women	18.8 million [16.4 million – 21.7 million]	–	–
Men	17.4 million [14.8 million – 20.5 million]	–	–
Children (<15 years)	1.7 million [1.3 million – 2.2 million]	160 000 [110 000 – 260 000]	100 000 [64 000 – 160 000]

Source: UNAIDS/WHO estimates

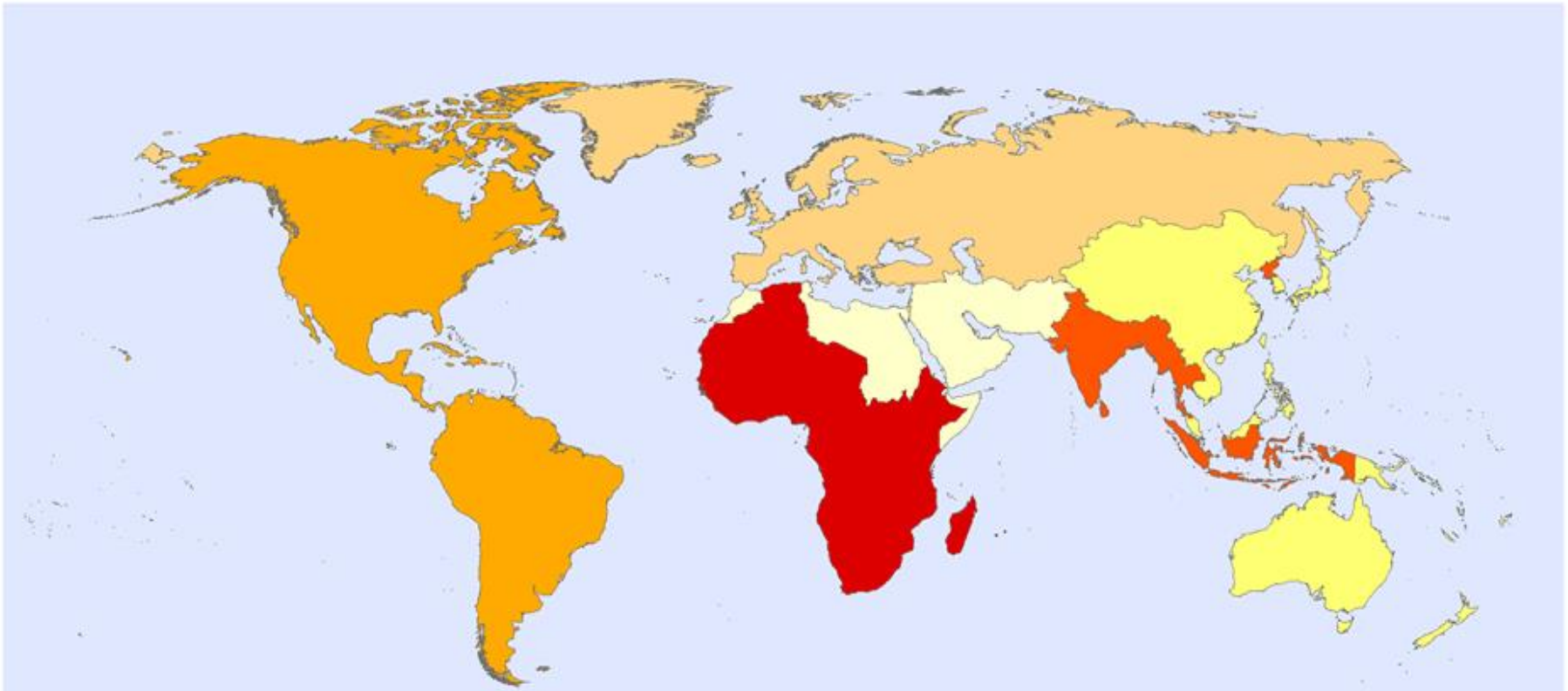
Global situation

- 75 million people have been infected with the HIV virus.
- 35 million people have died of HIV.

- Globally, 37.9 million people were living with HIV at the end of 2018.
- An estimated 0.8% [0.6-0.9%] of adults aged 15–49 years worldwide are living with HIV.
- African region remains most severely affected:

Nearly 1 in every 25 adults (3.9%) living with HIV and accounting for more than two-thirds of the people living with HIV worldwide.

Estimated number of people living with HIV, 2016
By WHO region



Number of people, by WHO region

- Eastern Mediterranean: 360 000 [290 000–500 000]
- Western Pacific: 1 500 000 [1 200 000–2 000 000]
- Europe: 2 400 000 [2 300 000–2 600 000]
- Americas: 3 300 000 [2 900 000–3 800 000]
- South-East Asia: 3 500 000 [2 500 000–8 200 000]
- Africa: 25 600 000 [22 900 000–28 600 000]

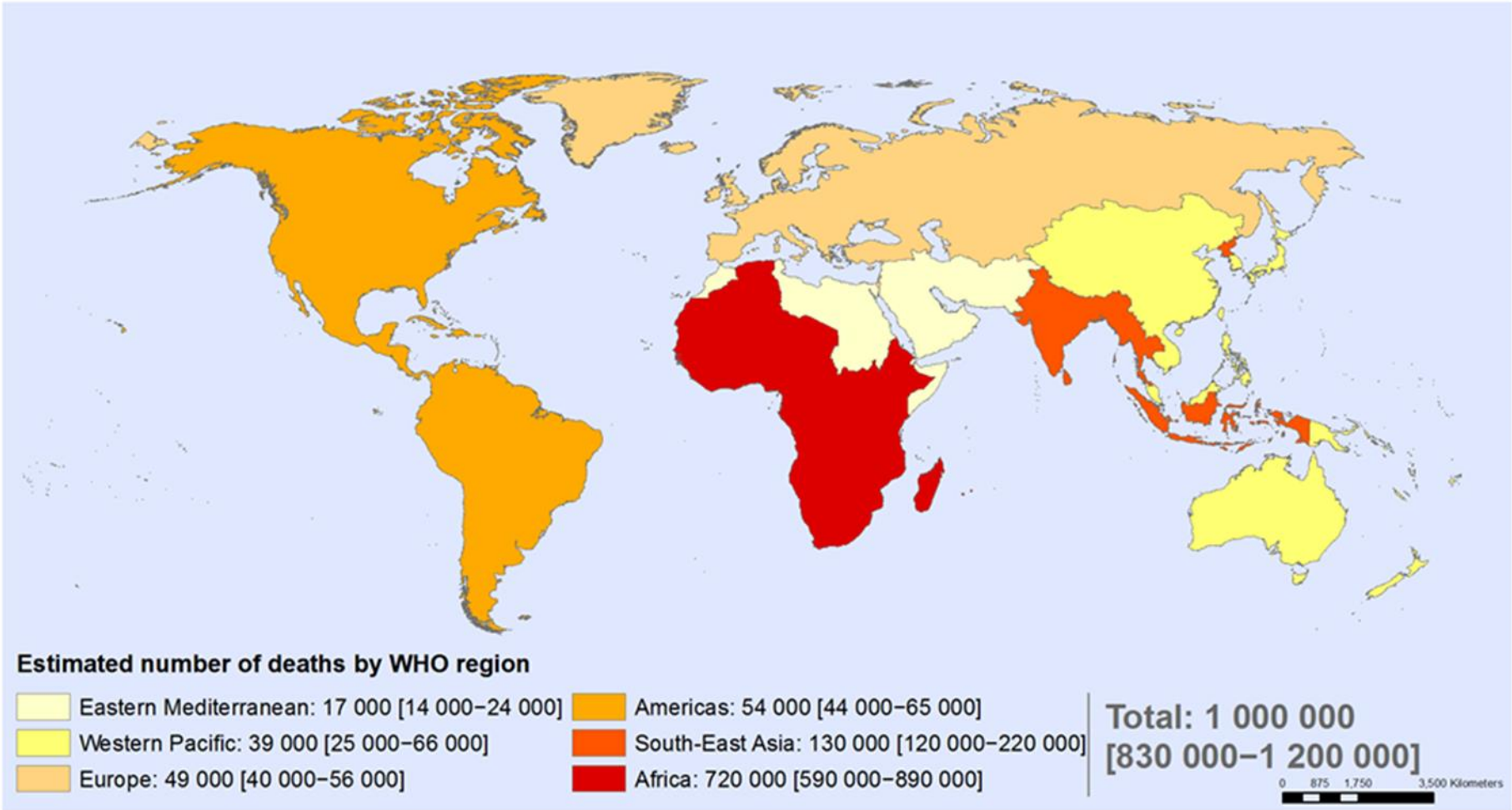
Total: 36 700 000
[30 800 000–42 900 000]

0 875 1,750 3,500 Kilometers

Data Source: World Health Organization
Map Production: Information Evidence and Research (IER)
World Health Organization

World Health Organization

Estimated number of people dying from HIV-related causes, 2016
By WHO region



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HIV and AIDS

Transmission

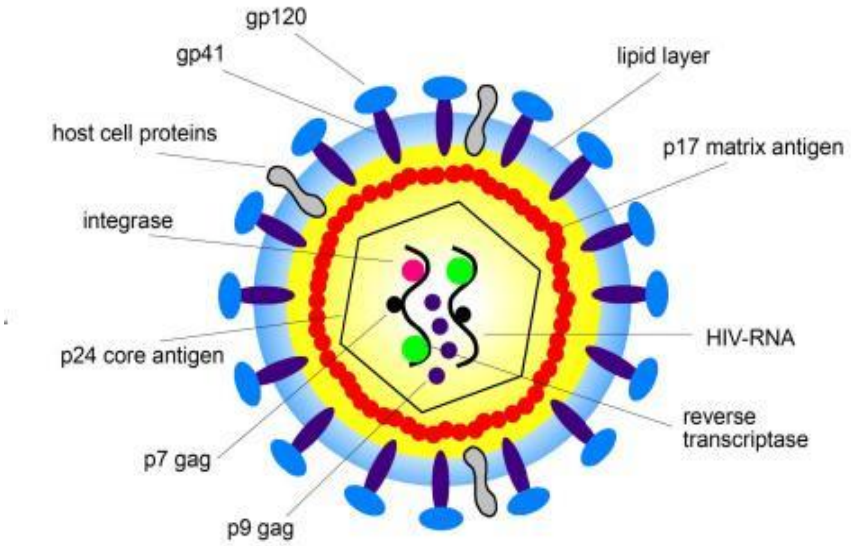
- **Sexual** (heterosexual ,msm ,others)

  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 protien . 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 :

CCXR5 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 structual 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

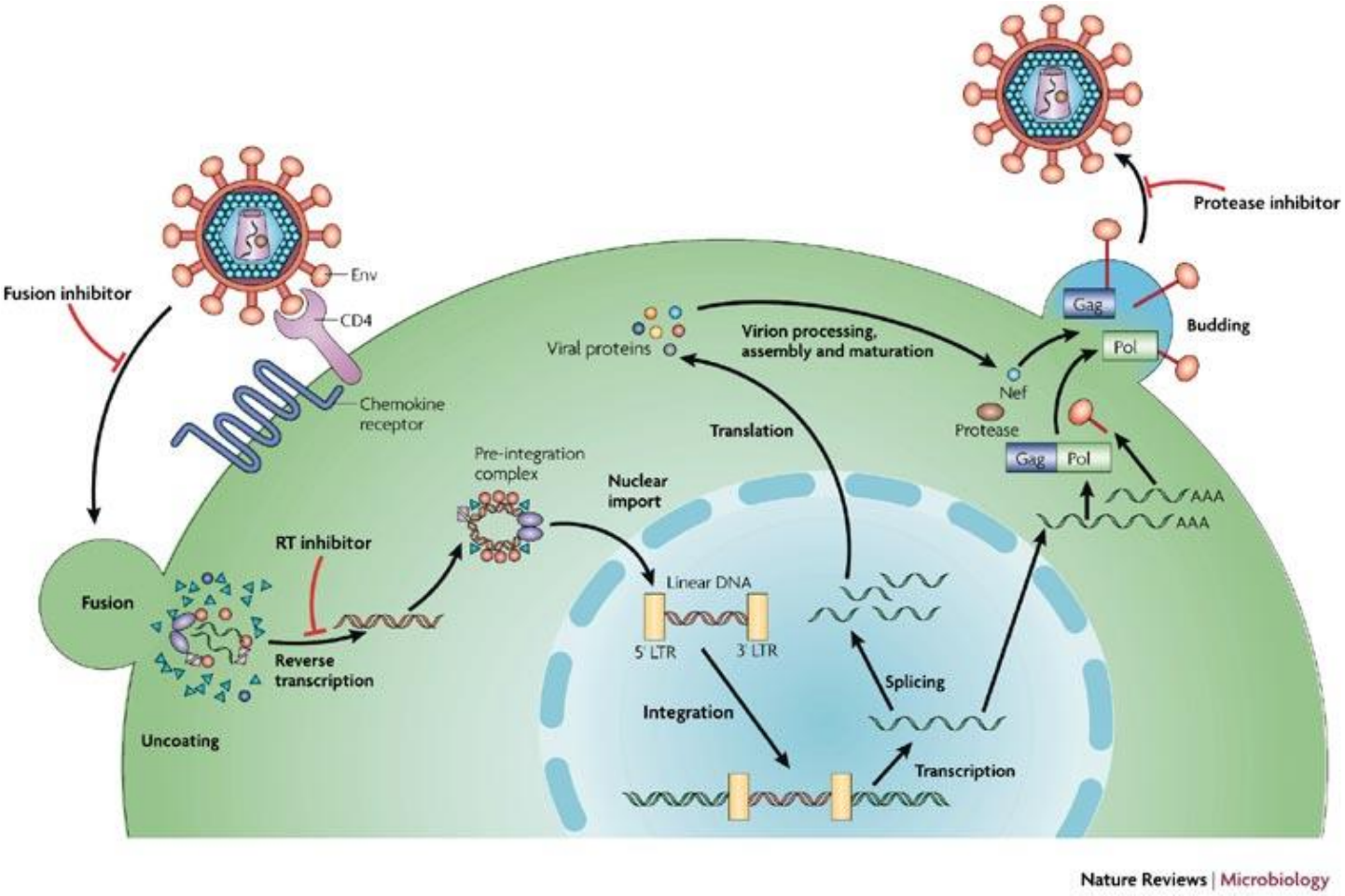
b) Budding

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

- Chronic immune system activation determine the course of the illness.

- 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)
- It resmble **infectious mononucleosis** with :
- **Fever , Pharyngitis , Adenopathy**
- **Rash , myalgia, fatigue, oral ulcer**
- **Diarrhoea, anorexia**.
- **THEN**.....
- HIV RNA level falls and the symptoms resolve.
- CD4 cell count rebounds but remains below the bassline

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 increaase the risk of Non-AIDS related comorbidities: CVD,Renal dysfunction and cancer

Diagnosis:

- ***HIV Antibody/Antigen immunoassay Test.*** is the screening test ,used to screen blood products and patients.
- It detect both HIV antigen (p24) and antibody.
- Result in 20 minutes
- shows up 2 to 4 weeks after infection..

- **In-home test kits**

- Kits that test your blood or oral.
- FDA-approved.

- Home tests are slightly less sensitive than in-person lab tests.

Diagnosis:

- **Confirmation :**
- The INNO-LIA™ (HIV I/II) Score is a Line Immuno 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 : diagnose HIV about 10 days

1) Confirmatory test for undetermined cases.

2) To asses the viral load .

3) Babies born to HIV-positive mothers, because their blood contains their mother's HIV antibodies for several months.

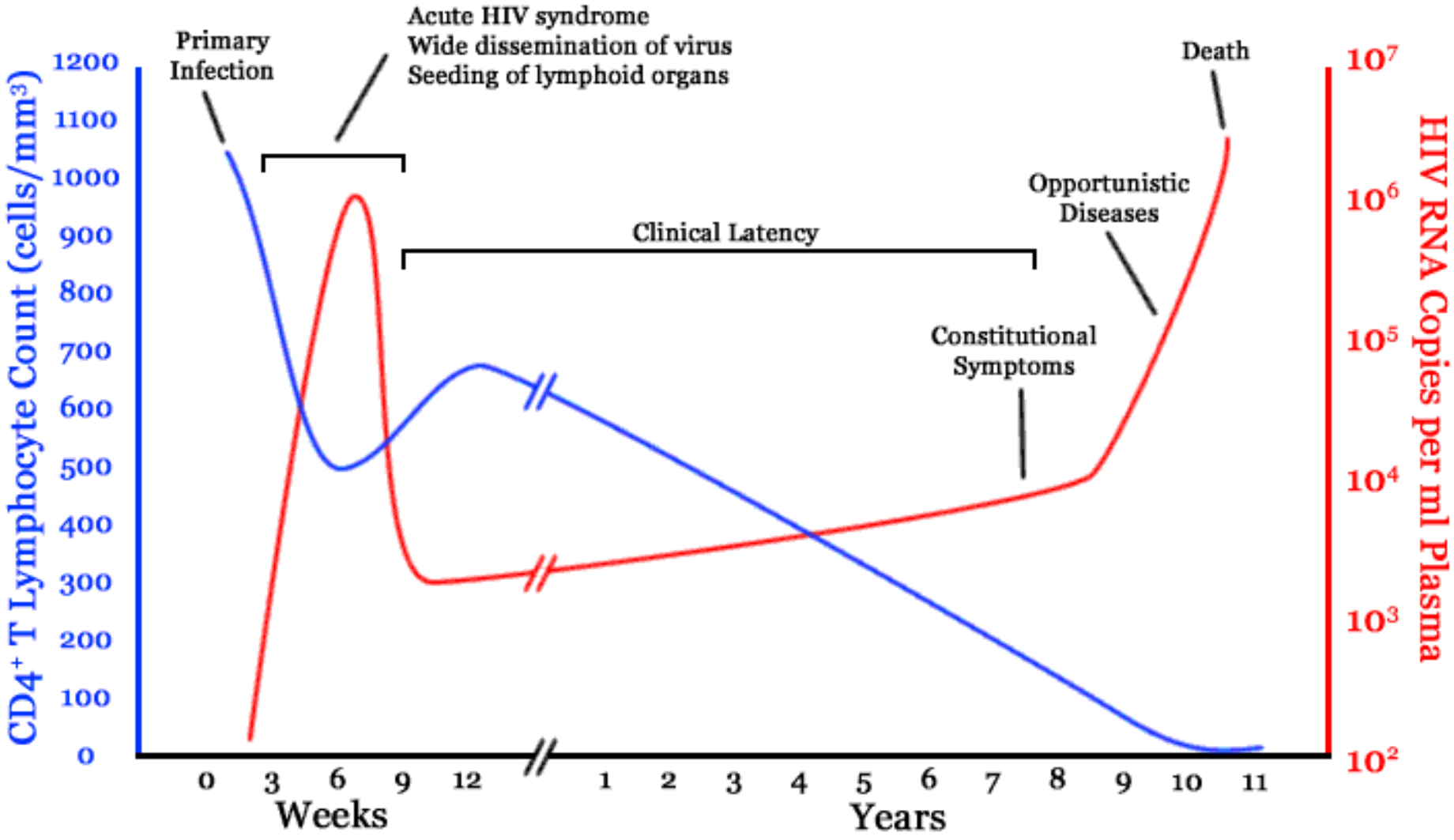
4) Blood supplies

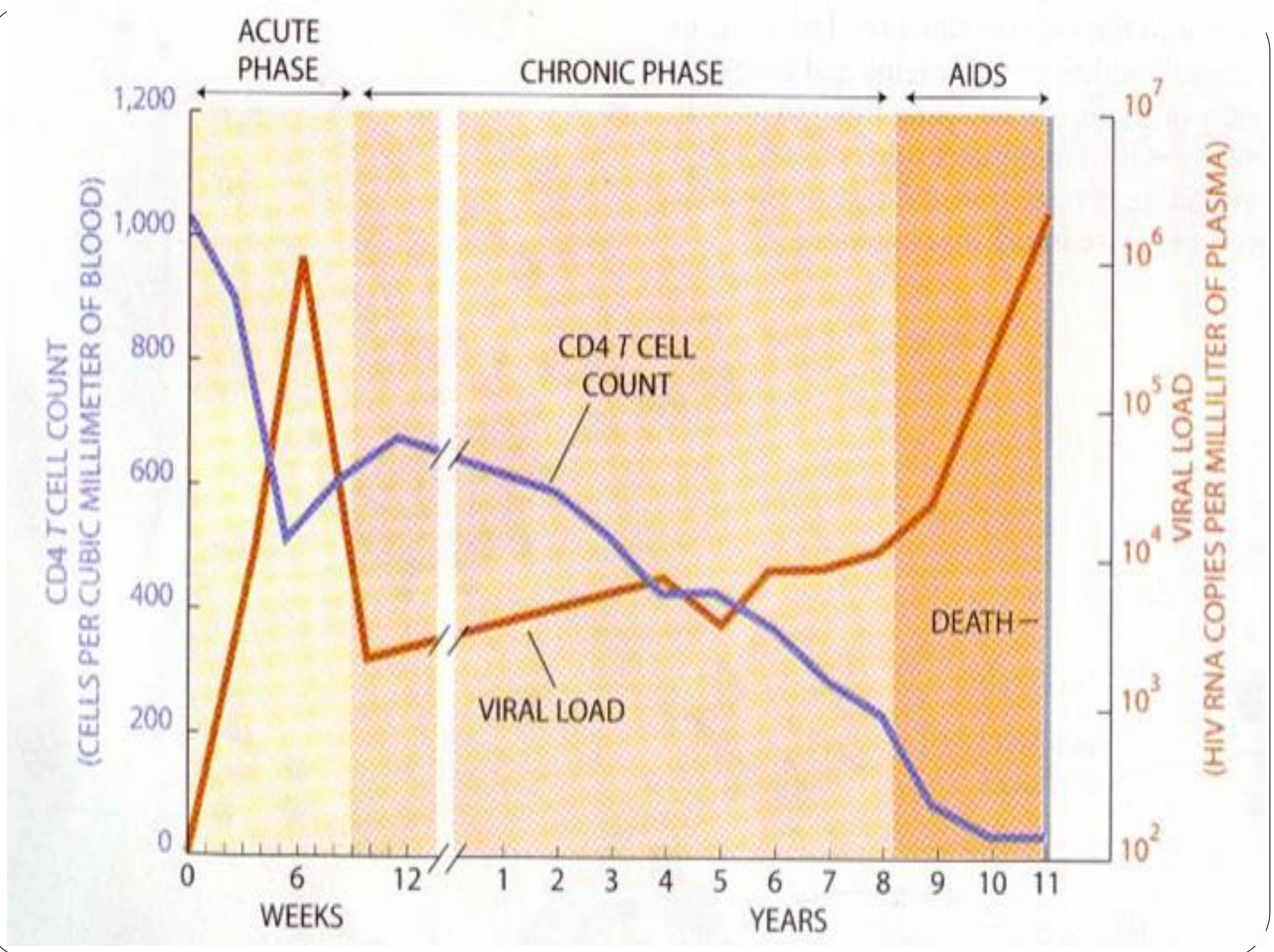
Not for routine testing:

a) Decreased sensitivity at lower viral load

b) Significant cost.

HIV Progression




ACUTE PHASE
CHRONIC PHASE
AIDS
1,200
1,000
800
600
400
200
0
CD4 T CELL COUNT (CELLS PER CUBIC MILLIMETER OF BLOOD)
10^7
10^6
10^5
10^4
10^3
10^2
VIRAL LOAD (HIV RNA COPIES PER MILLILITER OF PLASMA)
CD4 T CELL COUNT
VIRAL LOAD
DEATH
0
6
12
WEEKS
1
2
3
4
5
6
7
8
9
10
11
YEARS

HIV and AIDS

- **Immunological staging:**

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

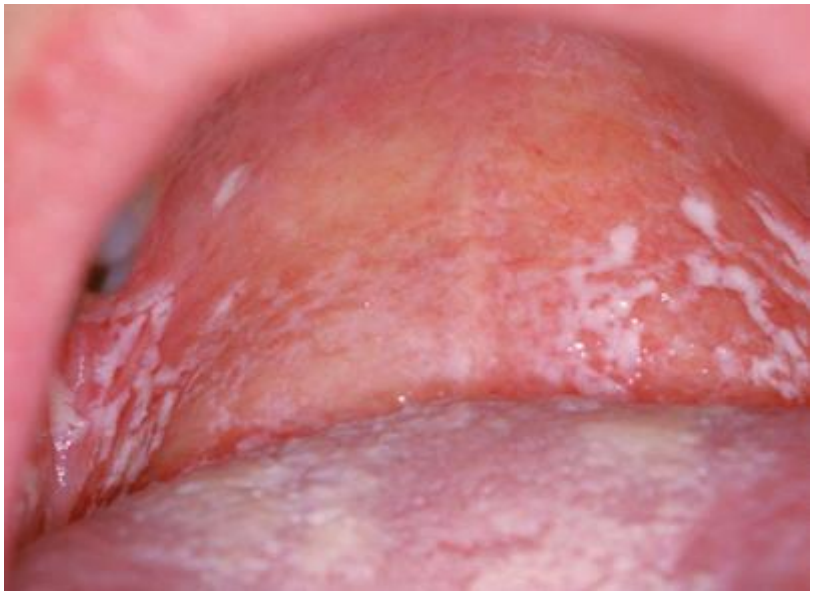
  1. >500 cells/mm³ normal immunity.
  2. 350-500 cells/mm³ mild deficiency.
  3. 200-350 cells/mm³ moderate immune deficiency.
  4. <200 cells/mm³ sever immune deficiency

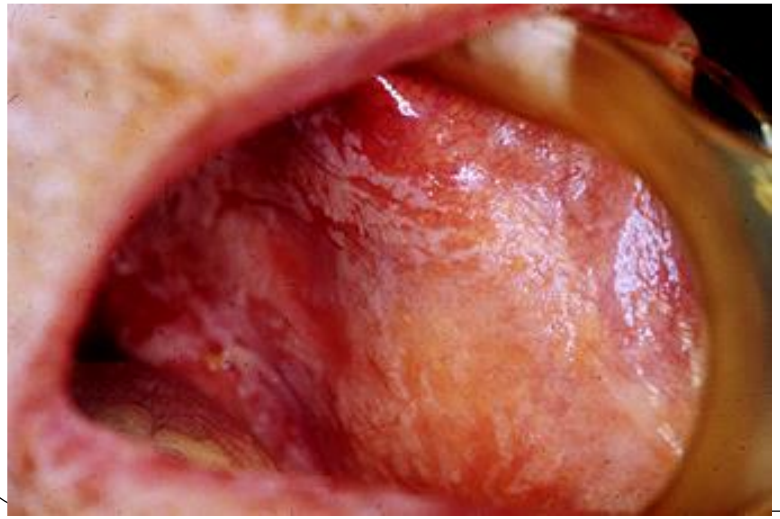
Clinical manifestation

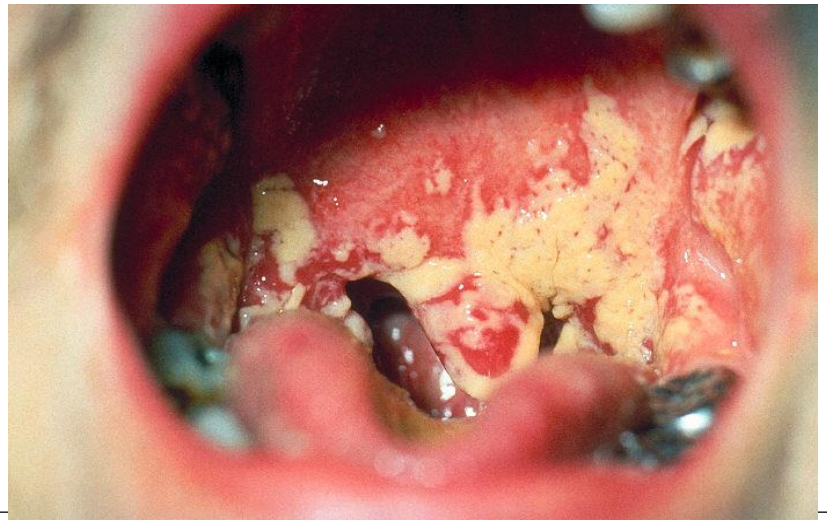
Physical examination:

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

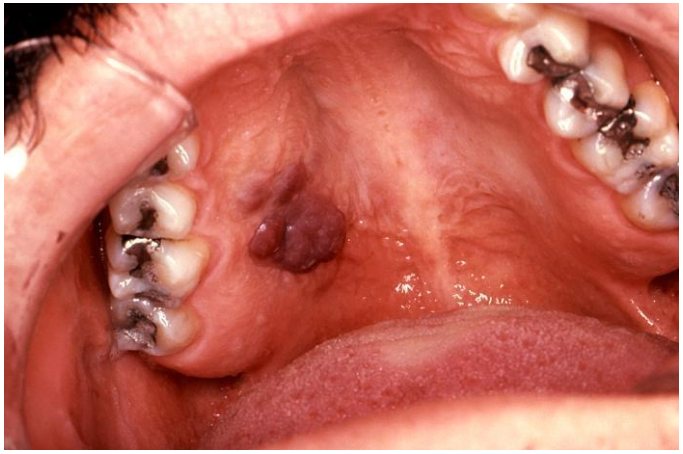
ORAL TRUSH







KAPOSI SARCOMA



Condyloma acuminatum

- Condylomatous lesions: genital wart

A pointed papilloma typically found on the skin or mucous membranes of the anus and external genitalia, caused by :

human papillomavirus ..HPV

Transmitted through sexual contact ..

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

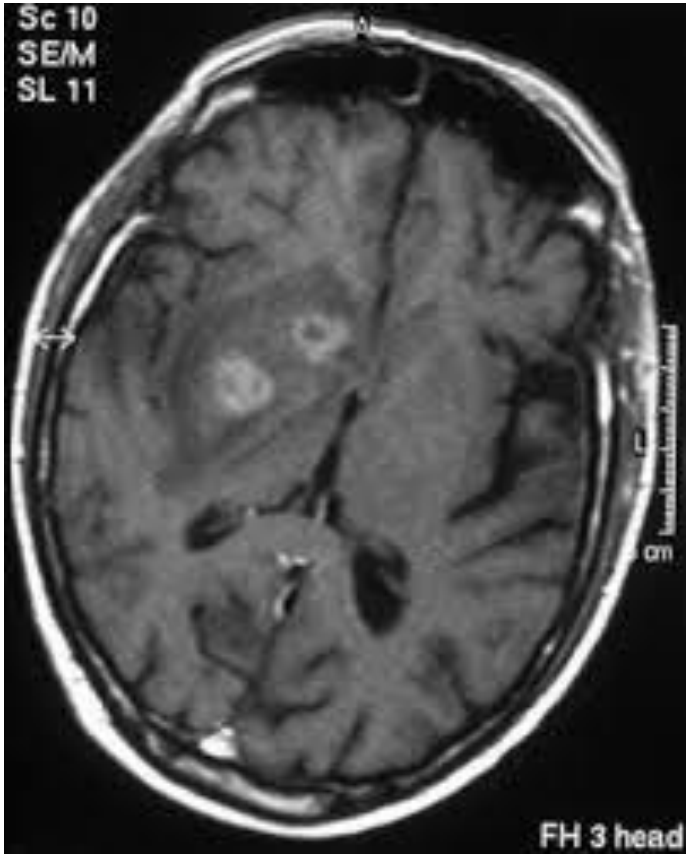
- **Tuberculosis (TB).** TB is the most common opportunistic infection and a leading cause of death .

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

COMPLICATION OF HIV/AIDS

- **Toxoplasmosis.** This potentially deadly infection is caused by Toxoplasma gondii, a parasite spread primarily by cats. It causes meningoenchephalitis.
- 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.

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**

Treatment:

- Prophylaxis:
- If CD4 is below 200 :
- Patient at high risk to develop :

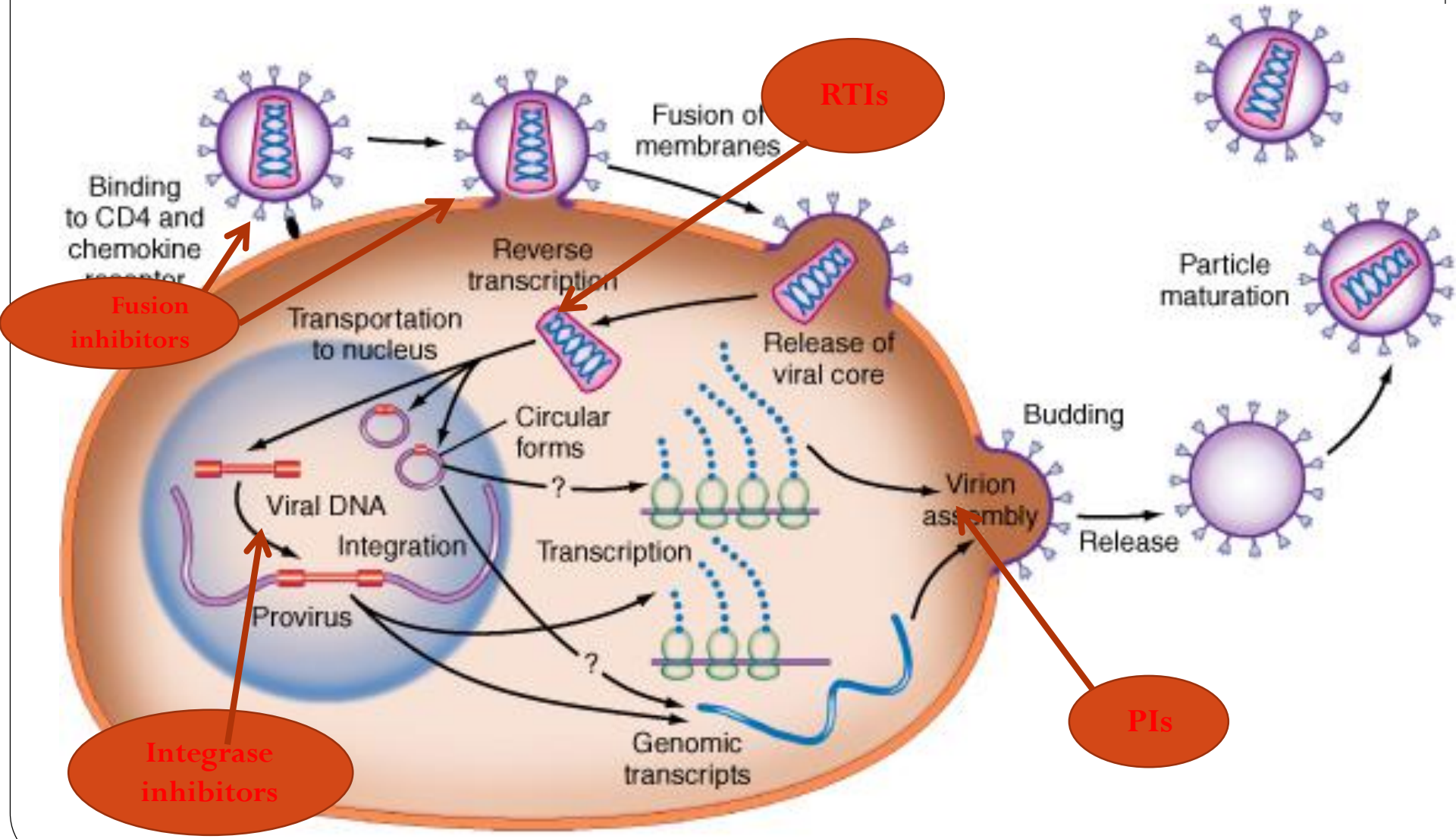
1) ***Pneumocystis jirovecii: Causing Pneumonia***

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**

❖ **Chronic infection**

a) Symptomatic disease .

b) A symptomatic disease with

1) CD4 count less than 350

2) Pregnancy

❖ **Post exposure prophylaxis.**

Prevention

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

{ وَلَا تَقْرَبُوا الزِّنَى 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)

Prevention

- Male circumcision for HIV prevention
- Mother-to-child transmission of HIV
- Pre-exposure prophylaxis (PrEP).

Pregnancy and HIV infection

Pregnant women infected with HIV infection caries 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 appropiate**
- ✓ **Formula feeding**

Thank you

Any Q