



Infections of Lymphocytes (1) HIV/AIDS

University of Jordan

Malik Sallam, M.D., Ph.D.

School of Medicine

Department of Pathology, Microbiology and Forensic Medicine



Background on AIDS

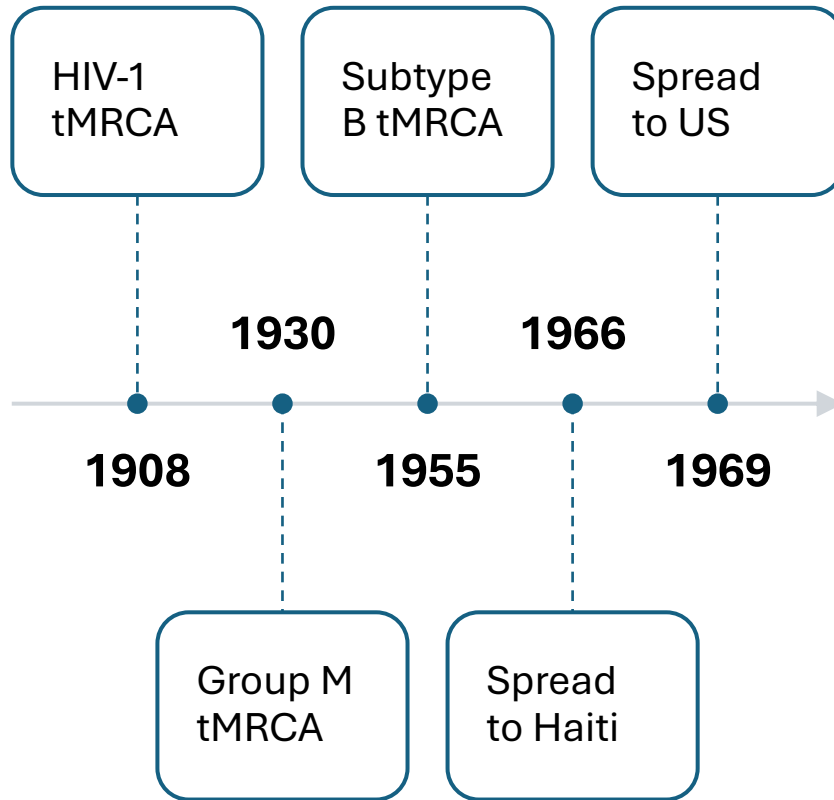
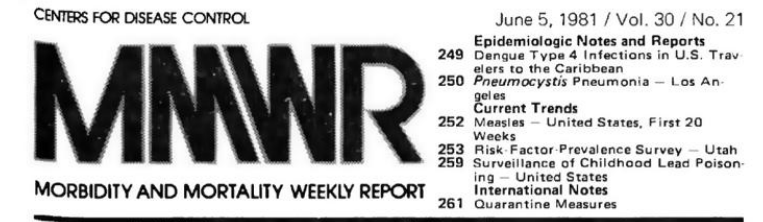
1981 Reporting of AIDS

1982 AIDS term coined

1983 HIV-1 isolated

1990 AZT approved

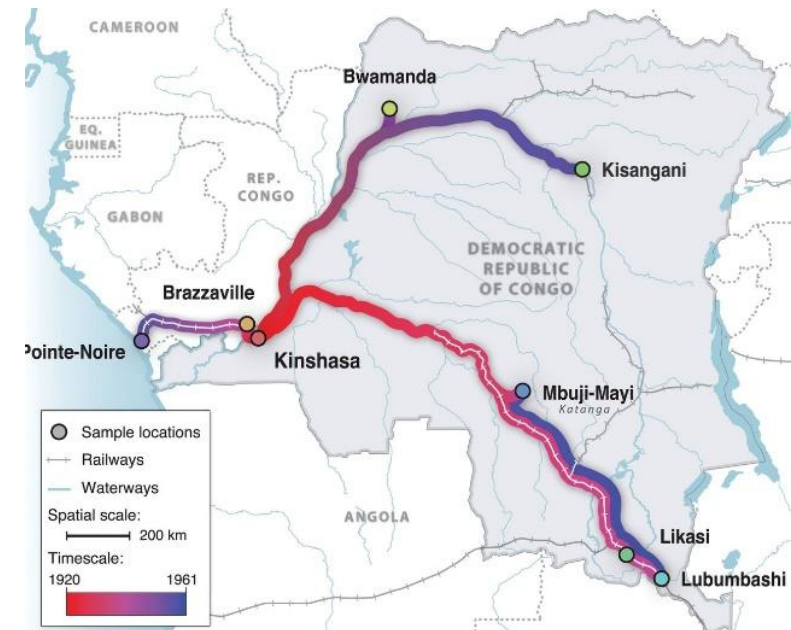
1996 Hit early hit hard



Pneumocystis Pneumonia — Los Angeles

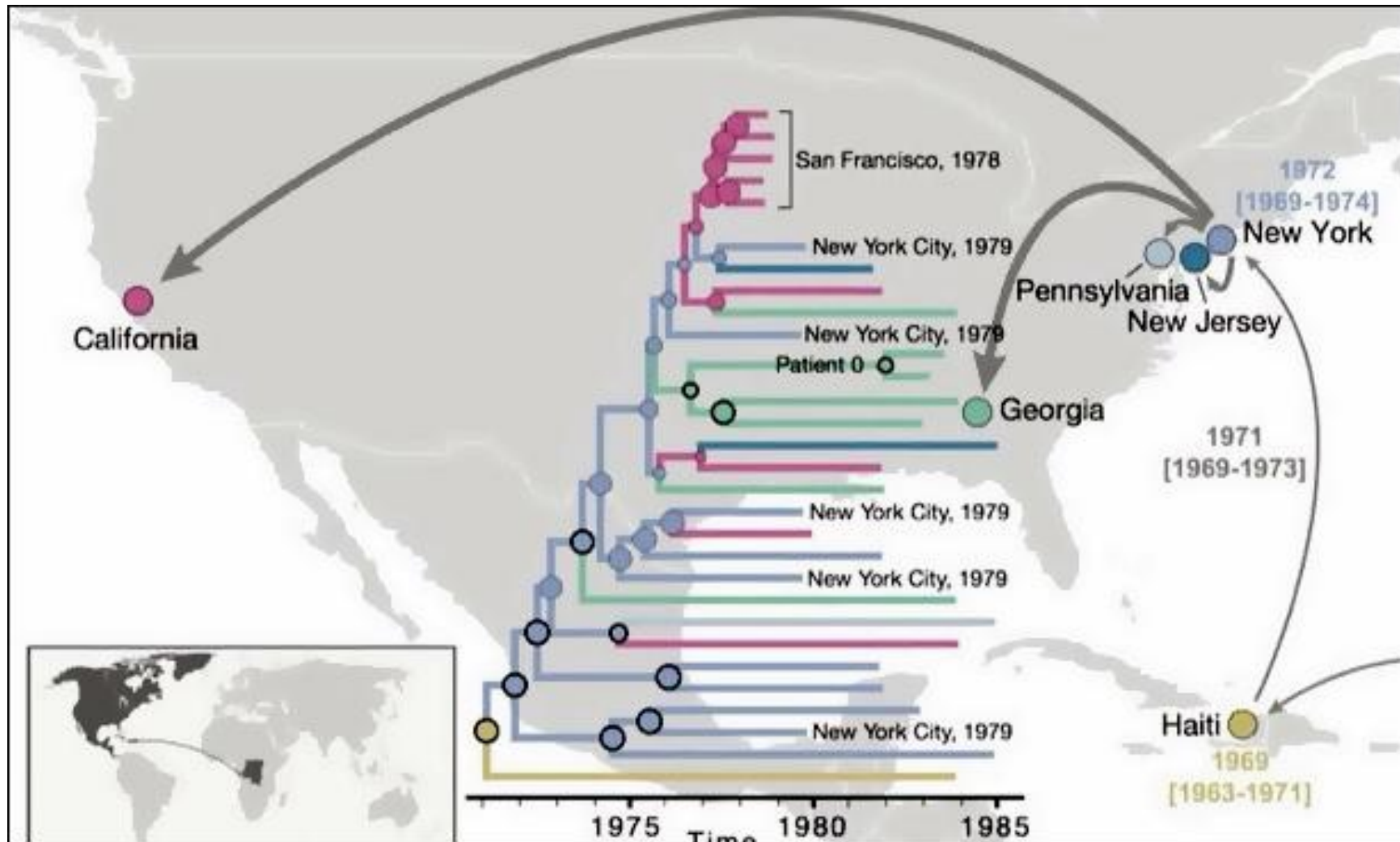
In the period October 1980-May 1981, 5 young men, all active homosexuals, were treated for biopsy-confirmed *Pneumocystis carinii* pneumonia at 3 different hospitals in Los Angeles, California. Two of the patients died. All 5 patients had laboratory-confirmed previous or current cytomegalovirus (CMV) infection and candidal mucosal infection. Case reports of these patients follow.

Patient 1: A previously healthy 33-year-old man developed *P. carinii* pneumonia and oral mucosal candidiasis in March 1981 after a 2-month history of fever associated with



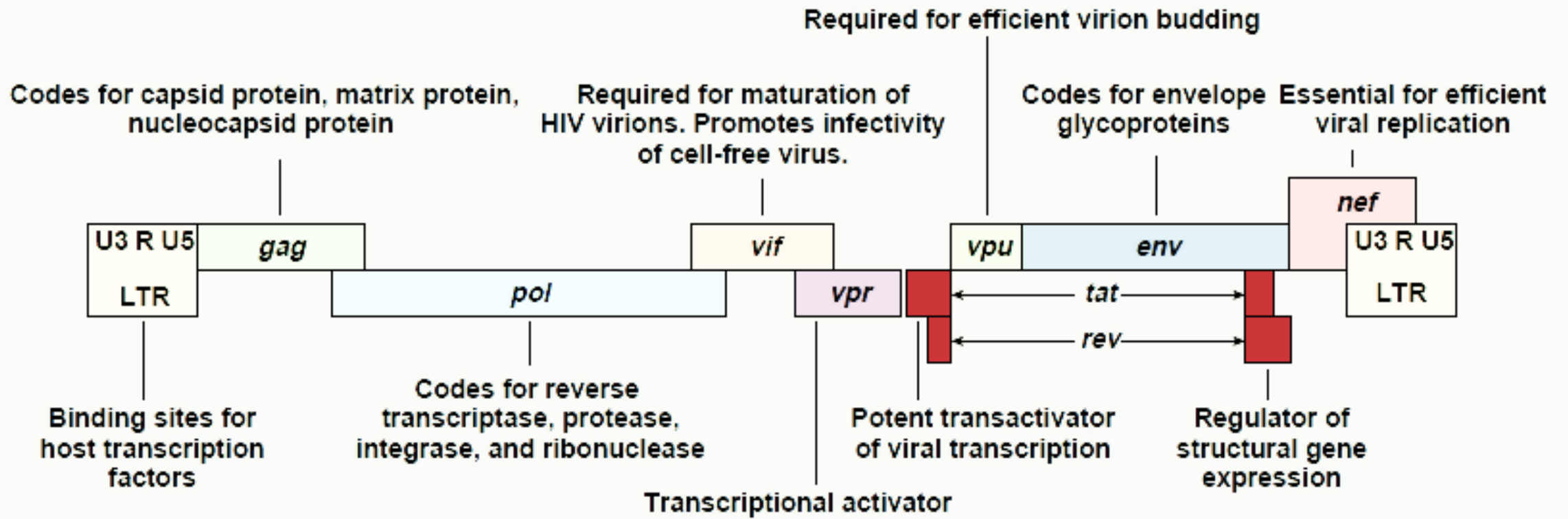


Background



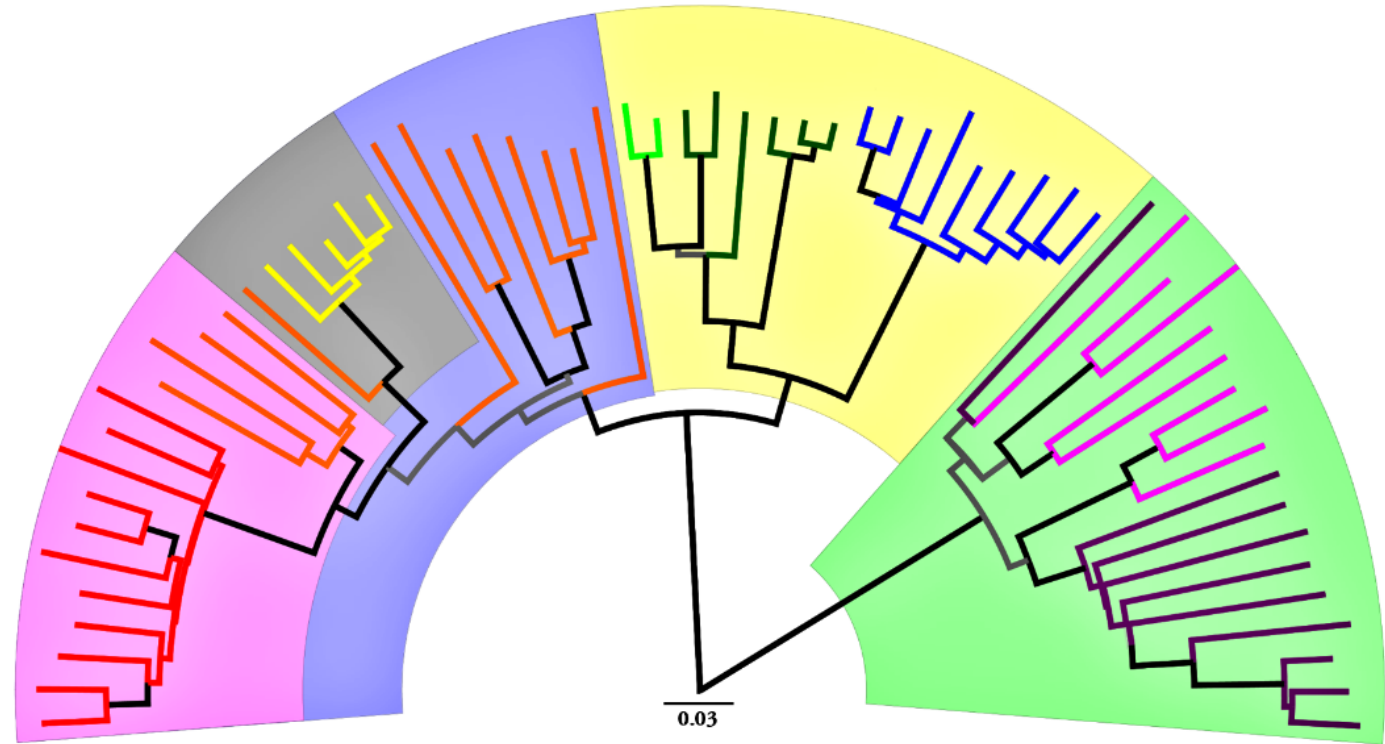


HIV Genome





Classification of HIV



Pan troglodytes



SIV_{cpz}

Homo sapiens



HIV-1
group M

HIV-1
group N

HIV-2

HIV-1
group O

HIV-1
group P

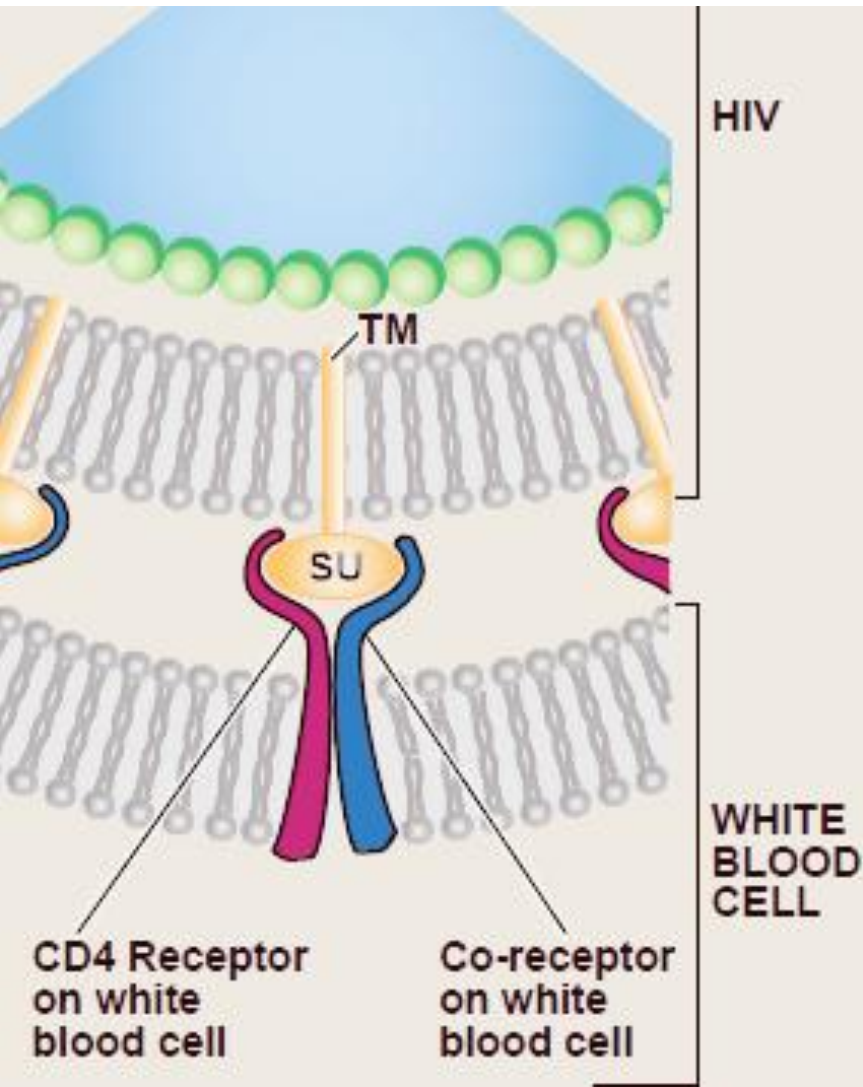
Gorilla gorilla



SIV_{gor}



HIV: Important Features



- *Natural Host:* Human.
- *Tropism:* CD4+ T cells, MΦ and DCs
- *Cellular receptors* CD4 + (CCR5 and/or CXCR4)
- *Geography:* Worldwide (HIV-1 group M); West Africa (HIV-2)



Epidemiologic characteristics of HIV-1/AIDS

- According to WHO, an estimated 41 million people were living with HIV at the end of 2025. 1.2 million people acquired HIV in 2025. Since 2010, the annual number of people acquiring HIV has been reduced by 42%
- In 2025, 570,000 people died from HIV-related causes globally. Since 2010, the annual number of HIV-related deaths has been reduced by 57%
- The unequal distribution of HIV/AIDS around the world is notable mostly in Sub-Saharan Africa.
- The global targets are that 95% of people living with HIV should know their HIV status (first 95), that 95% of people living with HIV who know their HIV status are on ART (second 95) and that 95% of people on ART have viral suppression (third 95).

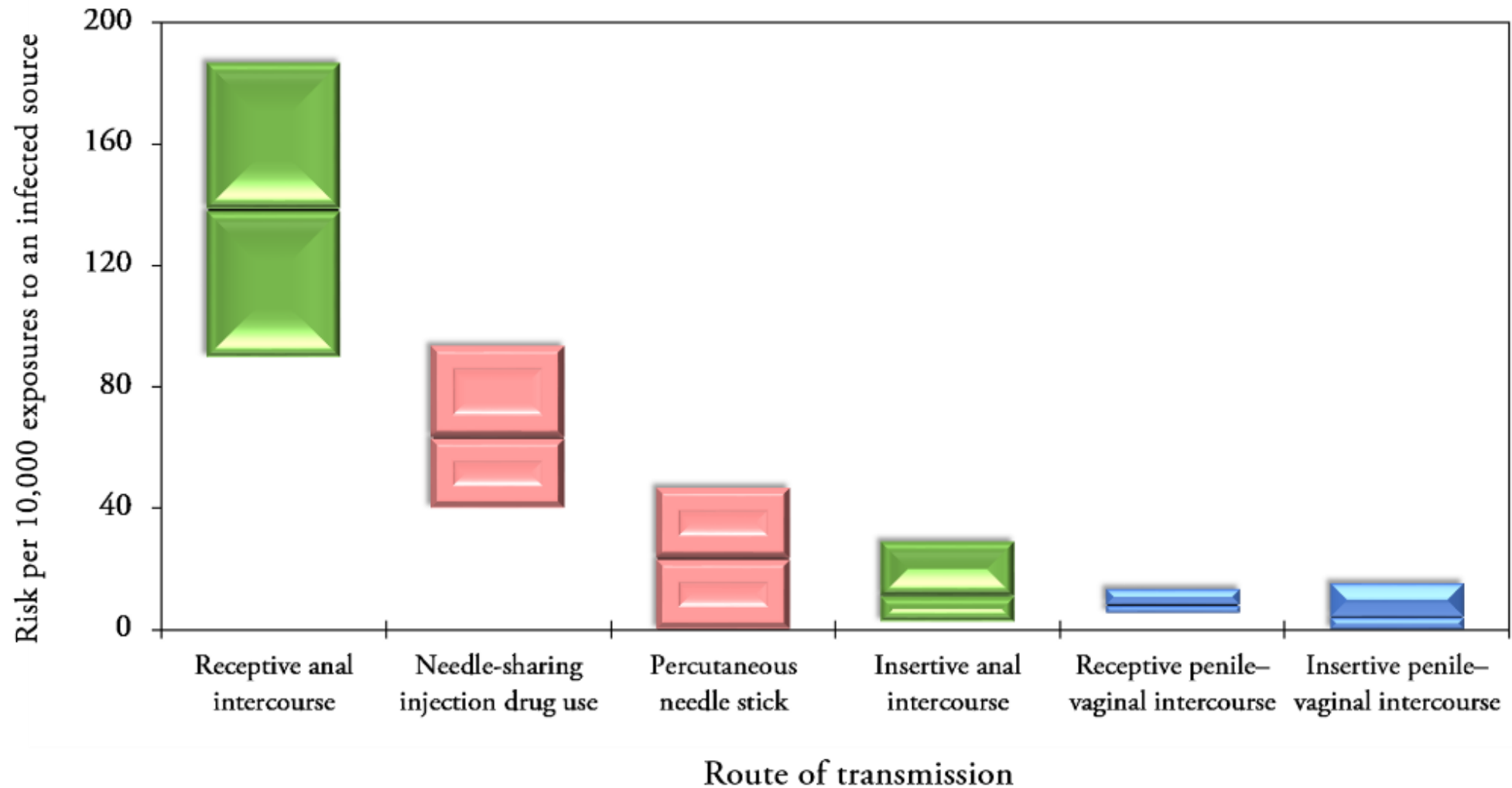


HIV-1 Transmission

- HIV-1 is a blood-borne virus (i.e. it can be transmitted through transfusion, needlestick injury and IDU) and the infection can be considered an STI (occurring through homosexual and heterosexual practices via vaginal, penile and anal mucosa).
- Vertical transmission can occur in utero, perinatally and through breast milk of infected mothers.
- Nowadays, the most common mode of transmission globally is HET contact but different regions differ in the most common route (e.g. MSM in US and Western Europe, IDU in Former Soviet Union countries and HET in sub-Saharan Africa).

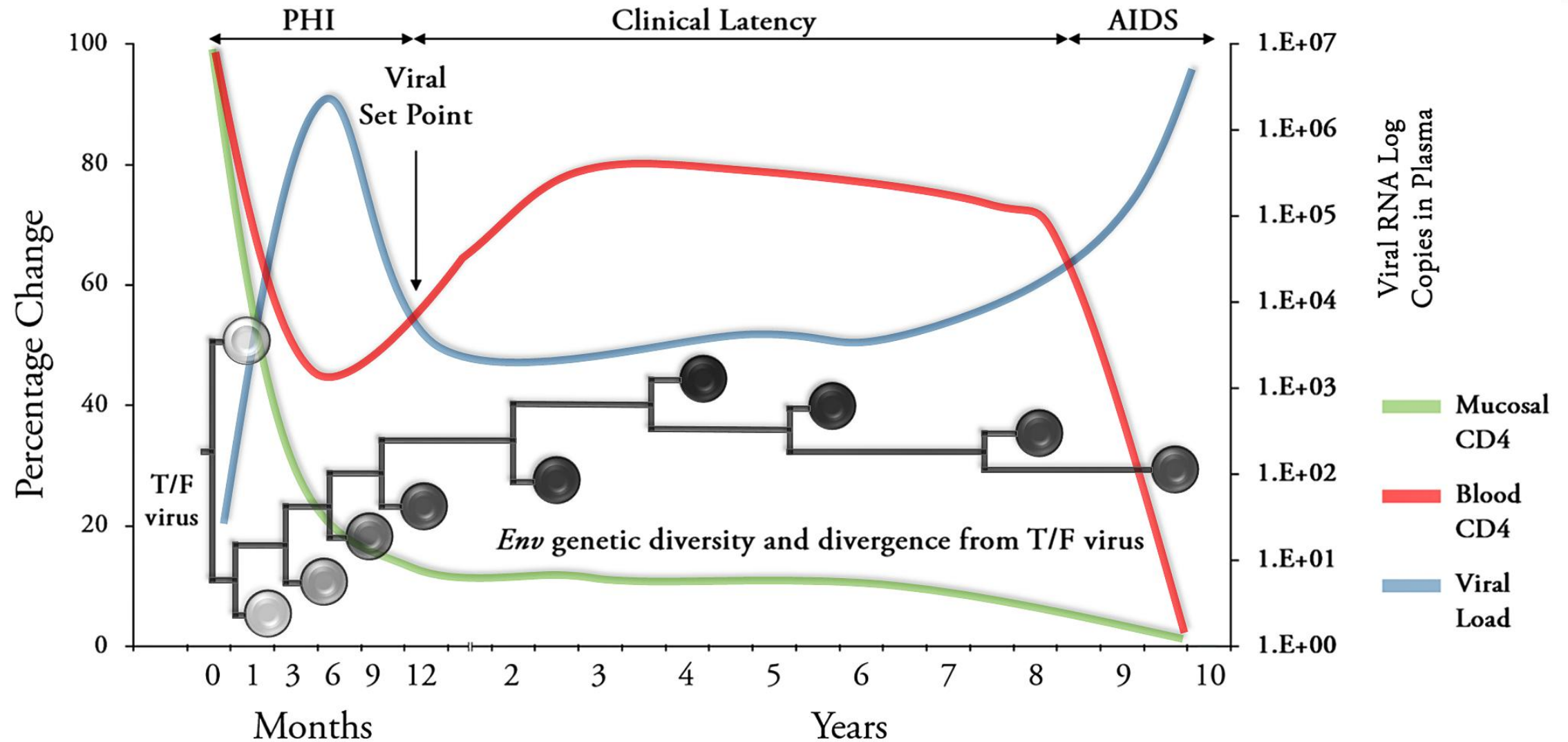


HIV-1 Transmission





HIV-1 Pathogenesis





HIV-1 Pathogenesis

The distinctive feature of HIV-1 infection is the progressive quantitative and qualitative deficiency of CD4⁺ T cells.

After HIV-1 inoculation, the virus infects its target cells, mostly macrophages through binding of gp120 (part of ENV) to CD4 and chemokine receptors CCR5 or CXCR4.

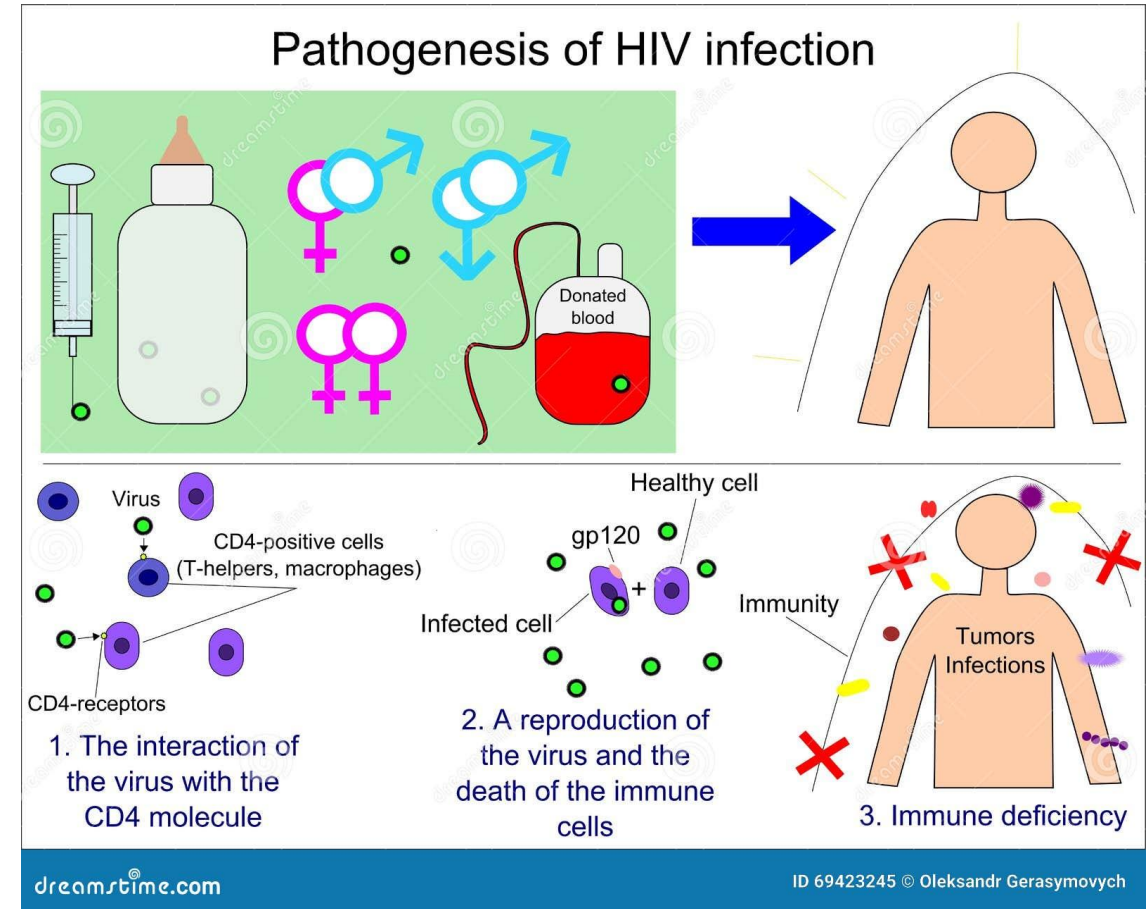
The virus starts to establish the infection for about 10 days locally before systemic spread.

Subsequent virus spread into the lymphoid tissues including the gut-associated lymphoid tissue (GALT), ends-up in the establishment of infection chronically.



HIV Pathogenesis

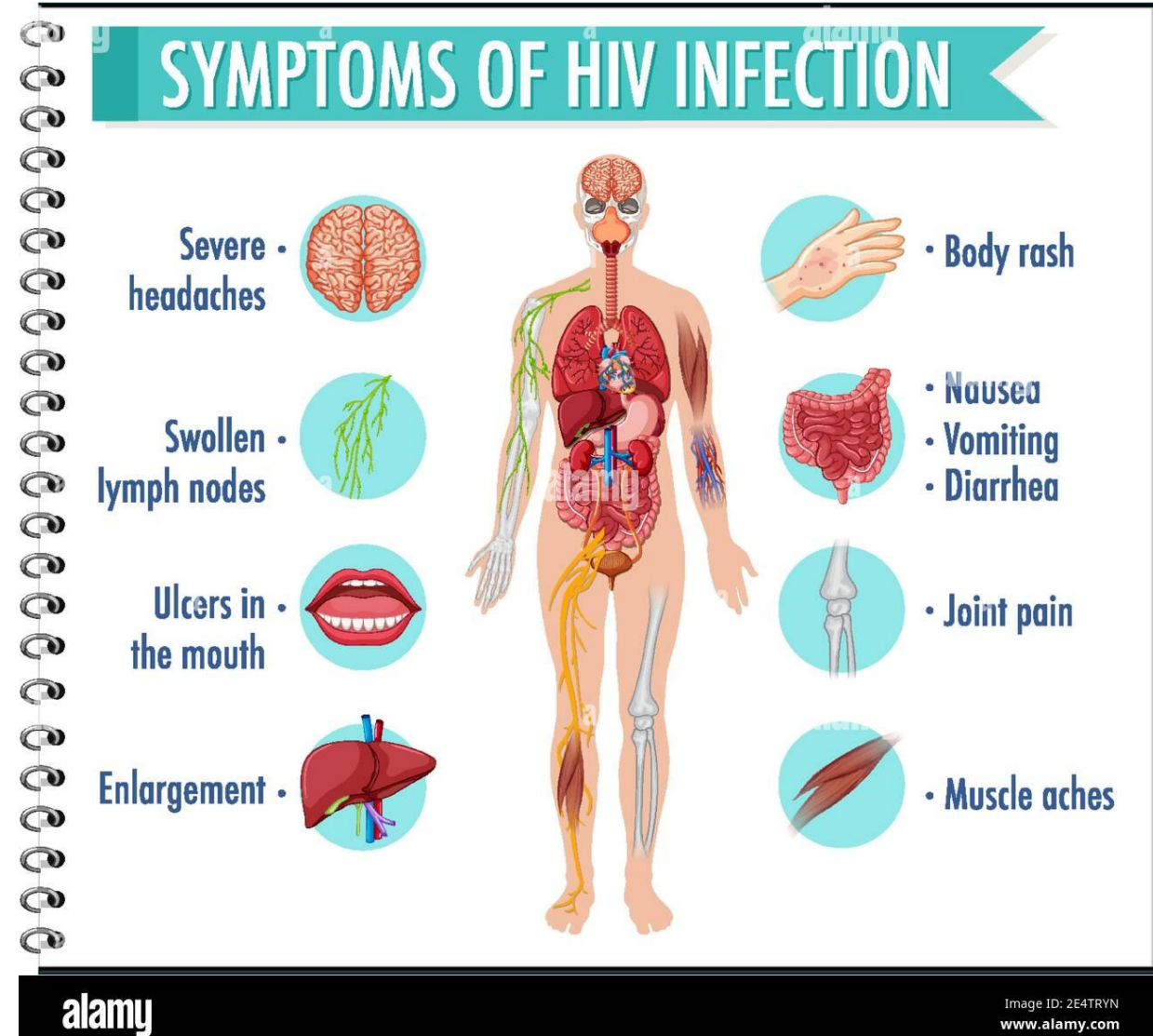
- Viremia follows, which remains at high levels for about 8-12 weeks, coinciding with mononucleosis-like features.
- The significant decline of CD4 cells at this phase is related to loss of memory cells in the GALT.
- The adaptive immune response takes over at this stage to control viral replication manifested in the decline of viral load to the lowest level “viral set-point”, which fluctuates at low level throughout the clinical latency.
- HIV-1 set-point is considered an important prognostic marker for assessment of disease progression.





HIV Infection: Clinical Features

- Primary infection (first few months): Nonspecific and resemble those of infectious mononucleosis.
- Clinical latency (3-20 years, average 8-10 years): The majority of HIV-1 infected individuals remain asymptomatic during the clinical latency period, nevertheless, generalized lymphadenopathy might persist from the primary infection period.
- AIDS: **The diagnosis of AIDS is made at CD4 T cell count of less than 200/ μ L or the presence of an AIDS defining condition** (MAC, PCP, extrapulmonary TB, PML, KS, toxoplasmosis, cryptococcosis, esophageal candidiasis, lymphomas, etc.).

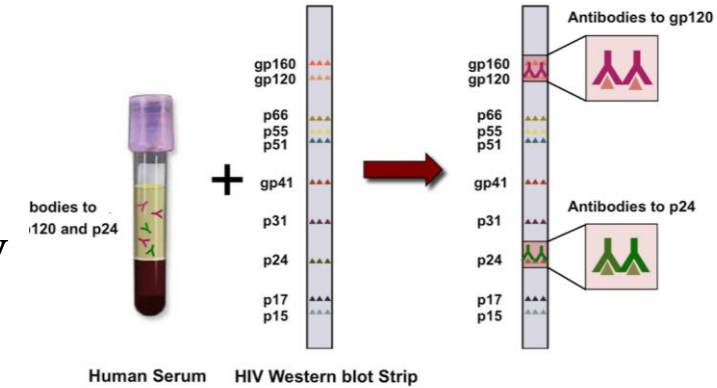
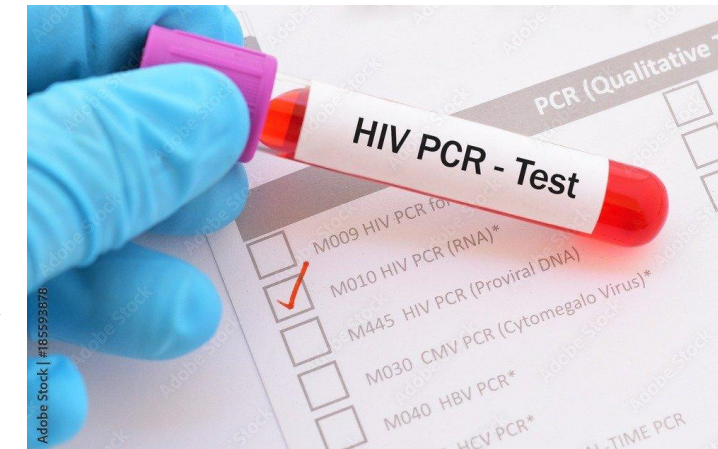




Diagnosis of HIV infection

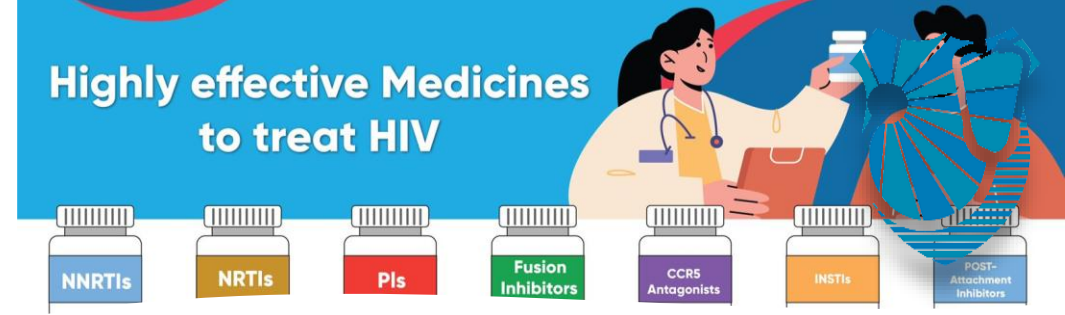


- Fourth-generation HIV-1/2 Ag-Ab immunoassays are used for screening. These simultaneously detect HIV-1 p24 antigen and antibodies to HIV-1 and HIV-2
- A reactive screening result is followed by an HIV-1/HIV-2 antibody differentiation immunoassay. If negative or indeterminate, HIV-1 NAT is performed to investigate possible acute HIV-1 infection
- The interval between HIV acquisition and test detectability varies according to the assay. A negative result during this period does not reliably exclude recent infection
- Western blot is no longer recommended as the routine confirmatory test in contemporary HIV diagnostic algorithms.





Management



- ART is recommended regardless of CD4 T-cell count or clinical stage, and should be initiated ASAP after diagnosis
- ART regimens consist of three ARV drugs, although selected two-drug regimens might be effective in certain cases
- HIV viral load is the marker of treatment response, while CD4 T-cell counts assess immune status to guide opportunistic infection prophylaxis
- Effective ART achieves sustained viral suppression, promotes immune recovery, prevents HIV-related complications, and enables people with HIV to achieve a near-normal life expectancy
- ART suppresses viral replication but does not eradicate persistent HIV reservoirs. Rare cases of sustained HIV remission or cure following specialized stem-cell transplantation do not represent a feasible routine treatment strategy



Management and prevention

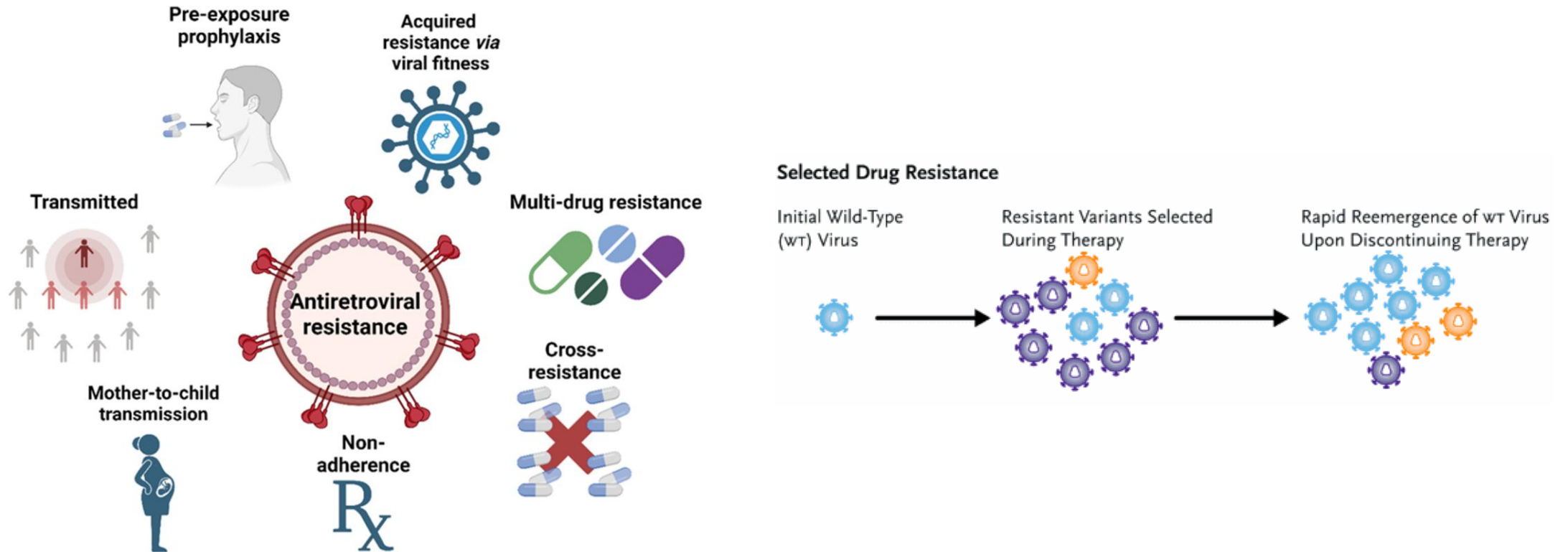
- The latency of HIV-1 infection is evident upon treatment interruption which will lead to resurgence of viral replication.
- ARV drugs are classified currently based on its mechanism of action

Drug class	Examples
NRTIs	Tenofovir, emtricitabine, lamivudine, abacavir
NNRTIs	Doravirine, rilpivirine, efavirenz
Protease inhibitors (PIs)	Darunavir, atazanavir
Integrase inhibitors (INSTIs)	Bictegravir, dolutegravir, cabotegravir
CCR5 antagonists	Maraviroc
Fusion inhibitors	Enfuvirtide
Attachment inhibitors	Fostemsavir
Post-attachment inhibitors	Ibalizumab
Capsid inhibitors	Lenacapavir



Management

Several biologic properties of HIV-1 make the emergence of drug resistance an inevitable outcome in the individuals receiving suboptimal ART (high rate of mutation, possibility of recombination).





HIV infection prevention



National Centre for
Infectious Diseases

NATIONAL
HIV
PROGRAMME

PRE-EXPOSURE
PROPHYLAXIS

PrEP

Pre-exposure prophylaxis (PrEP) is a risk-reduction treatment against HIV. This treatment involves HIV medicine for people who do not have HIV but are at risk of HIV infection. When taken as prescribed, PrEP is highly effective at preventing HIV infection.



In the absence of an effective vaccine prevention relies on:

- Early diagnosis and timely initiation of ART reduce disease progression and onward transmission
- Sustained viral suppression through effective ART prevents sexual transmission of HIV and substantially reduces vertical transmission
- Oral or long-acting injectable PrEP prevents HIV acquisition, while PEP must be initiated within 72 hours of exposure and continued for 28 days
- Behavioral and harm-reduction measures



Thank You!