Infectious diseases

	4/5th Semester Classes on Infectious Diseases, 8-9AM, Tuesdays (LT-1)
	Topics
1	Approach to Infectious Diseases and their prevention
2	Antibiotic stewardship practices
3	Community-Acquired Infections
4	Health Care–Associated Infections
5	Gram-Positive Bacteria (part-1)
6	Gram-Positive Bacteria (part-2)
7	Gram-Negative Bacteria (part-1)
8	Gram-Negative Bacteria (part-2)
9	Spirochetal Diseases
10	Diseases Caused by Atypical/Miscellaneous Bacterial Infections
11	**Revision-cum-exam on bacteria (Must to know type)**
12	Infections Due to DNA Viruses
13	Infections Due to RNA Viruses (part 1)
14	Infections Due to RNA Viruses (part 2)
15	HIV/AIDS – part 1
16	HIV/AIDS – part 2
17	Fungal Infections
18	Parasitic Infections (part 1)
19	Parasitic Infections (part 2)
20	**Revision-cum-exam on Virus, Fungal, and Parasite (Must to know type)**

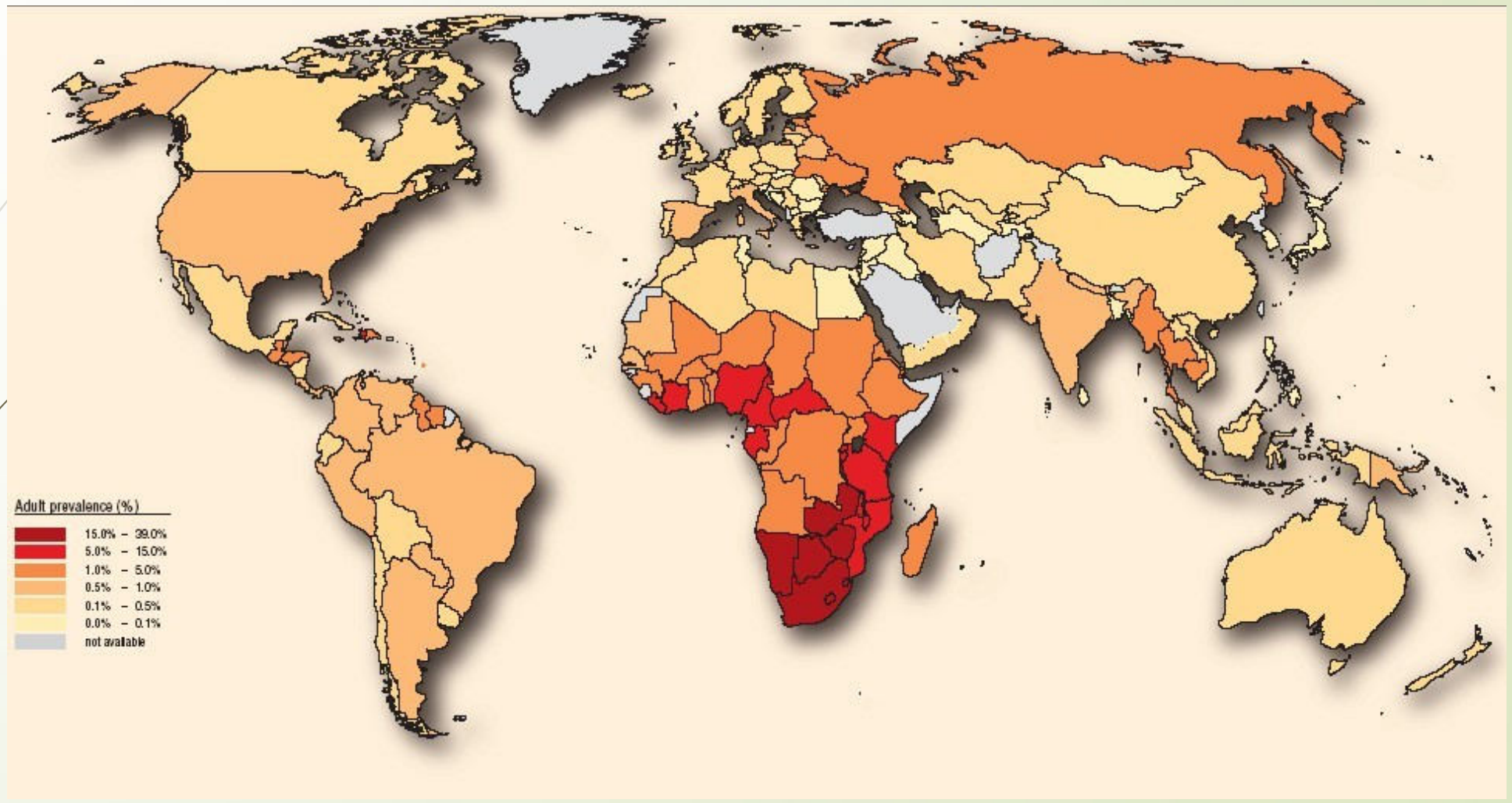
1

HIV/AIDS

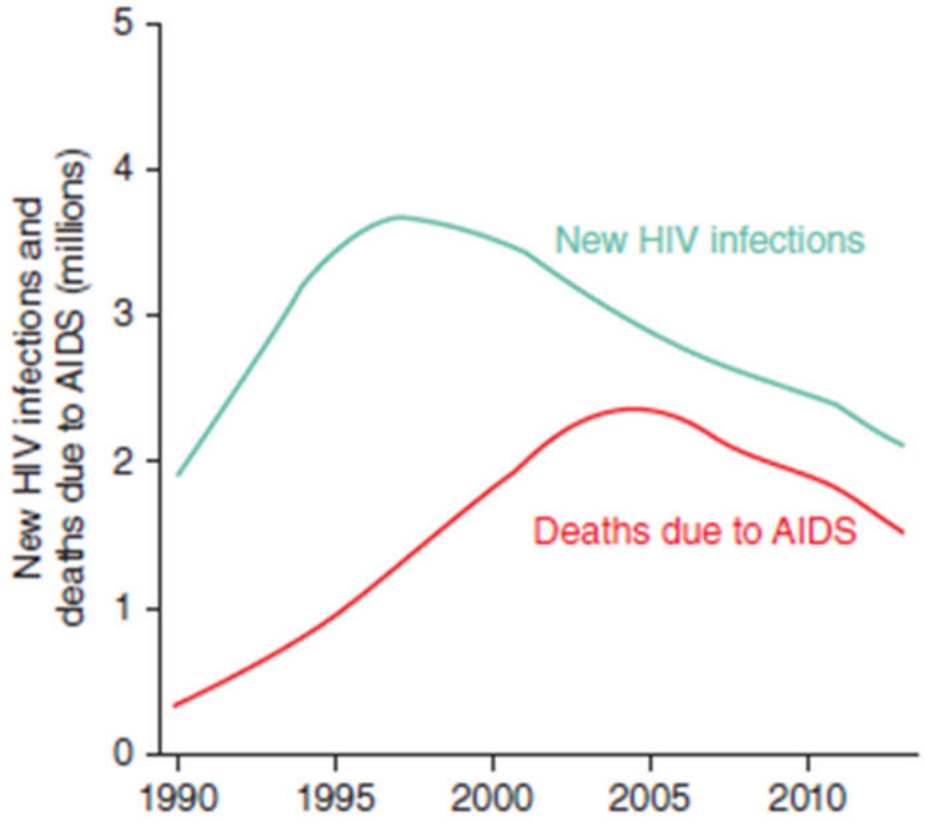
- **HIV** is a retrovirus which **attacks the T-cells** in the immune system

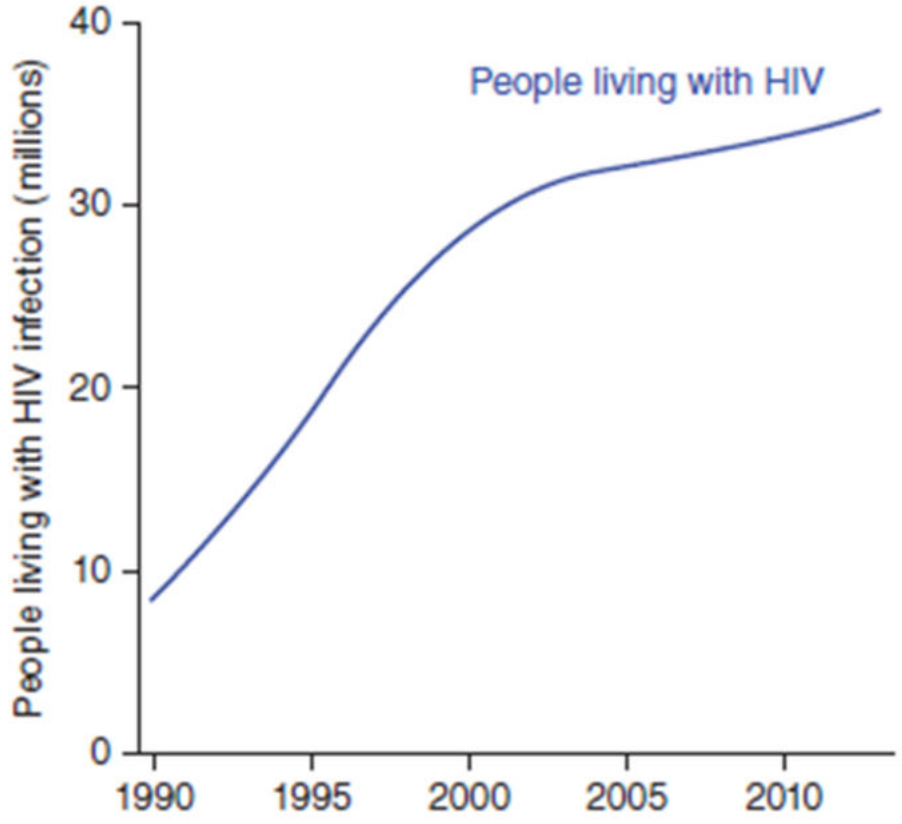
- Acquired Immuno deficiency syndrome or AIDS, is a collection of symptoms due to underlying infections and malignancies resulting from specific damage to immune system caused by human immunodeficiency virus (HIV).

A Global view of HIV Infection



- Approximately > 40 million people are currently living with HIV infection, and 25 million have already died





AIDS

- The first indication of this new syndrome came in 1981 in homosexual drug addict males;
- They had two things in common- *Pneumocystis* pneumonia and Kaposi's sarcoma

- In 1983, HIV was isolated from a patient with lymphadenopathy, and by 1984 it was demonstrated clearly to be the causative agent of AIDS

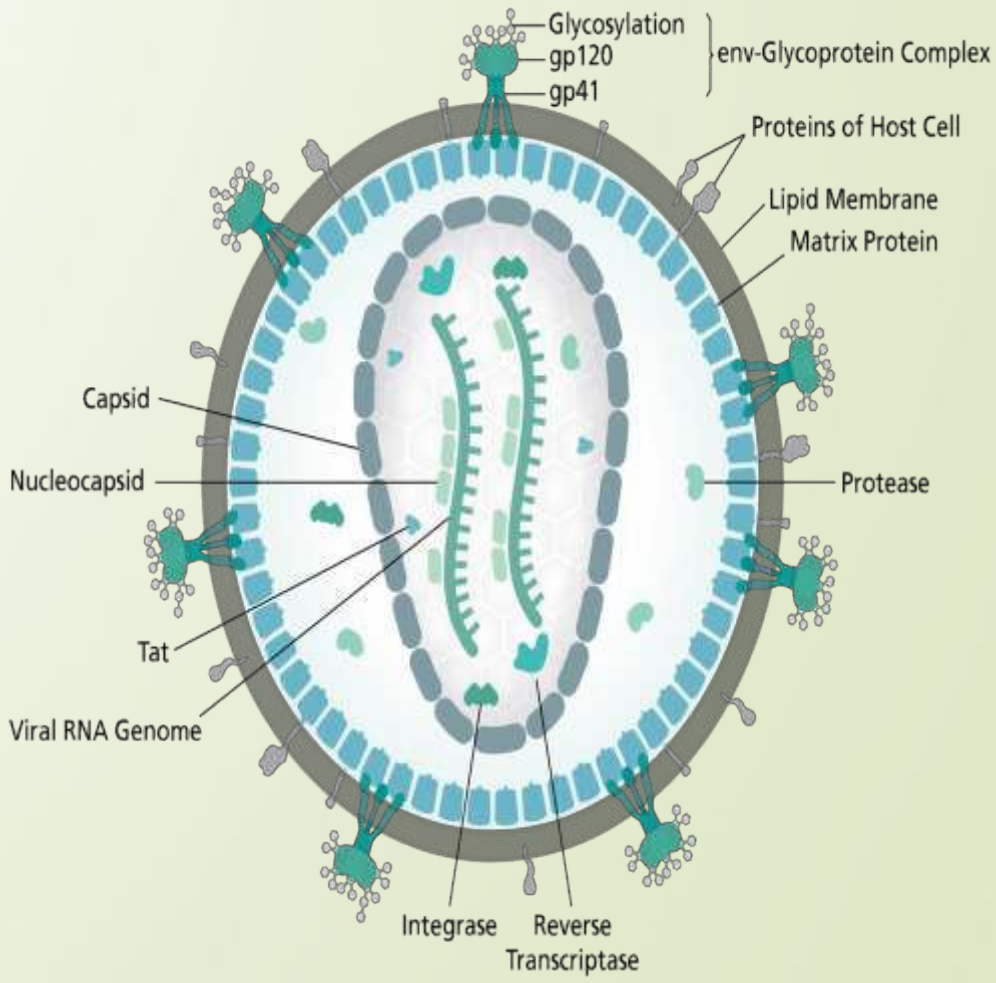
- In 1986, The International Committee on virus Nomenclature decided on the generic name of the causative virus as the **Human Immunodeficiency Virus**

TABLE 225e-1 CLASSIFICATION OF RETROVIRUSES: THE FAMILY RETROVIRIDAE

Genus	Example(s)	Feature
Alpharetrovirus	Rous sarcoma virus	Contains *src* oncogene
Betaretrovirus	Mouse mammary tumor virus	Exogenous or endogenous
Gammaretrovirus	Abelson murine leukemia virus	Contains *abl* oncogene
Deltaretrovirus	HTLV-1	Causes T cell lymphoma and neurologic disease
Epsilonretrovirus	Walleye dermal sarcoma virus	Not known to be pathogenic in humans
Lentivirus	HIV-1, -2	Causes AIDS
Spumavirus	Simian foamy virus	Not known to be pathogenic in humans

Structure of HIV

- It has a diameter of 100-120 nm with a spherical morphology
- Cone-shaped core surrounded by lipid matrix containing key surface antigens and glycoproteins
- Viral core contains 2 copies of genomic RNA, reverse transcriptase, integrase and protease



Based on molecular and antigenic differences, two types of HIV have been recognized

HIV 1

- HIV-1 is more common in india
- Easily transmitted.
- Pathogenic in nature
- Duration of infection is quite long.
- classified in to at least ten subtypes based on sequence analysis of their *gag* and *env* genes (Group M (For major) is largest.

HIV 2

- HIV-2 is found in West Africa, Mozambique, and Angola.
- Less easily transmitted.
- Less pathogenic.
- Duration of infection is shorter .
- Relatively rare and has not been reported from India.

Antigenic variations in HIV

- HIV is a **highly mutable virus** and exhibits frequent antigenic variations as well as differences in other features such as **nucleotide sequences, cell tropism, growth characteristics and cytopathology**
- Not only are there differences between isolates of HIV from different races or persons but also between sequential isolates from the same person, and even between those obtained from different sites of the same person at the same time.
- This great variability is believed to be **due to error prone nature of reverse transcription**

Mode of transmission

1. **Sexual contact-** In 75 % cases , trans
   is by sexual contact.

- People who already have a sexually
  transmitted disease, such as **syphilis,**
  herpes, chlamydial infection, gonorrhea,
  bacterial vaginitis, are more likely to acc
  infection during sex with an infected par

TABLE 226-3 ESTIMATED PER-ACT PROBABILITY OF ACQUIRING HIV FROM AN INFECTED SOURCE, BY EXPOSURE ACT

Type of Exposure	Risk per 10,000 Exposures
Parenteral	
Blood transfusion	9250
Needle-sharing during injection drug use	63
Percutaneous (needle-stick)	23
Sexual	
Receptive anal intercourse	138
Insertive anal intercourse	11
Receptive penile-vaginal intercourse	8
Insertive penile-vaginal intercourse	4
Receptive oral intercourse	Low
Insertive oral intercourse	Low
Other[a]	
Biting	Negligible
Spitting	Negligible
Throwing body fluids (including semen or saliva)	Negligible
Sharing sex toys	Negligible

Mode of transmission

2. **Parenteral**- In 15 % cases, it is by blood transfusion or blood product transfusion.

3. **Sharing of** unsterilized **needles** or syringes in drug addicts contaminated with blood from an infected person can spread virus.

4. HIV can be spread in health-care settings through **accidental needle sticks** or contact with contaminated fluids.

5. HIV can also spread through **organ transplantation**.

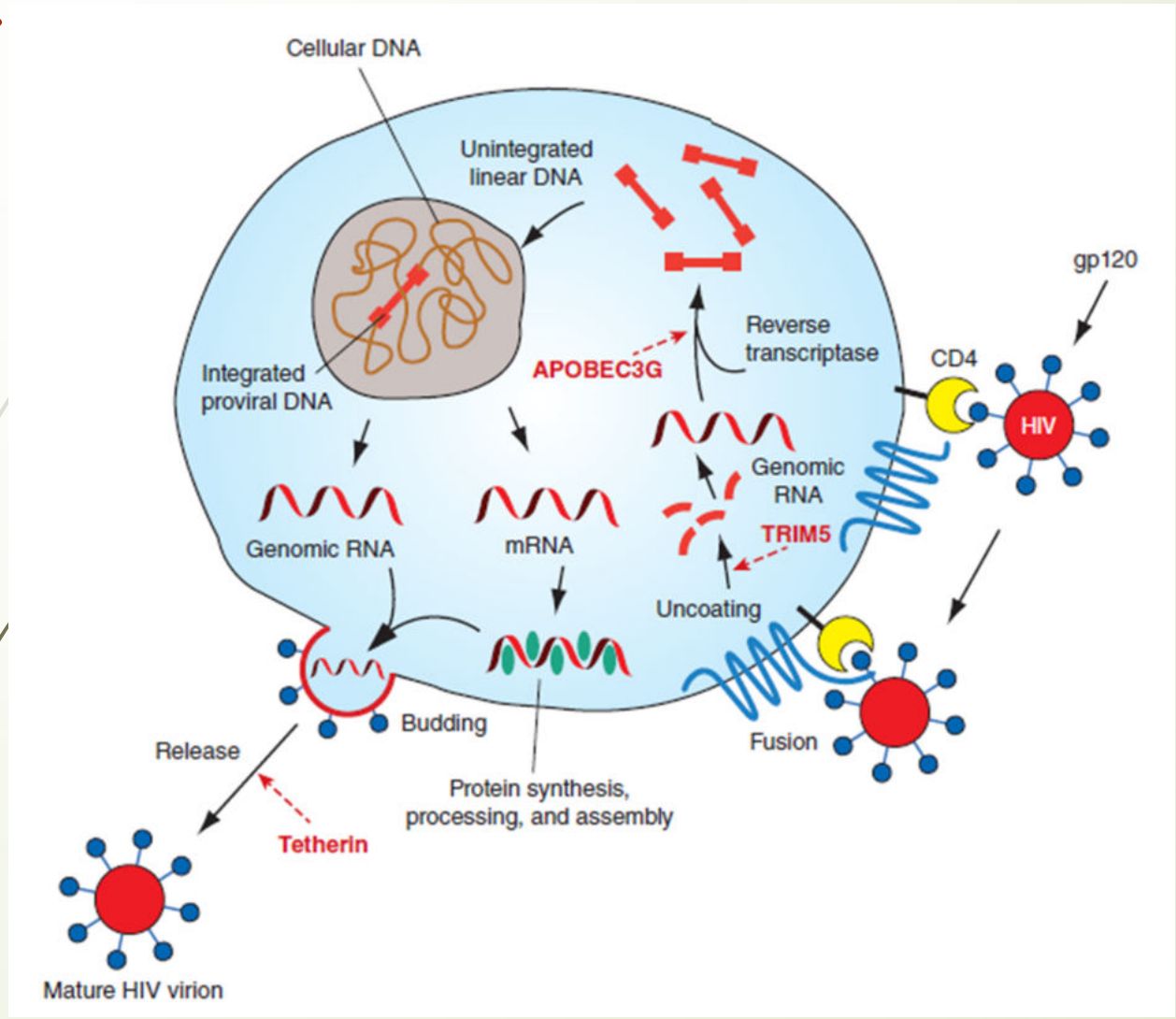
6. **Mother to child**

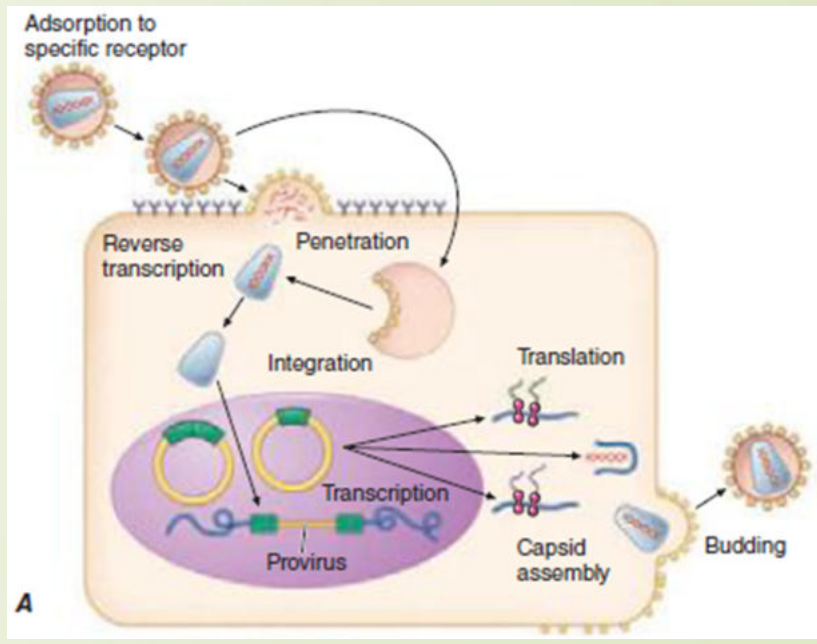
From mother to child

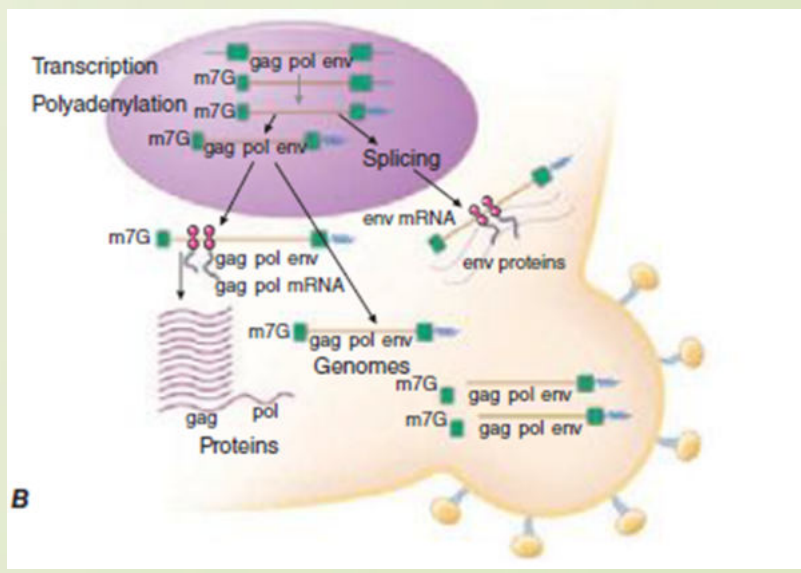
- 30% of children born to infected mothers have the acquired infection unless virus is treated by antiviral drugs before pregnancy.
- **In nursing mothers** transmission can occur through breast milk.

Timing of HIV Infection	% of Chidlren at risk
During pregnancy	5–10
During labour and delivery	10–15%
During breast feeding	5–20%
Overall risk without breast feeding	15–25%
Overall risk with breast feeding to 6 months	20–35%
Overall risk with breast feeding to 18 to 24 months	30–45%

Pathogenesis



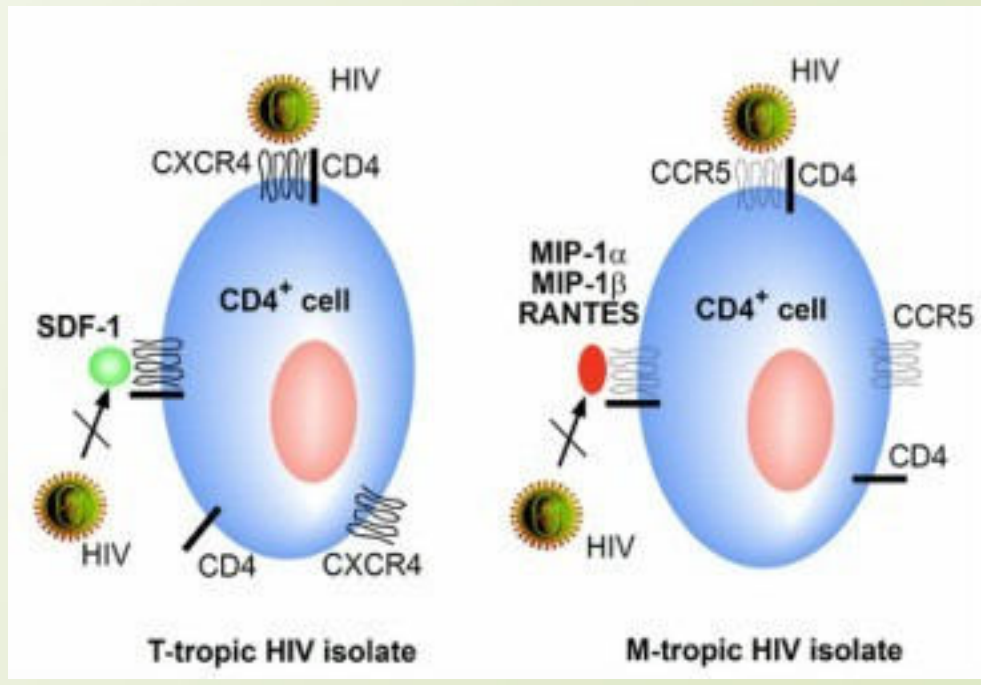


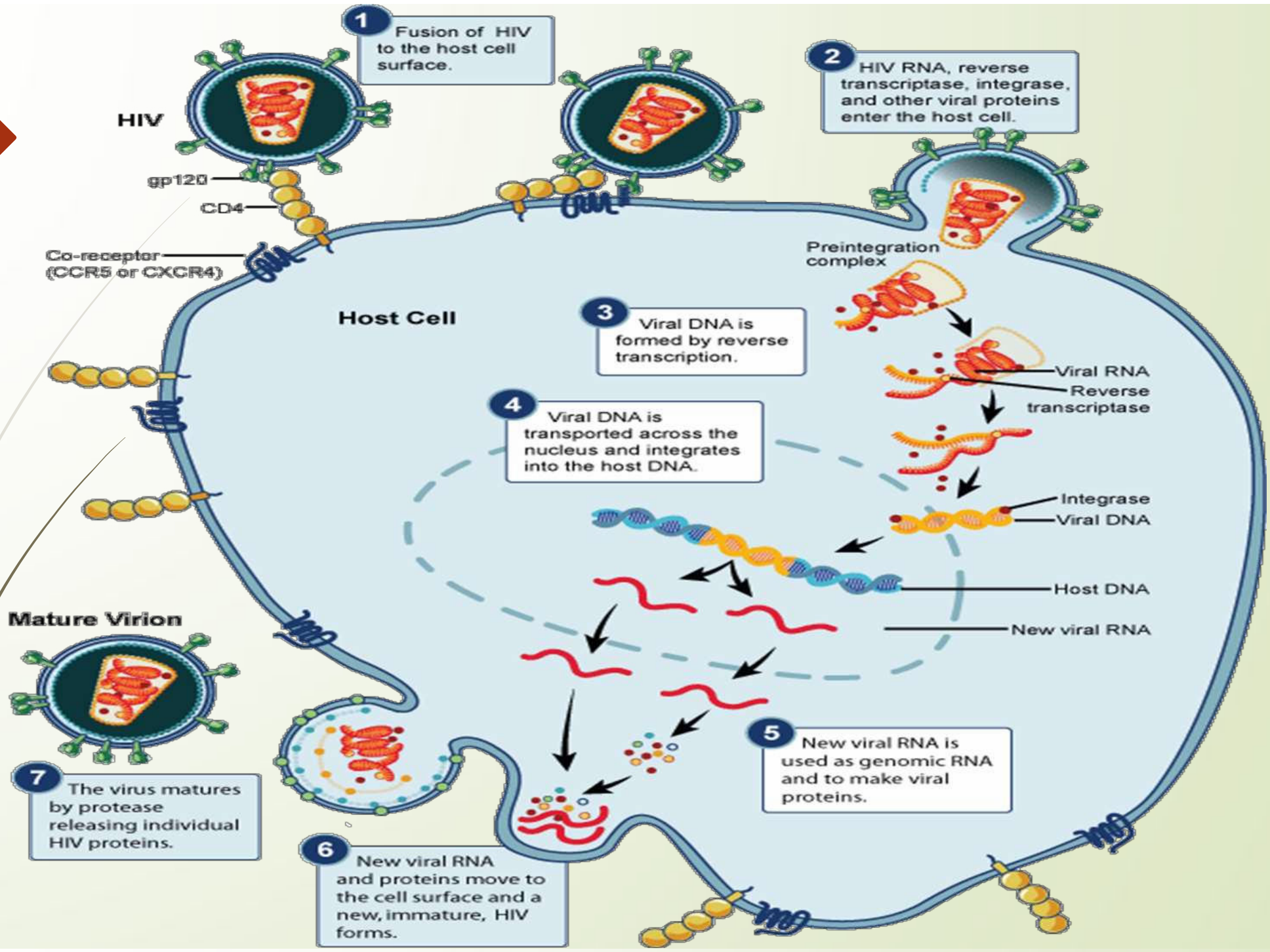


CD4+cells are present in- **T helper cells, B-lymphocytes , macrophages, monocytes , and dendritic cells**

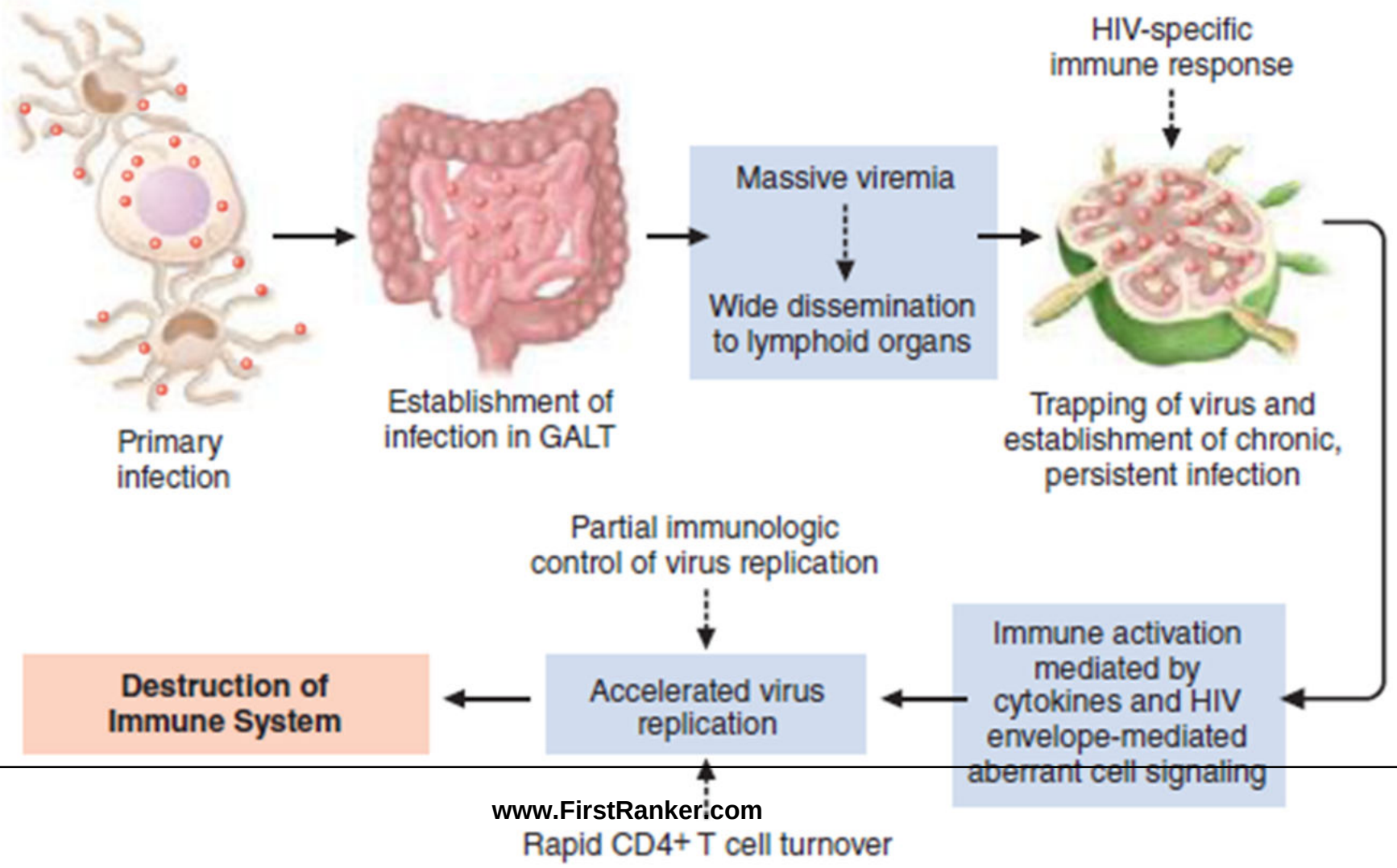
Steps of viral entry in to the host cell

- Strains of HIV that utilize CCR5 as a co-receptor are referred to as **macrophage tropic viruses (M –tropic viruses)**
- Strains of HIV that utilize CXCR4 are referred to as **T-tropic viruses**.
- Many virus strains are dual tropic in that they utilize both CCR5 and CXCR4.

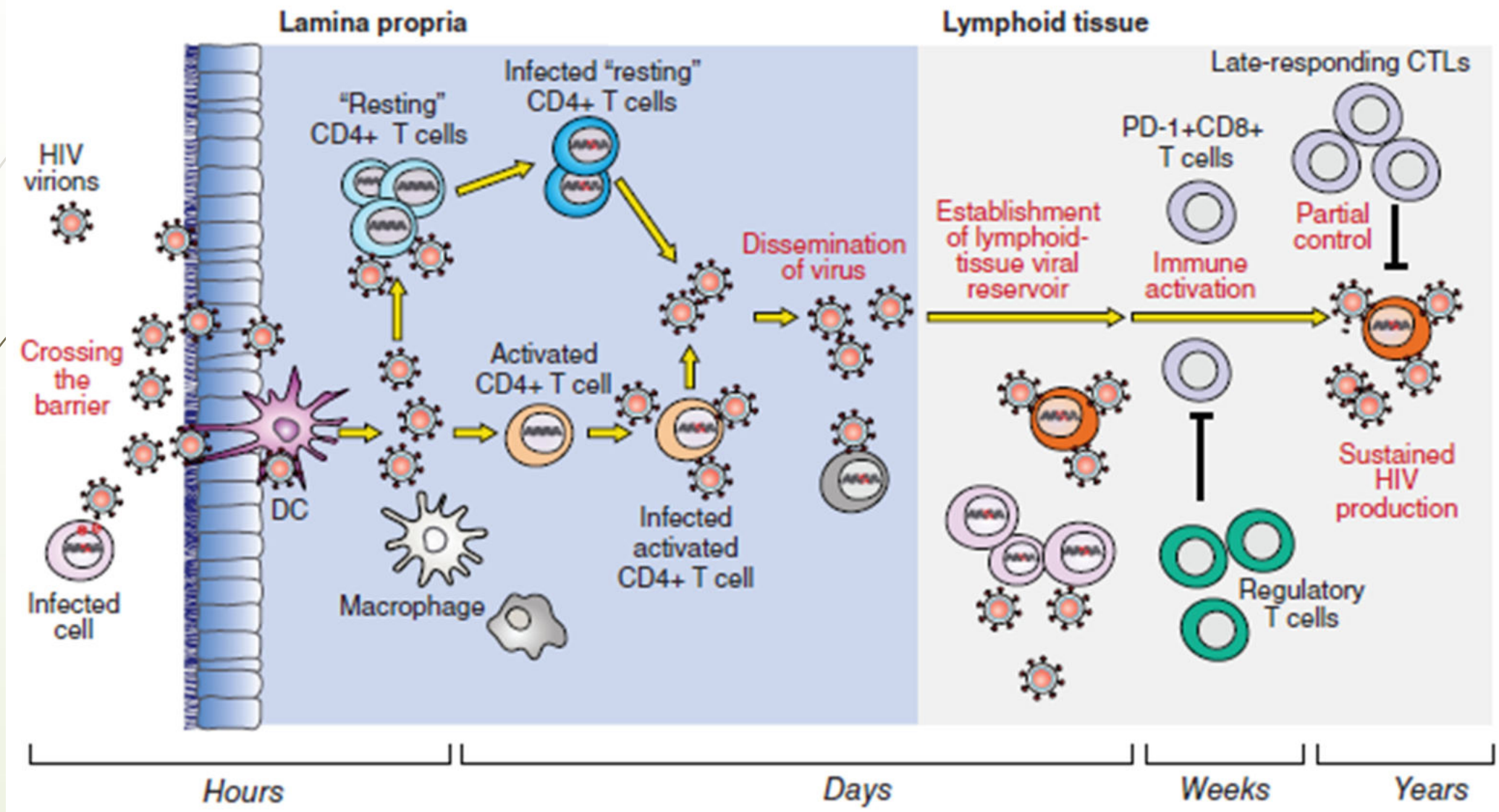




Events that transpire from primary HIV infection



Summary of early events in HIV infection



- **Lymphoid tissues are the major anatomic sites** for the establishment and propagation of HIV infection
- **Immune activation and inflammation** contribute substantially to:

  (1) the replication of HIV,

  (2) the induction of immune dysfunction, and

  (3) the increased incidence of chronic conditions associated with persistent immune activation and inflammation

  - *Accelerated aging syndrome*
  - *Bone fragility*
  - *Cancers*
  - *Cardiovascular disease*
  - *Diabetes*
  - *Kidney disease*
  - *Liver disease*
  - *Neurocognitive dysfunction*

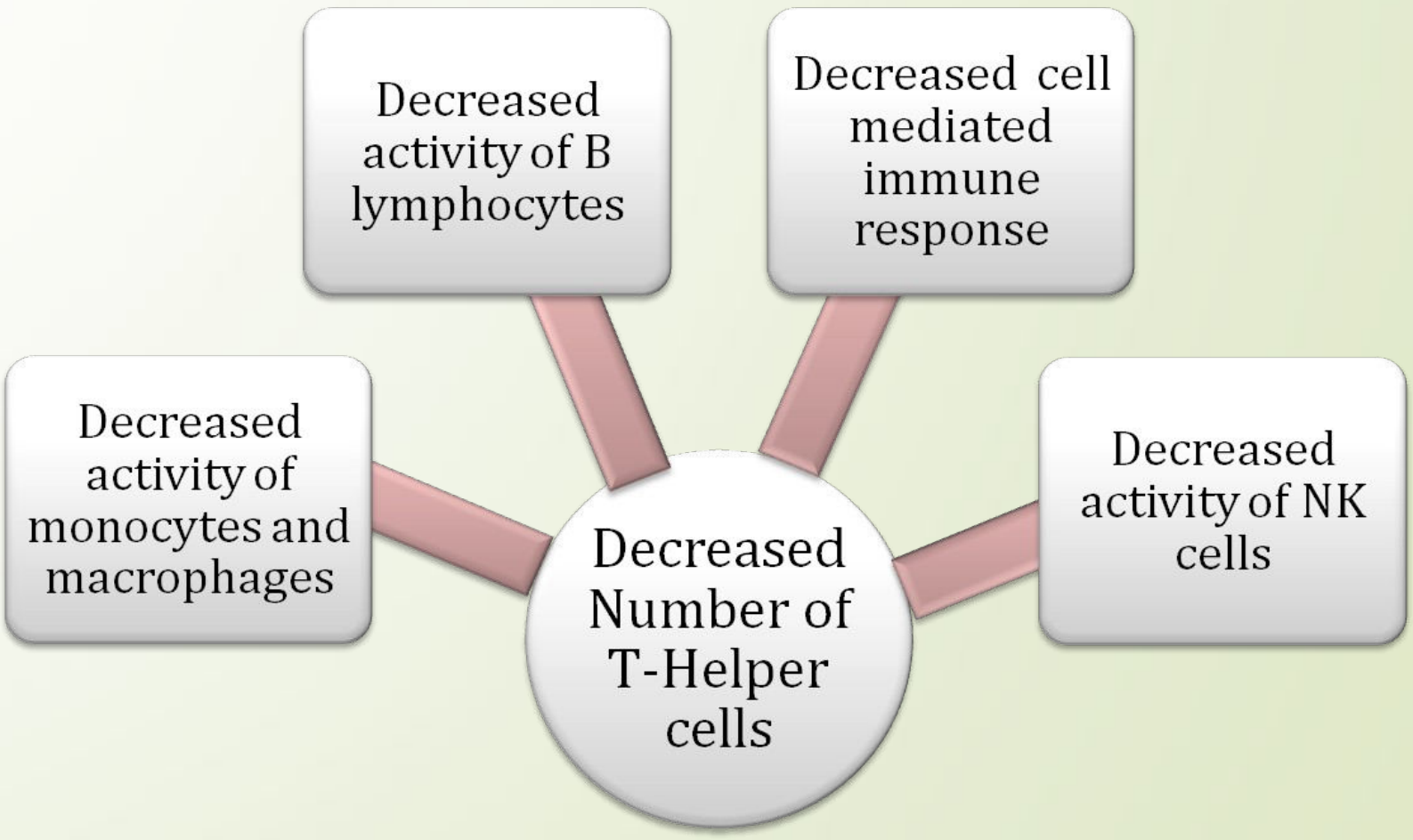
I**ncreased** occurrence and/or exacerbation of certain **autoimmune diseases** like:

- *Psoriasis,*
- *Idiopathic thrombocytopenic purpura,*
- *Graves' disease,*
- *Antiphospholipid syndrome, and*
- *Primary biliary cirrhosis*

Immune reconstitution inflammatory syndrome (IRIS) is an autoimmune-like phenomenon characterized by a paradoxical deterioration of clinical condition, which is usually compartmentalized to a particular organ system, in individuals in whom cART has recently been initiated.

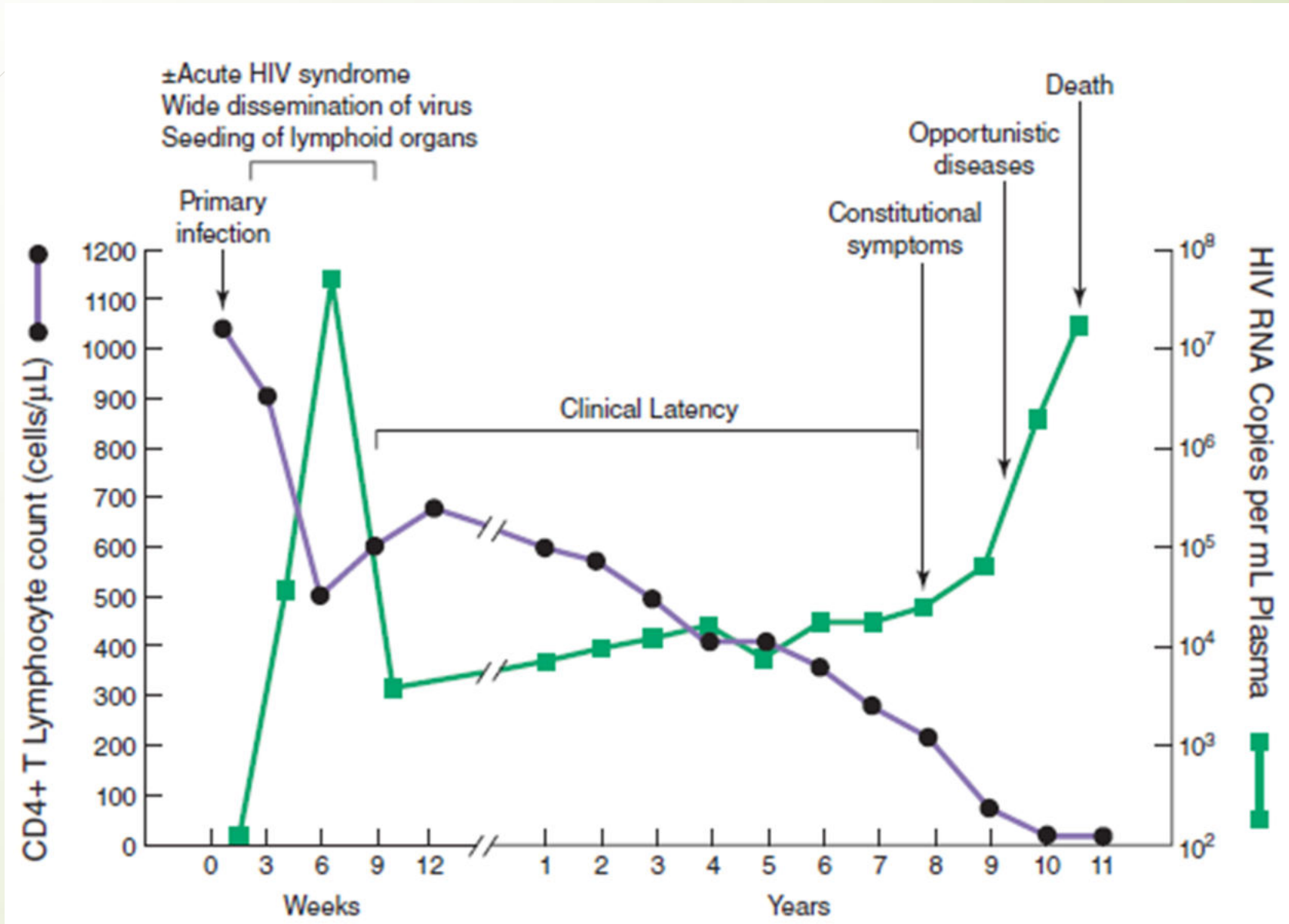
- It is associated with a decrease in viral load and at least partial recovery of immune competence, which is usually associated with increases in CD4+ T cell counts.
- Commonly seen with underlying *Mycobacterium tuberculosis* and cryptococcosis

Immune deficiency in HIV Infection



Typical course of an untreated HIV-infected individual

(The combination of viral pathogenic and immunopathogenic events decides the disease)



- **Long-term nonprogressors** are by definition **long-term survivors**; however, the reverse is not always true

- Long-term nonprogressors were first described in the 1990s, defined if
  - They had been infected with HIV for a long period (≥10 years),
  - Their CD4+ T cell counts were in the normal range, and
  - They remained stable over years without receiving Cart

Laboratory Diagnosis of HIV infection

1) **Non Specific Tests-** The following tests help to establish the immunodeficiency in HIV infection.
   - **Total Leukocyte and lymphocyte count-** to demonstrate leucopenia and lymphopenia. The lymphocytic count is usually below 2000/mm^3
   - **T cell subset Assays**- Absolute CD4+ cell count is reduced with T4 : T8 ratio is reversed
   - **Platelet count**-shows Thrombocytopenia.
   - **IgA and Ig Glevels** are raised
   - **Diminished cell mediated Immunity** as indicated by skin tests
   - **Lymph node biopsy** shows profound abnormalities

Laboratory Diagnosis of HIV infection

2.Specific Tests for HIV infection- Diagnosis depends on the demonstration of antibodies to HIV and/or the direct detection of HIV or one of its components

Detection of antigen - p24 Capture ELISA assay, is positive in about 30% of the infected persons.

- In the first few weeks after infection and in the terminal phase, the test is uniformly positive

Detection of antibodies - It takes 2-8 weeks to months for the antibodies to appear in circulation

Recently, the interval **between infection and detection (window period) has decreased** from 22 days for antibody testing to 16 days with p24 antigen testing and subsequently to 12 days with NAT

Laboratory Diagnosis of HIV infection

ELISA (most frequently used method for screening for HIV antibody)

1)First generation - whole viral lysates

2)Second generation - recombinant antigen

3)Third generation - synthetic peptide

4)Fourth generation - antigen + antibody (Simultaneous detection of HIV antigen and antibody) - HIV duo

Laboratory Diagnosis of HIV infection

Supplemental Tests

- Western Blot Test (*gold standard*)
- Indirect Immunoflorescence test
- Radio ImmunoPrecipitaion Assay

Rapid Tests

a) Dot Blot assay

b) Particle Agglutination tests

c) HIV spot and comb test

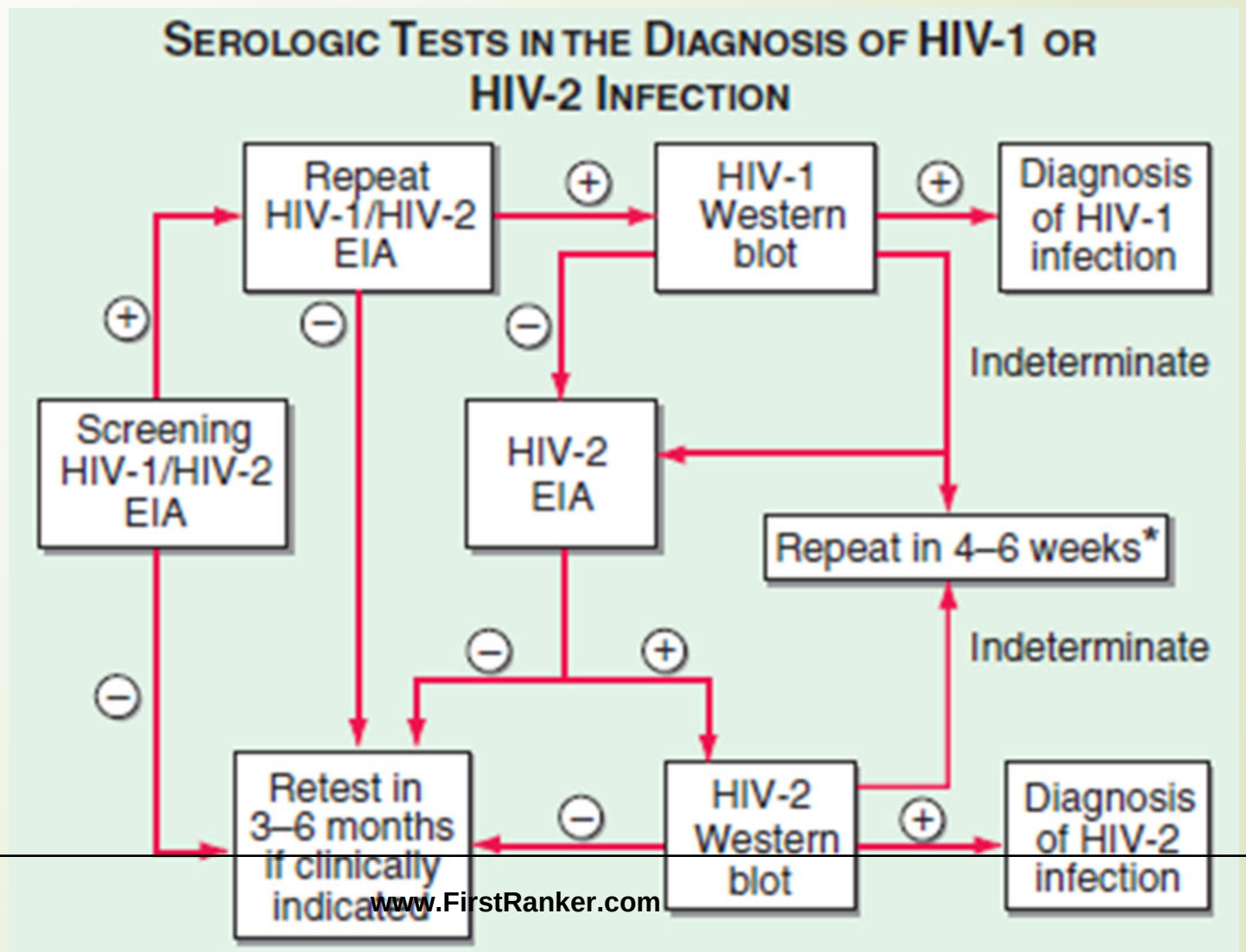
d) Flurimetric microparticle techn

Laboratory Diagnosis of HIV infection

Demonstration of viral Nucleic acid

- Three different **PCR** techniques namely
  - RT- PCR,
  - Nucleic acid sequence based amplification (NASBA) and
  - branched-DNA (b-DNA) assay have been employed to develop commercial kits

Extremely high sensitivity



Clinical Manifestations

The center for disease control (CDC) has classified the clinical course of HIV infection under various groups.

1. **Acute HIV infection**
2. **Asymptomatic or Latent infection**
3. **Persistent generalized lymphadenopathy (PGL)**
4. **AIDS related complex**
5. **Full blown AIDS (Last stage)**

Thank you