



Infections of Lymphocytes (1) HIV/AIDS

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Background on AIDS

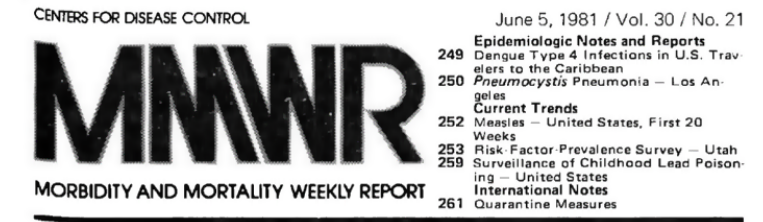
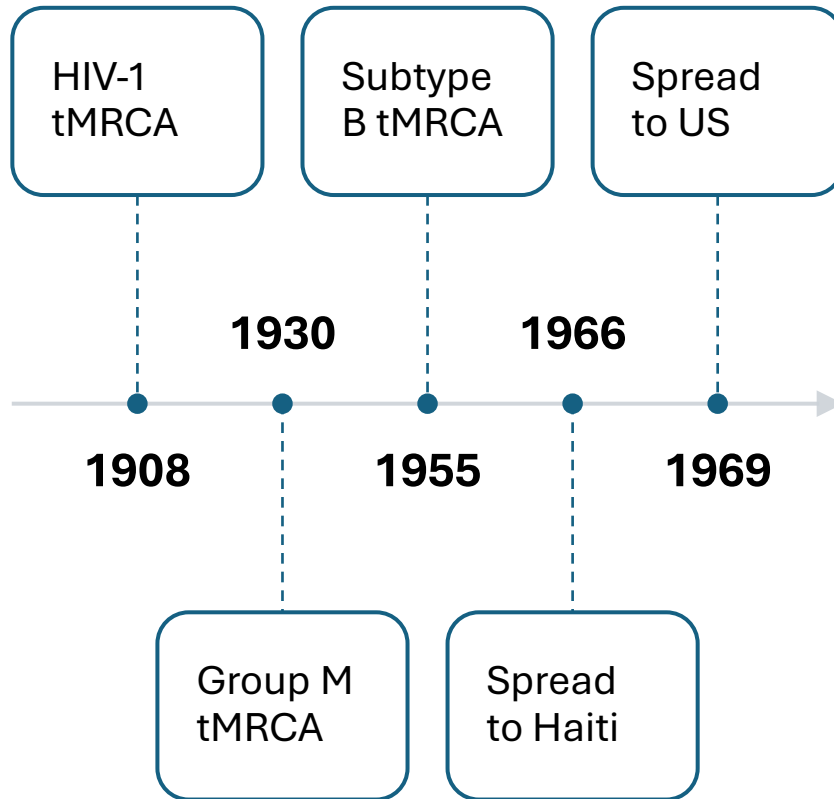
1981 Reporting of AIDS

1982 AIDS term coined

1983 HIV-1 isolated

1990 AZT approved

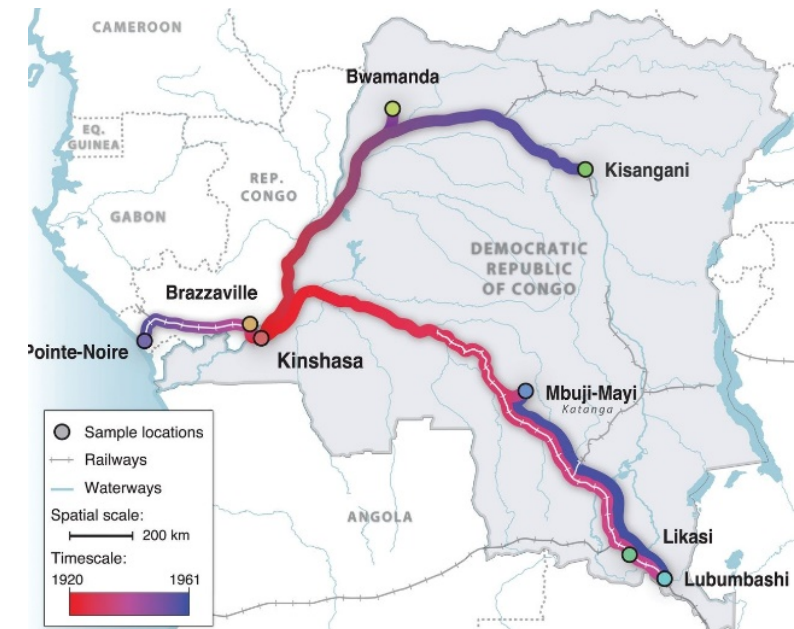
1996 Hit early hit hard



Pneumocystis Pneumonia — Los Angeles

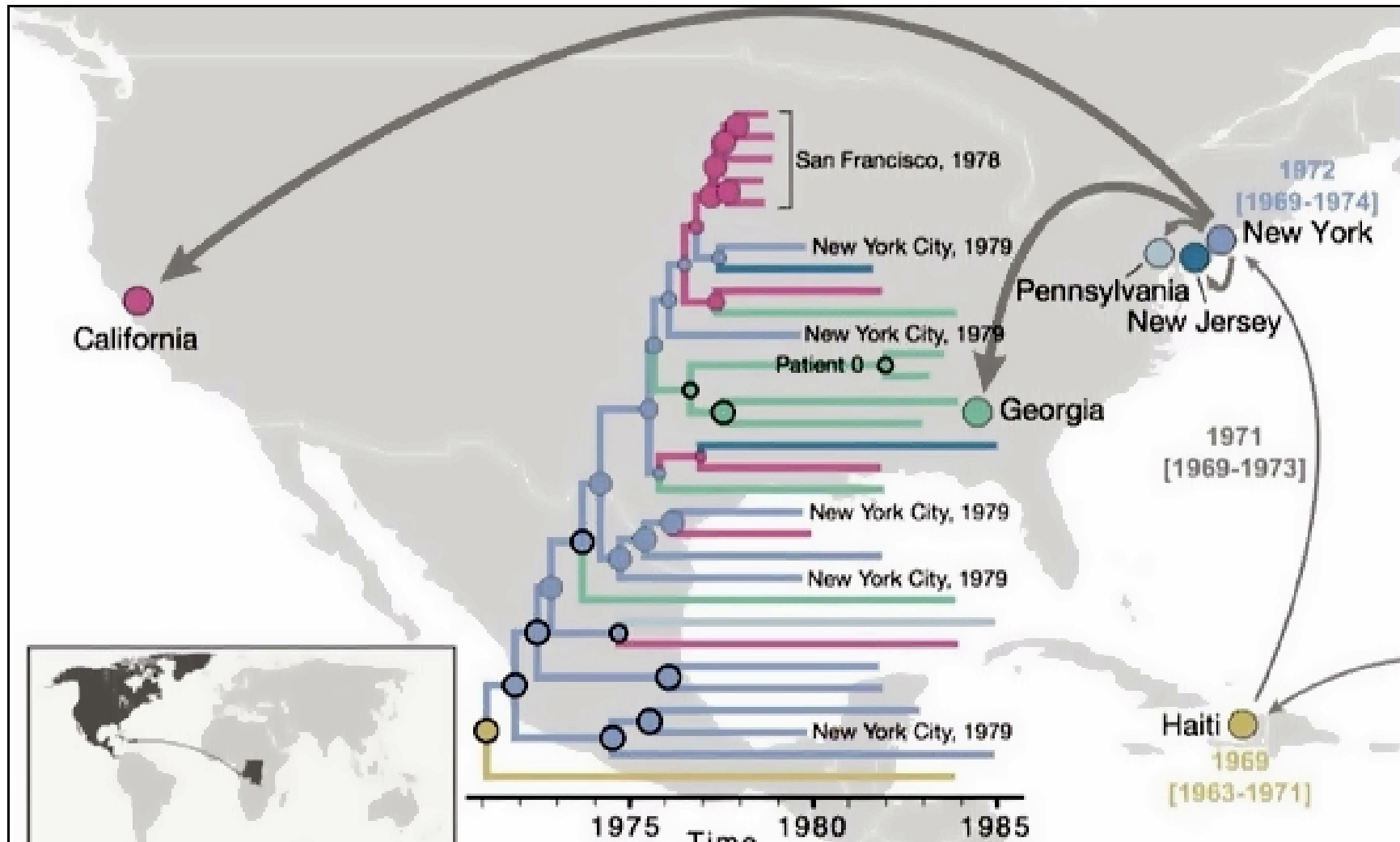
In the period October 1980-May 1981, 5 young men, all active homosexuals, were treated for biopsy-confirmed *Pneumocystis carinii* pneumonia at 3 different hospitals in Los Angeles, California. Two of the patients died. All 5 patients had laboratory-confirmed previous or current cytomegalovirus (CMV)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



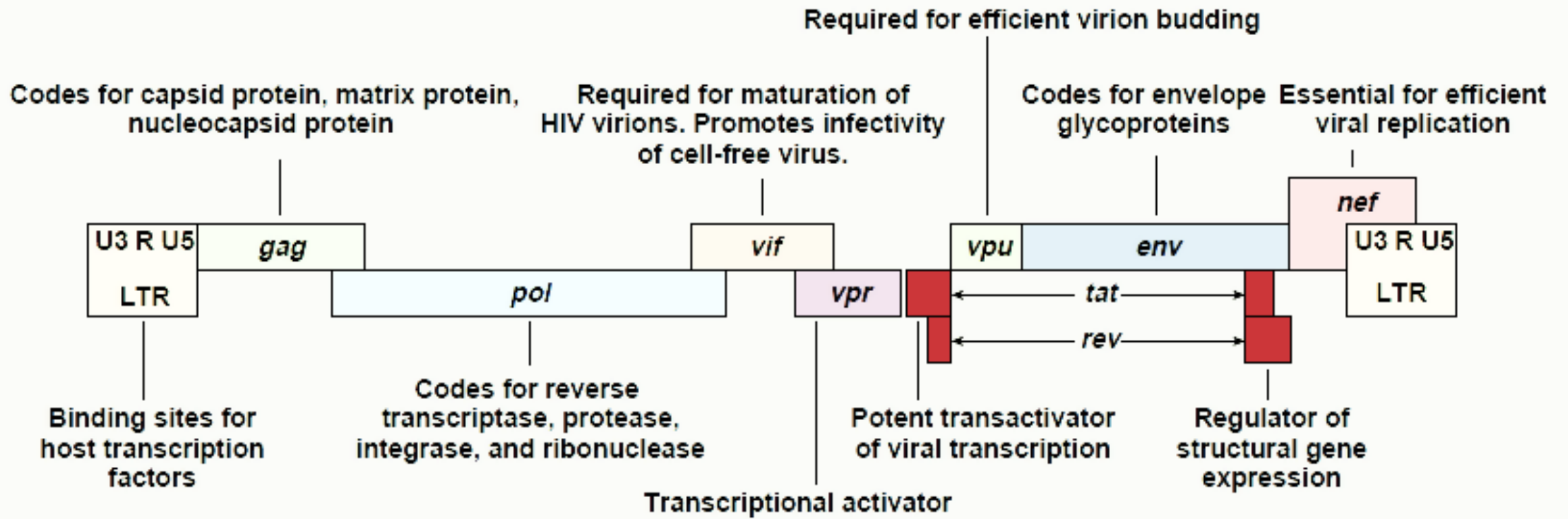


Background



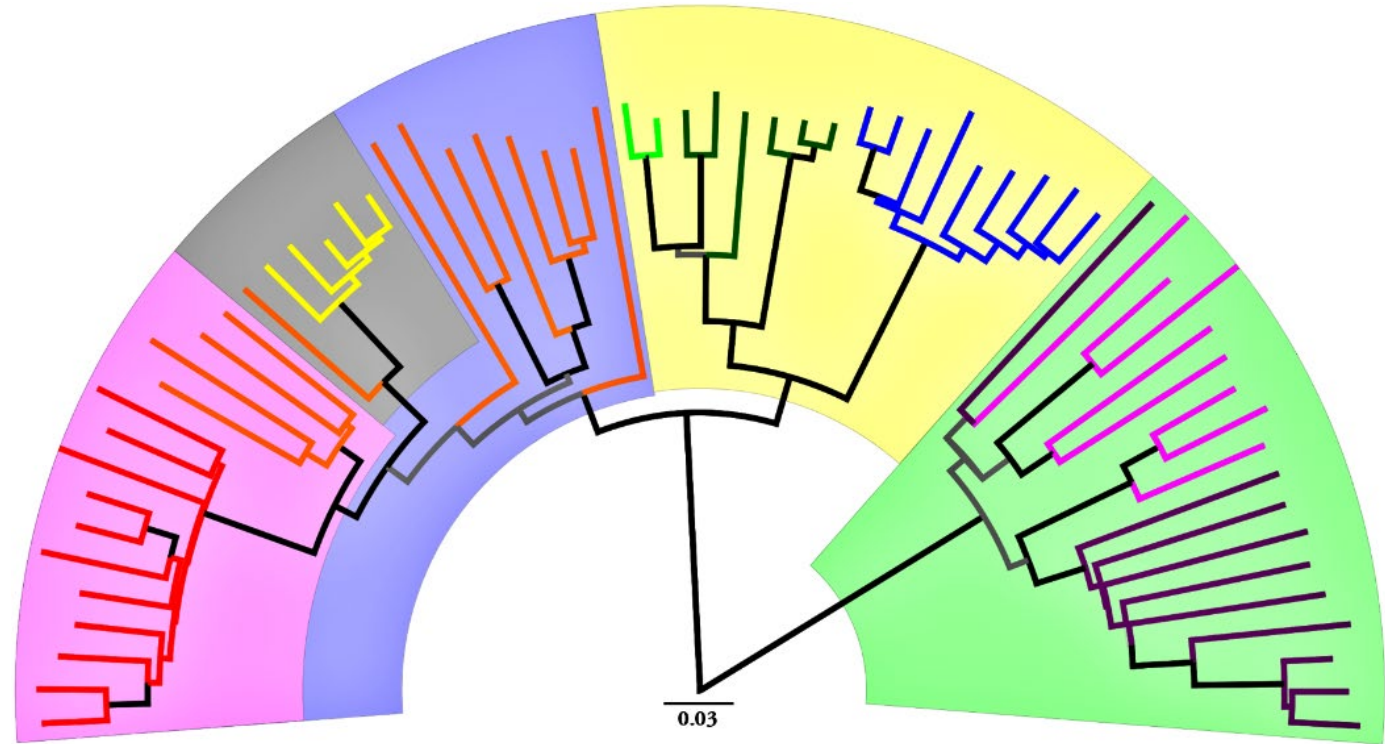


HIV Genome





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

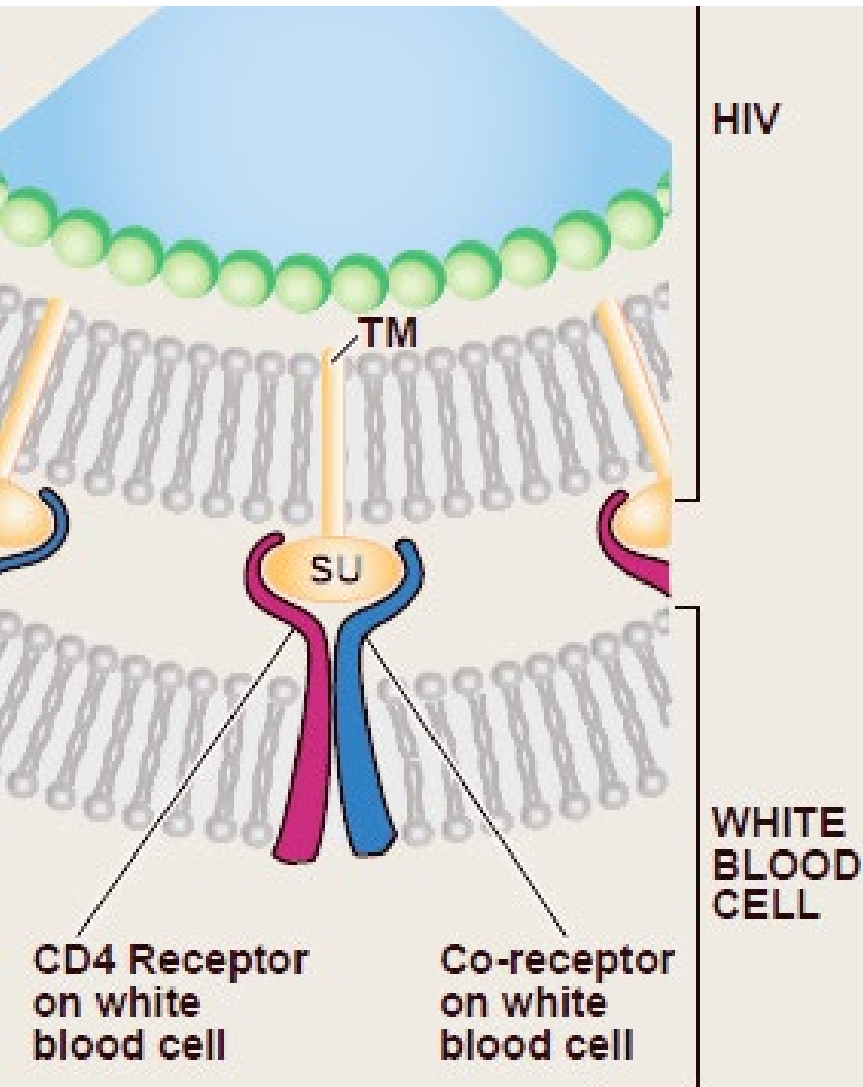
Gorilla gorilla



SIV_{gor}



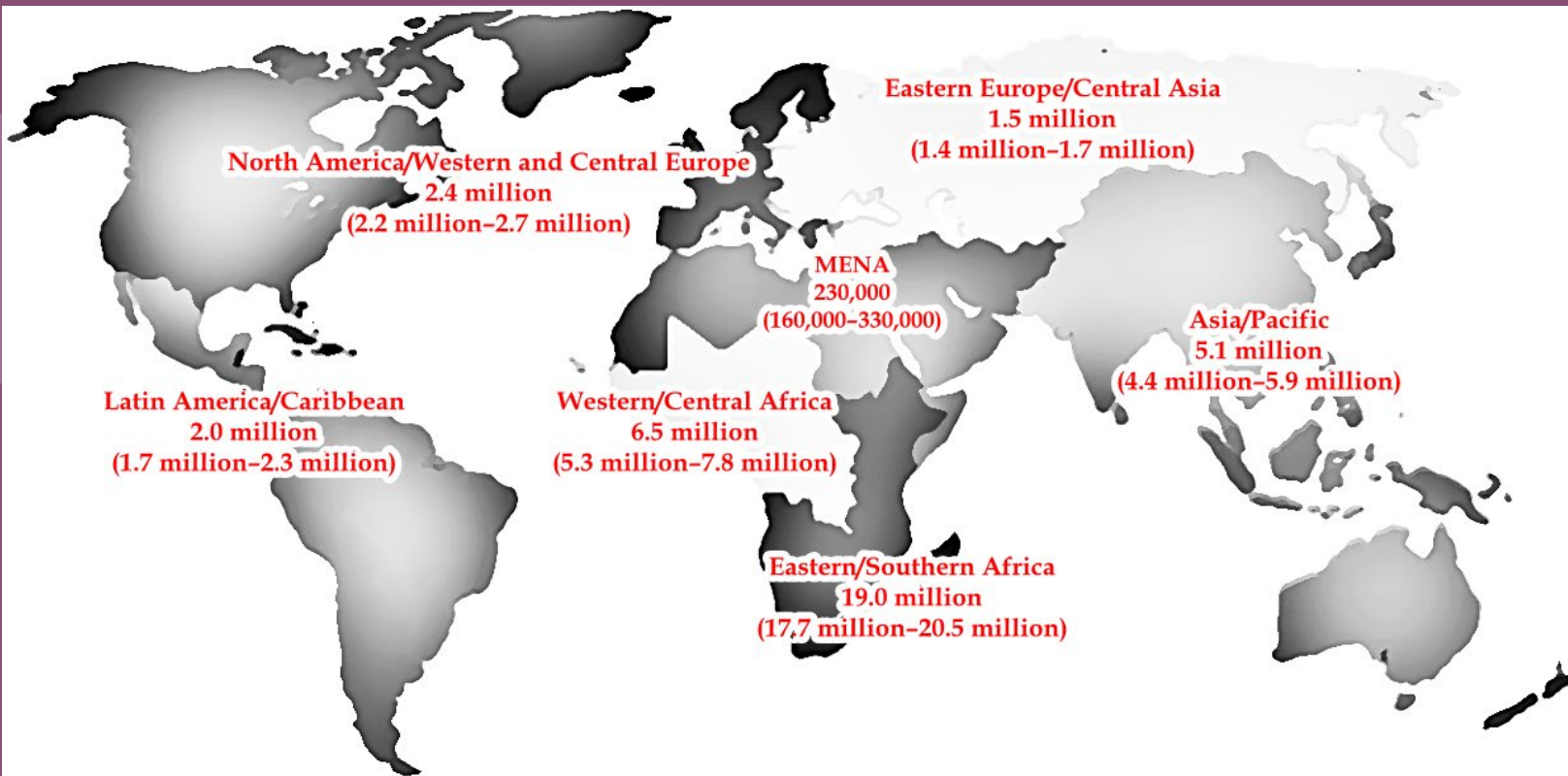
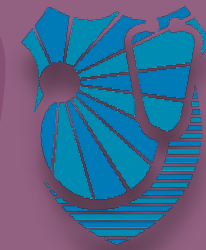
HIV: Important Features



- *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 UNAIDS, and by the end of 2024, about 40.8 million people were living with HIV/AIDS (PLWHA), of which about 1.3 million individuals acquired the infection in 2024.
- The unequal distribution of HIV/AIDS around the world is notable mostly in Sub-Saharan Africa, with more than two-thirds of PLWHA.

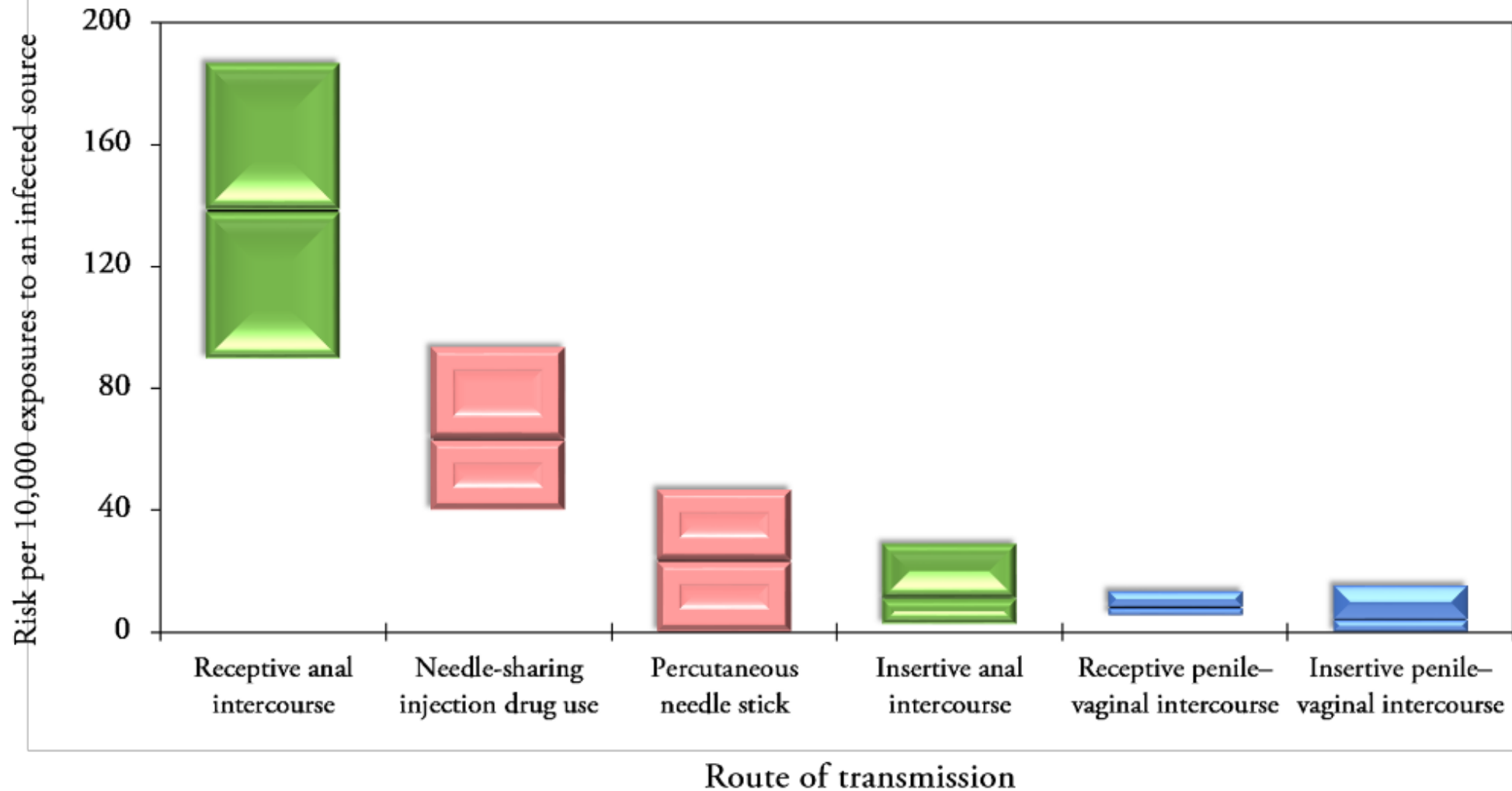


HIV-1 Transmission

- 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).

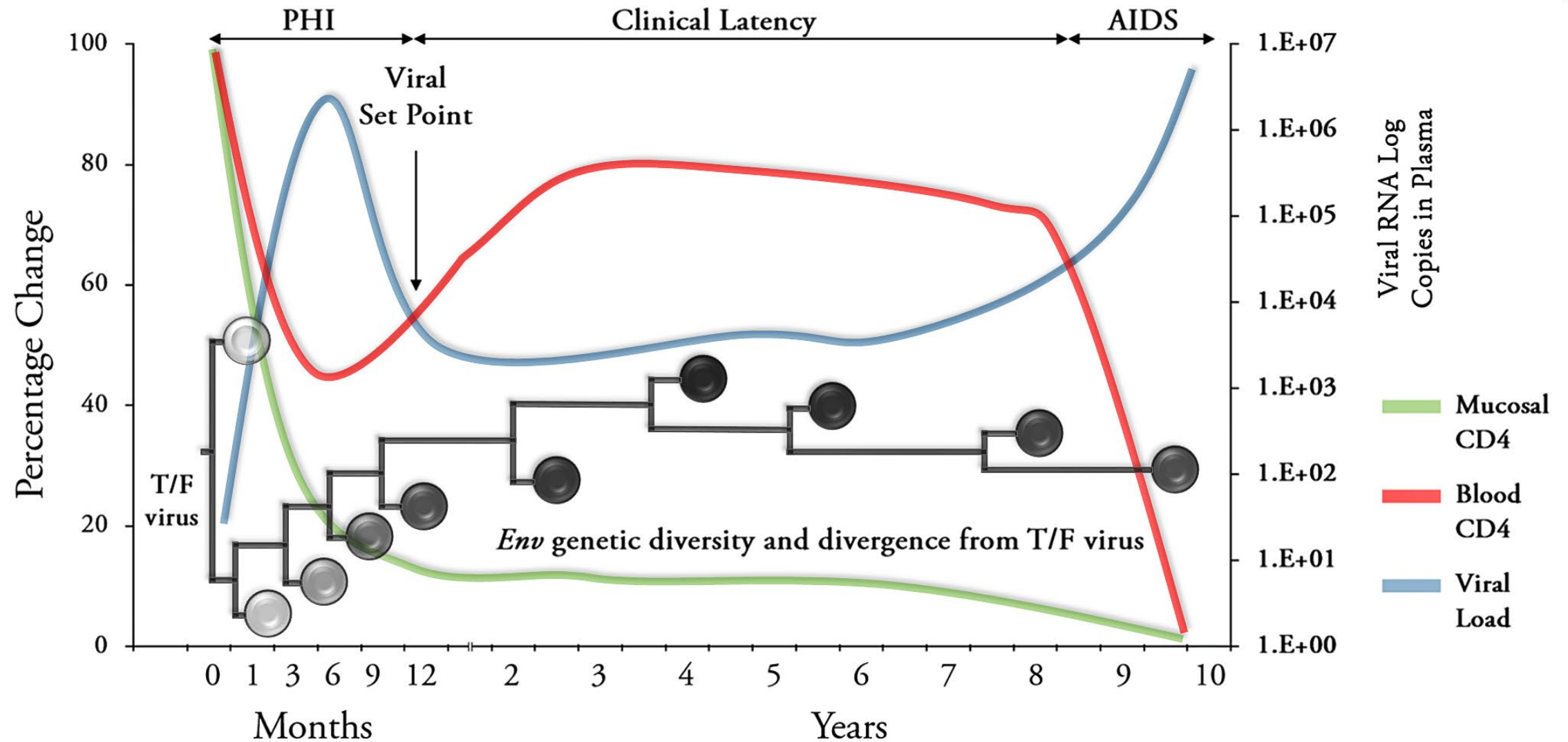


HIV-1 Transmission





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.

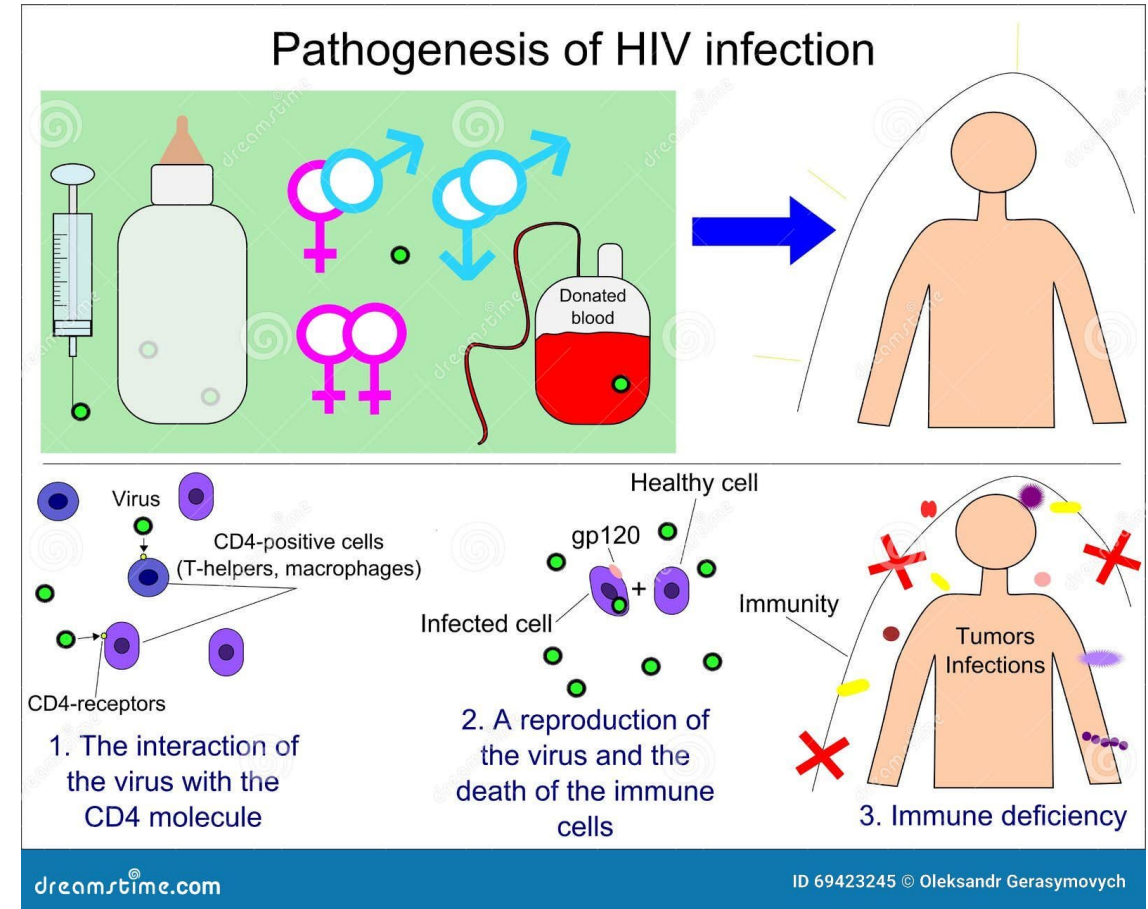
The virus starts to establish the infection for about 10 days locally before systemic spread.

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



HIV Pathogenesis

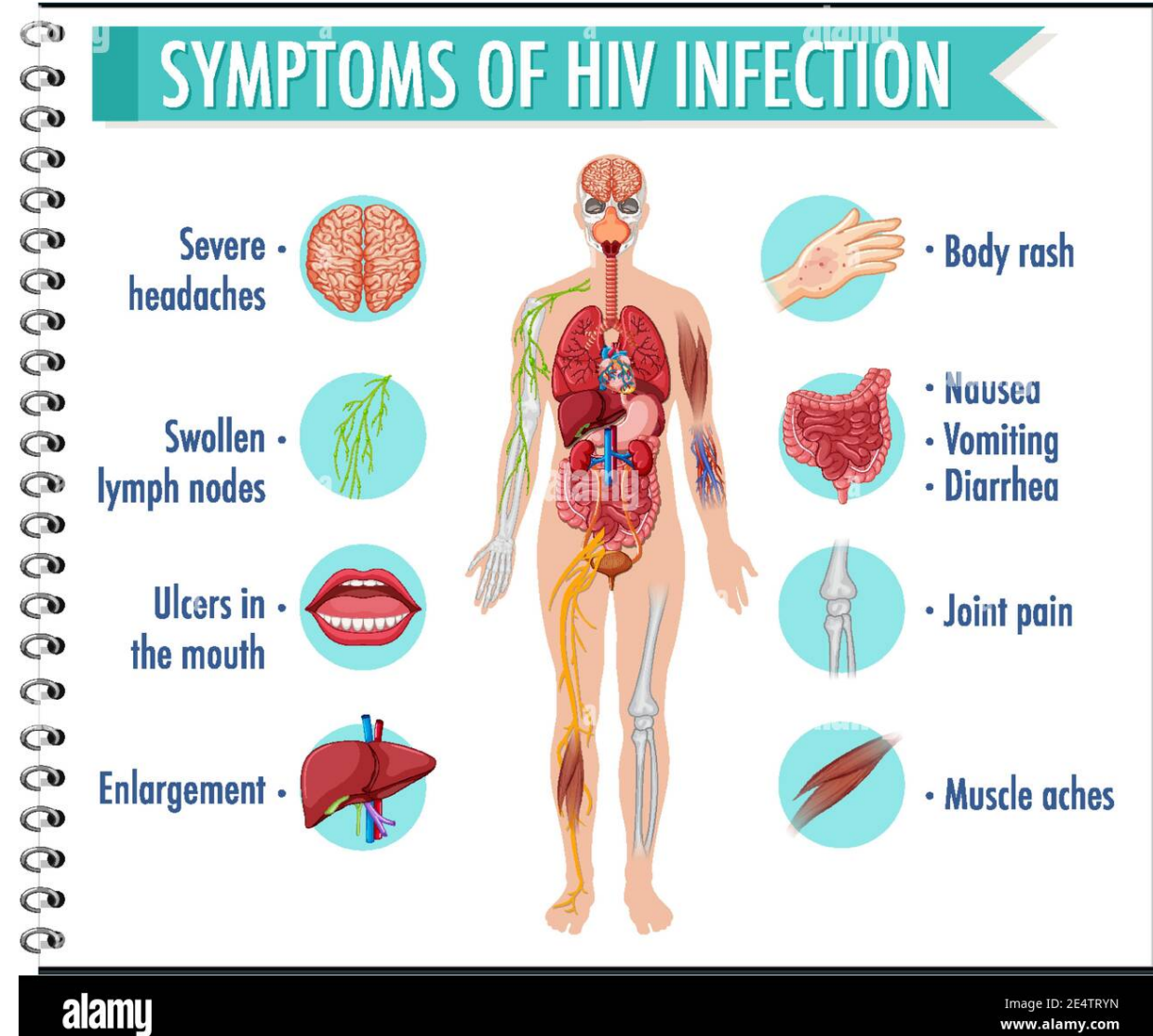
- Viremia follows, which remains at high levels for about 8-12 weeks, coinciding with mononucleosis-like features.
- The significant decline of CD4 cells at this phase is related to loss of memory cells in the GALT.
- The adaptive immune response takes over at this stage to control viral replication 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

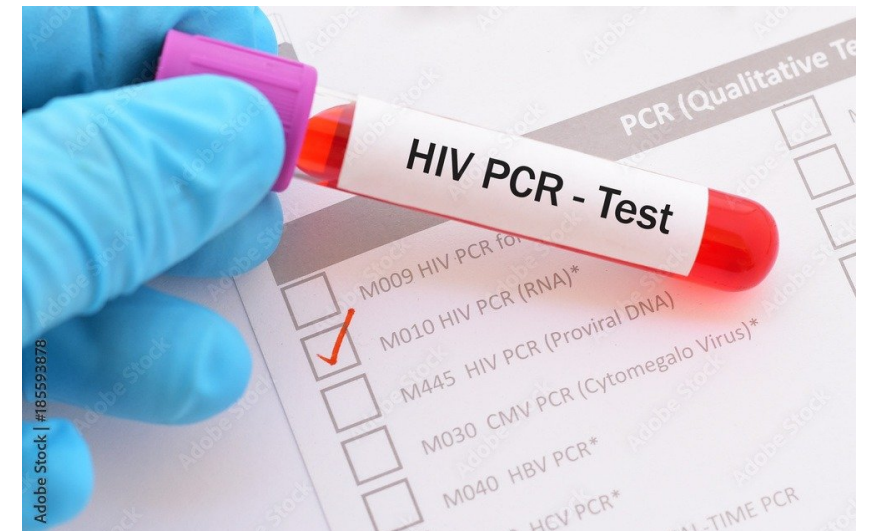
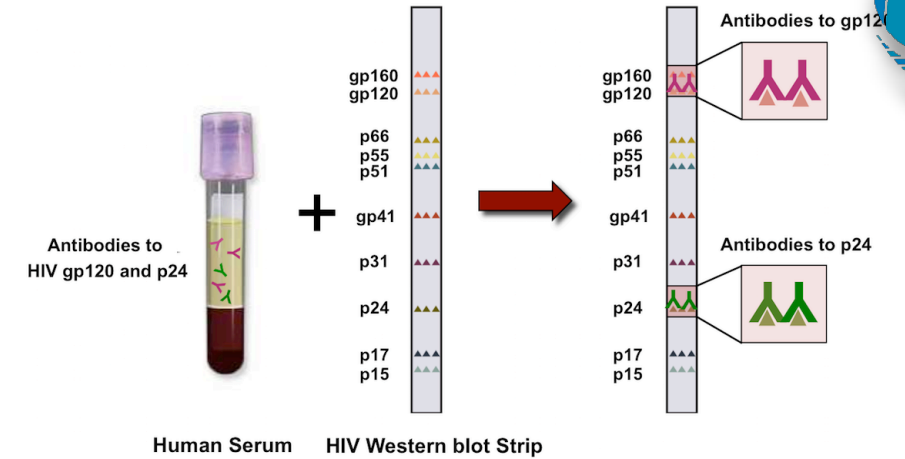
- Primary infection (first few months): Nonspecific and resemble those of infectious mononucleosis.
- Clinical latency (3-20 years, average 8-10 years): The majority of HIV-1 infected individuals remain asymptomatic during the clinical latency period, nevertheless, generalized lymphadenopathy might persist 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

- Screening for HIV-1 infection relies on enzyme immune assays combining the detection of Abs (IgM and IgG) to HIV-1 (groups M, O, and N) and HIV-2 together with detection of p24.
- This is followed if positive by a confirmatory test, mostly western blot or detection of HIV RNA.
- The biggest challenge in diagnosis is the presence of an interval between infection and detection (window period).





Highly effective Medicines to treat HIV



- CD4 T cell count and viral load measurements are used for evaluation of disease progression and response to ART.
- The cornerstone of HIV-1 management is the so-called HAART.
- Despite the incurable nature of HIV-1 infection so far (with the exception of the Berlin patient) the treatment with combinations of ART aims to suppress viral replication to a degree that permits the recovery of immune system responses to prolong the infected-individuals' survival.

Management



Diagnosis, management and prevention

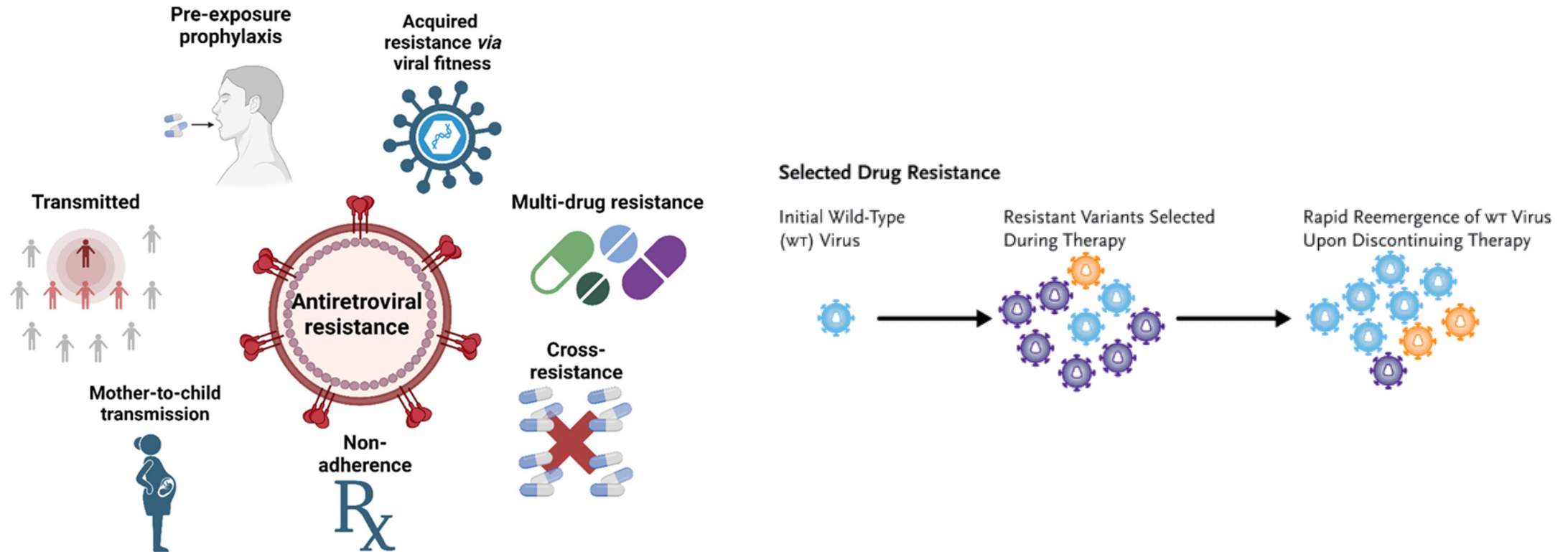
- The latency of HIV-1 infection is evident upon treatment interruption which will lead to resurgence of viral replication.
- ARV drugs are classified currently based on its mechanism of action into six classes.

NRTI	NNRTI	PI	Integrase Inhibitor	Fusion Inhibitor	CCR5 antagonist
Zidovudine	Nevirapine	Saquinavir	Raltegravir	Enfuvirtide	Maraviroc
Didanosine	Delavirdine	Ritonavir	Dolutegravir		
Stavudine	Efavirenz	Indinavir	Elvitegravir		
Lamivudine	Etravirine	Nelfinavir			
Abacavir	Rilpivirine	Atazanavir			
Tenofovir		Tipranavir			
Emtricitabine		Darunavir			



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 towards HIV-1 infection, the preventive efforts rely on the following measures:

- HIV-1 testing among most-at-risk groups
- Consideration of PrEP and PEP among individuals at risk with early initiation of ART among HIV-1 infected people
- Counselling and education of at-risk groups regarding the behavioral practices that are associated with higher probability of transmission (e.g. needle-sharing, unprotected sex, etc.), along with implementing protective measures (needle exchange program [NEP], STI screening and condom use).



Thank You!