Human immunodeficiency virus (HIV)

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Outline

- Introduction
- Epidemiology
- Virus biology
- Transmission
- Basics of Pathogenesis
- Diagnosis
- Acute HIV infection
- Principles of management

First report (1981)

*Dec 10, **1981** :* Gottlieb et al.

"*Pneumocystic carinii* pneumonia and mucosal candidiasis in previously healthy homosexual men"

4 patients: PCP, candidiasis, prolonged fever, CMV, Kaposi's sarcoma, lymphopenia, homosexuals, absent CD4.

Discovery of the HIV (1983)

WHO DISCOVERED THE AIDS VIRUS?

LUC MONTAGNIER

On a spring day in 1984, Dr. Robert Gallo stood before a press conference at the National Cancer Institute to announce that he had discovered the virus that causes AIDS. What he neglected to mention was that Dr. Luc Montagnier of the Pasteur Institute in Paris had also identified what turned out to be the same virus. The two institutes had previously shared samples; they agreed to publish together and even make a joint announcement. But when the press got wind of the news, the NCI felt compelled to proceed without the French. "If I could relive those days, I wish they had been at the press conference," says Gallo today. "I was a little swept away." It took three years—and the intercession of the French and U.S. Presidents—to smooth the ruffled scientific feathers and work out a settlement in which both researchers call themselves co-discoverers. "It could have happened differently," says Montagnier. "But everybody has their personality."

—By Alice Park

ROBERT GALLO

Epidemiology

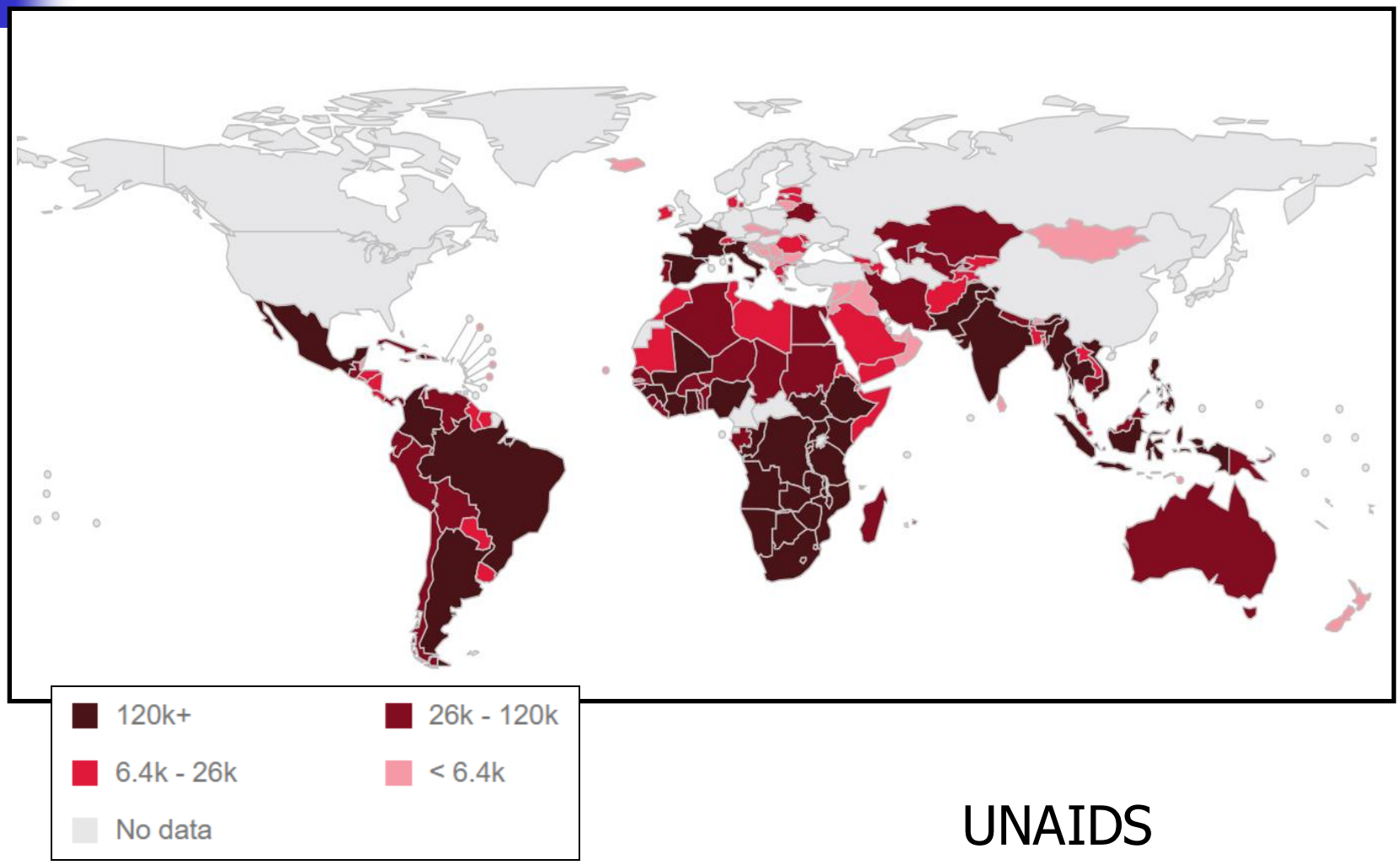
- What is the global distribution of HIV?
- What is the trend of mortality?
- What is the trend of incidence?
- The effect of treatment on mortality.
- Africa and AIDS.
- HIV and MENA region.
- HIV in Jordan.

HIV burden (2023)

- **88.4 million** [71.3–112.8] **total** since start of epidemic
- **39.9 million** [36.1 million–44.6 million] **living** with HIV
- **42.3 million** [35.7–51.1] **died** since start of epidemic

Global HIV & AIDS statistics — Fact sheet
https://www.unaids.org/en/resources/fact-sheet

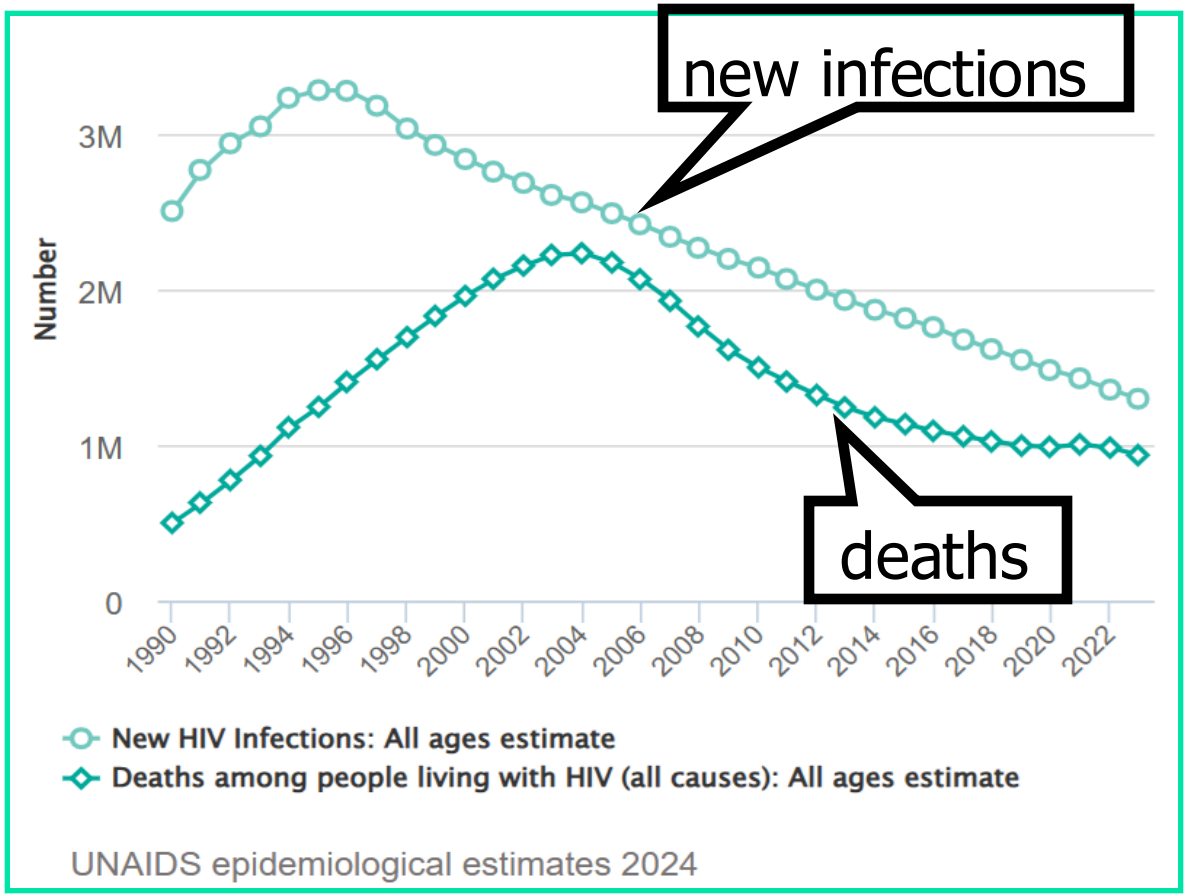
People living with HIV (2023)



UNAIDS

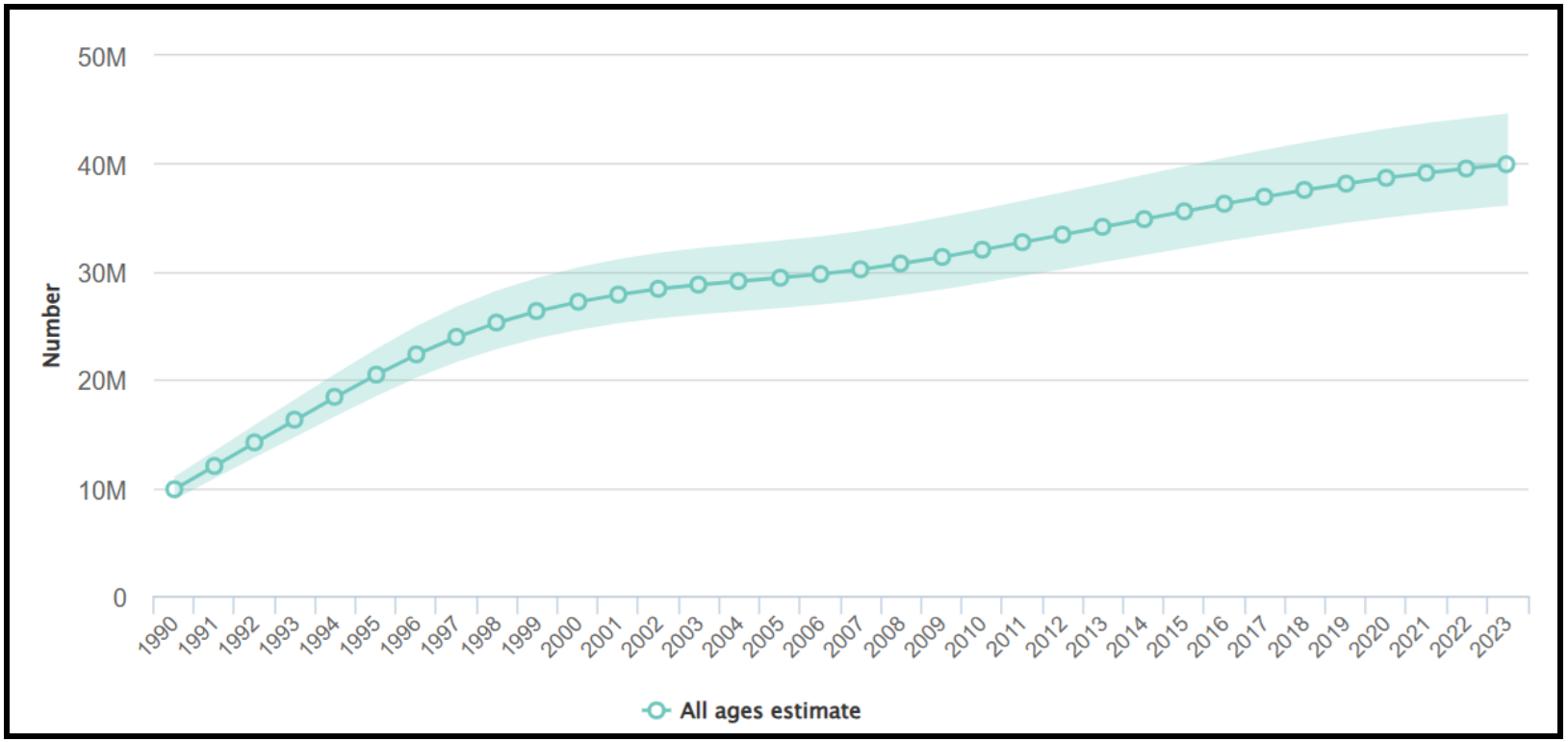
Incidence vs mortality (2023)

Decline in number of people acquiring HIV and HIV deaths



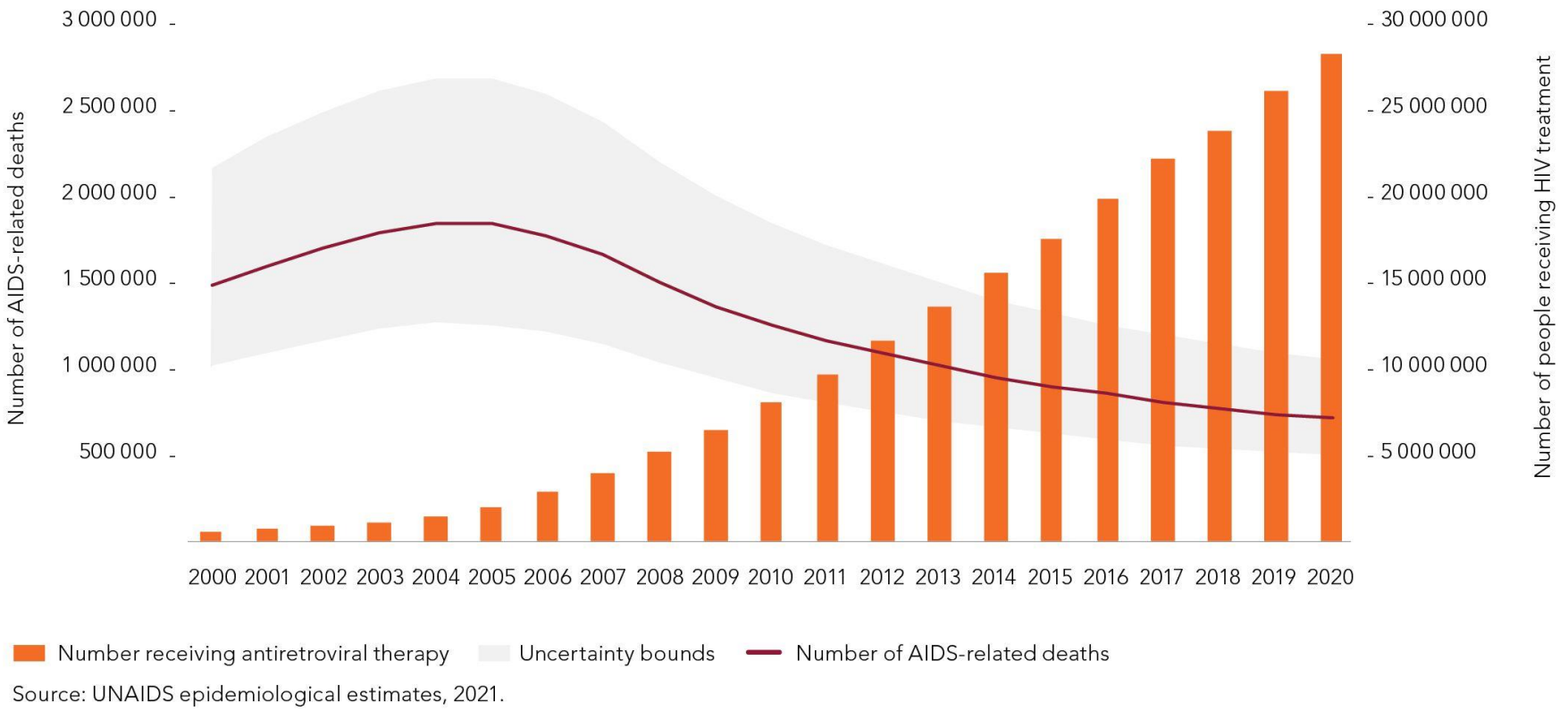
Global data on HIV epidemiology and response https://aidsinfo.unaids.org/

People living with HIV (2024)

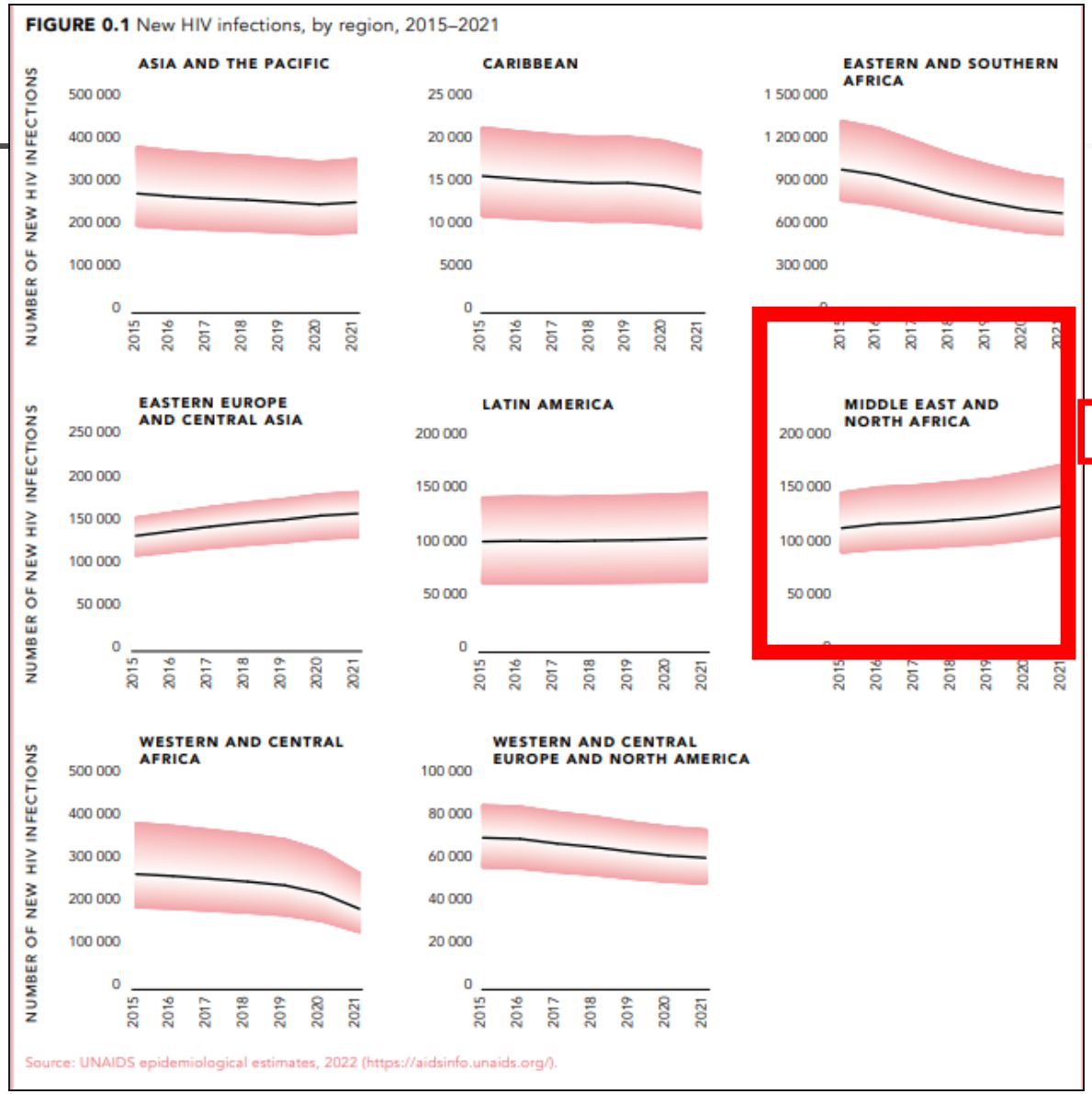


UNAIDS epidemiological estimates 2024 https://aidsinfo.unaids.org/

HIV **treatment** and **mortality**



2015-2021 trends



Incidence ↑

- 38.4 million are alive in 2021
- 36.7 million adults (15 years or older).
- 1.7 million children (0–14 years).
- 54% of all people living with HIV were women and girls.

- 1.5 million new cases / in 2021
- 1.3 million in adults
- 0.64 million in women (ie. 50% of infected were women)
- 0.16 were children
- 95 % in developing countries
- 66% in subsaharan Africa
- 16 million children were orphaned

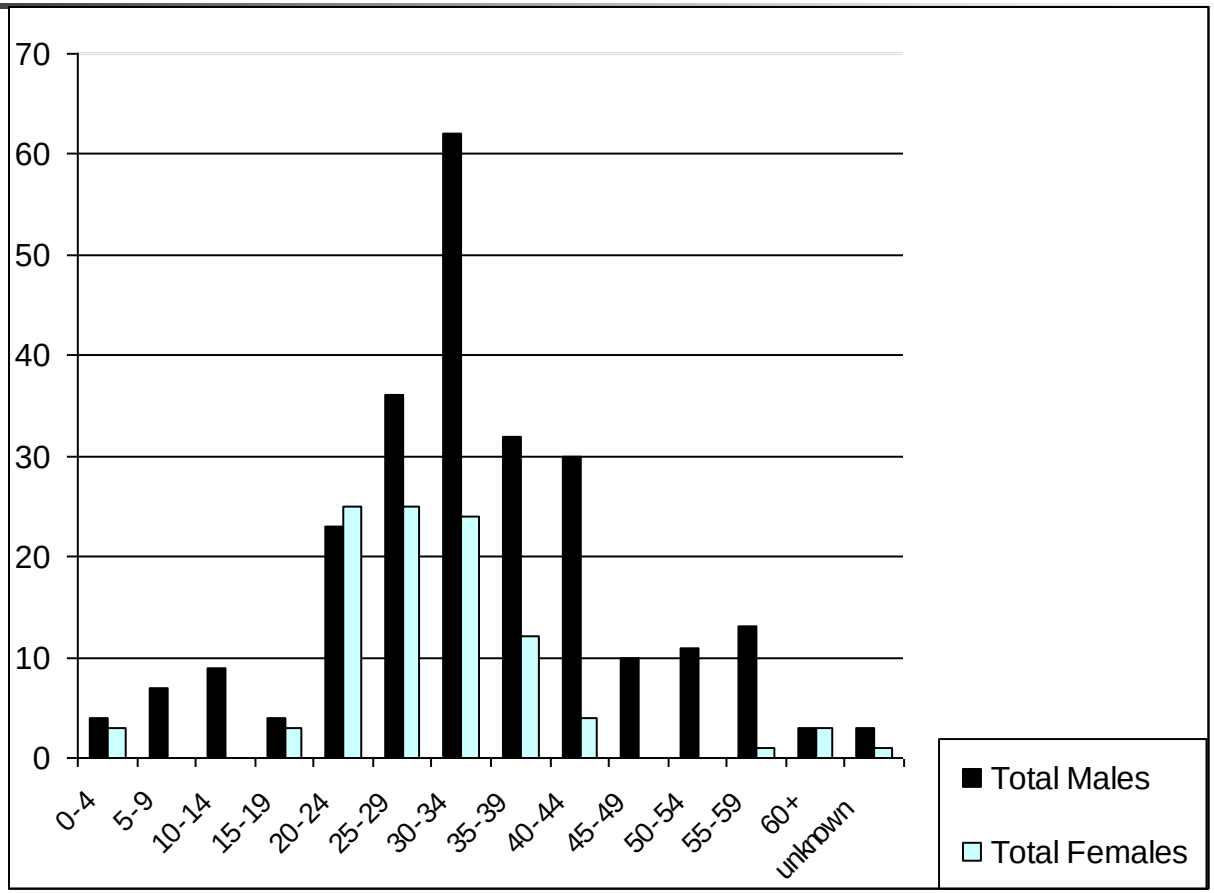
Africa and HIV

- 8% of adults < 45
- > 80% of prostitutes
- In 2013: **70% of the global total**
- **Life expectancy < 40 years**
- Causes:
  - Multiple sex partners
  - Prostitution
  - STD's
  - Mother to child transmission

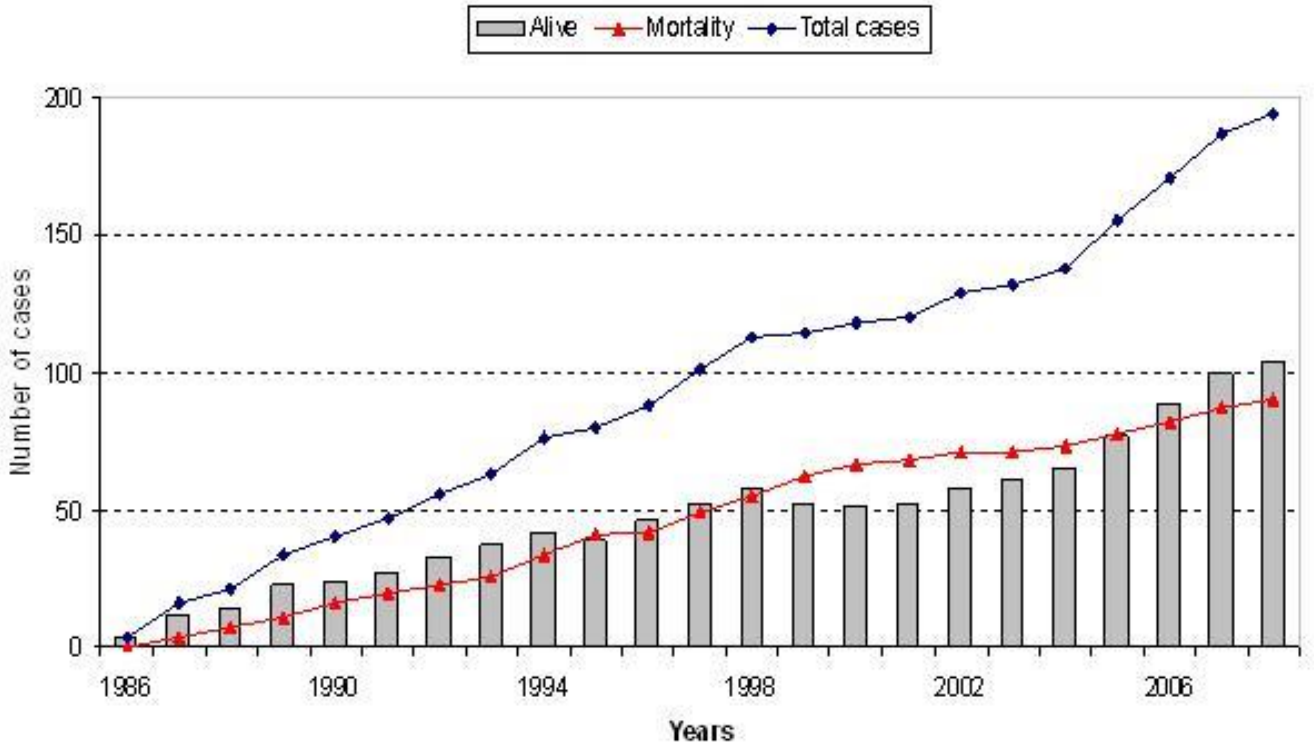
Time cover 2001

A 15 year old boy in Botswana has 90% chance of dying of AIDS

HIV in Jordan



HIV – Jordan: mortality



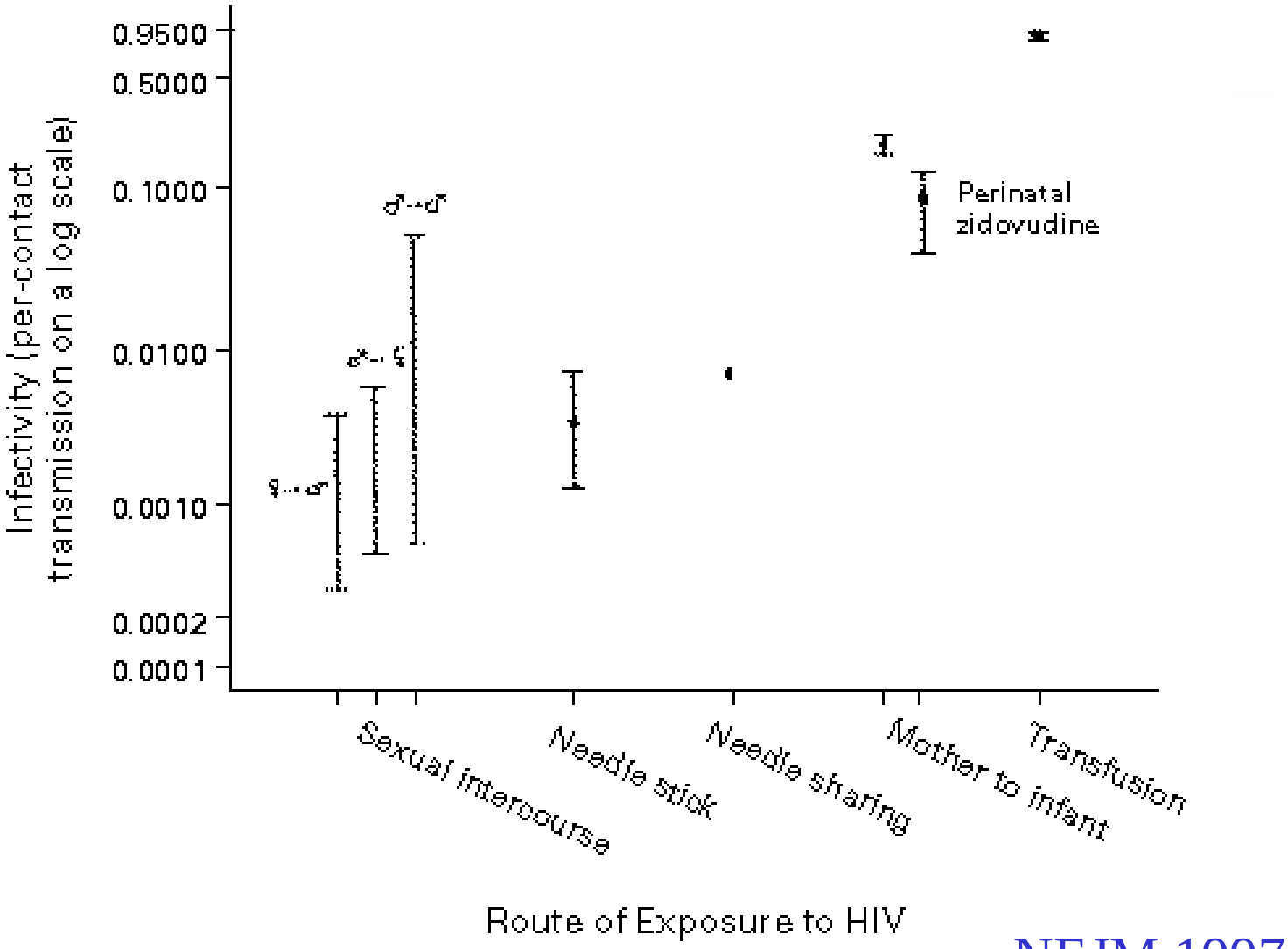
Transmission

- Sexual intercourse
- Mother $\rightarrow$ child
- IV drug use
- Blood transfusion
- Needlestick injury

All body fluids…

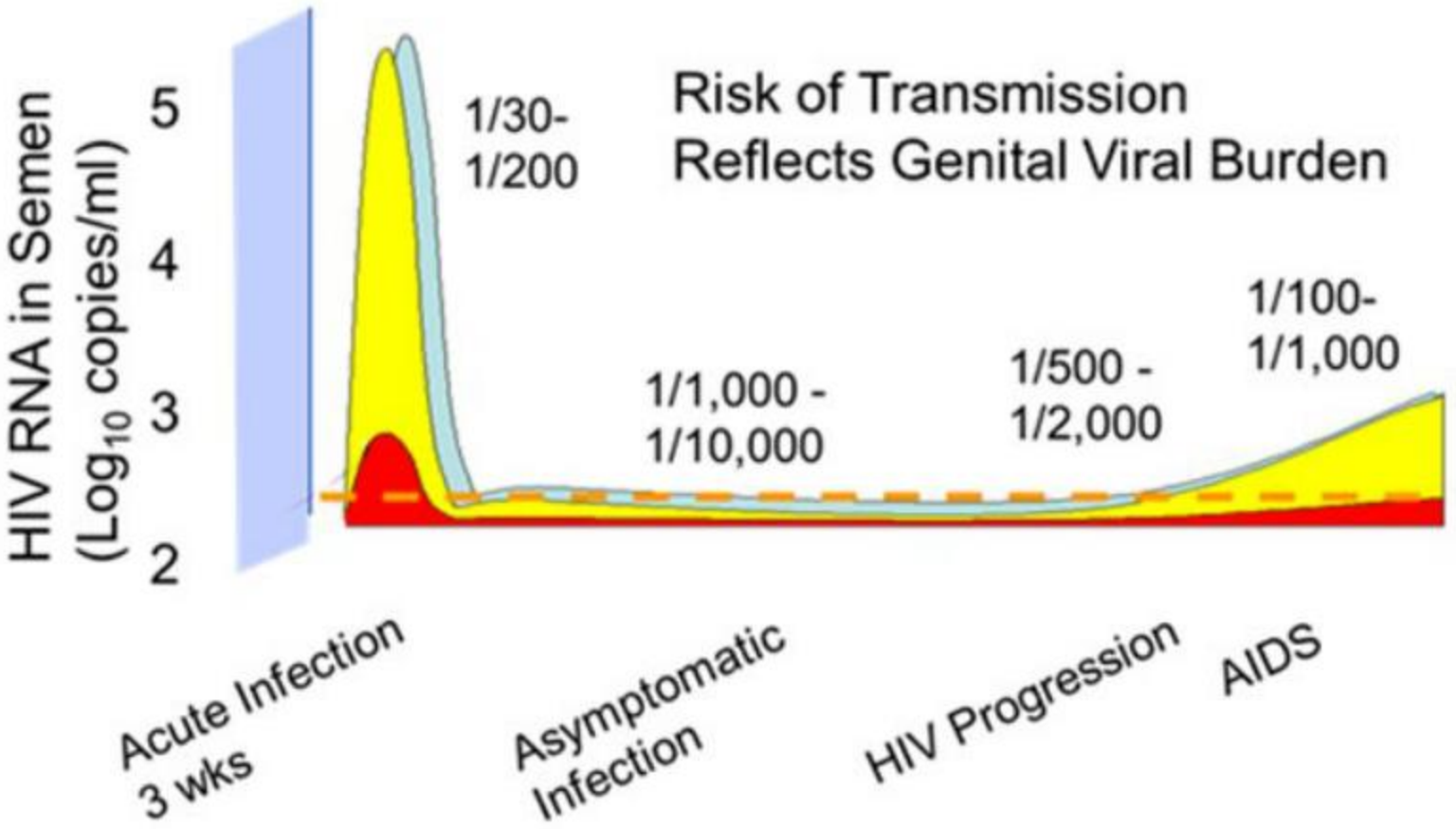
- Blood: PRBCs, FFP, cryo., clotting factors, platelets, IVIG
- Semen
- Vaginal secretion
- Saliva
- Tears
- Breast milk
- CSF
- BAL fluid
- Amniotic fluid
- Transplanted organs (liver, kidney, heart, bone)

Transmission risk estimates



NEJM 1997

Risk of Sexual Transmission of HIV



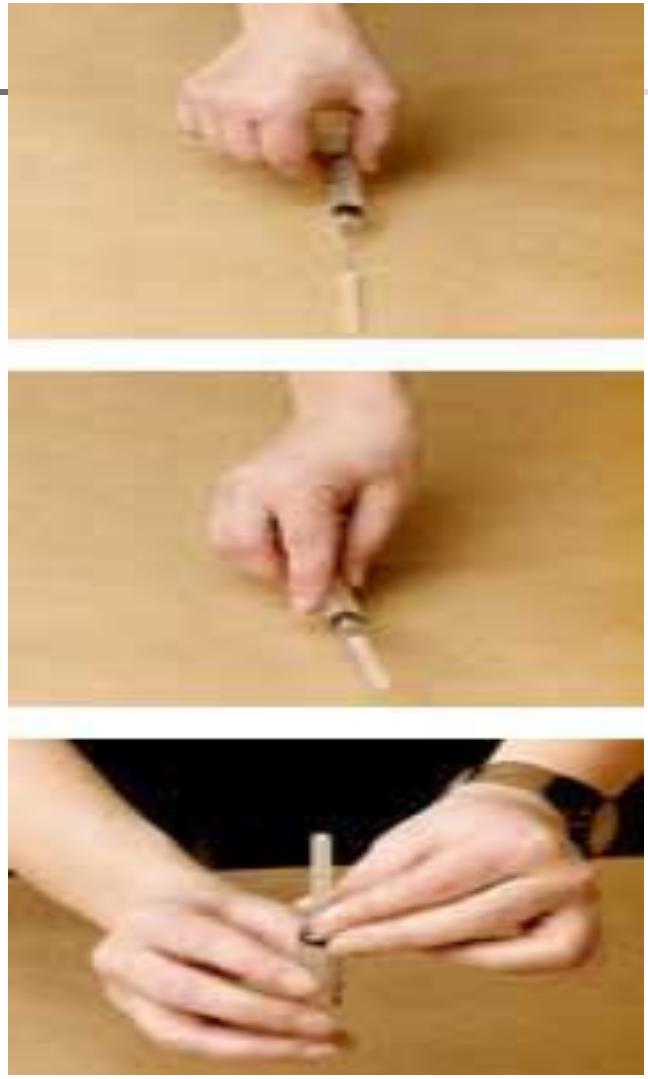
Cohen MS, et al. *J Infect Dis.* 2005; 191:1391-3.

Healthcare workers

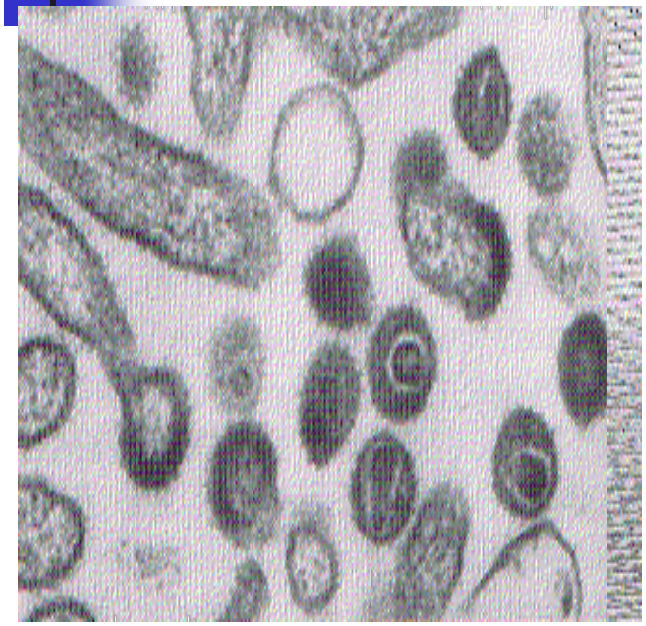
- Low risk
- 0.3%
- Universal precautions *****
  - Hand washing
  - Gloves, gowns, masks
  - Sharps
  - Open lesions…

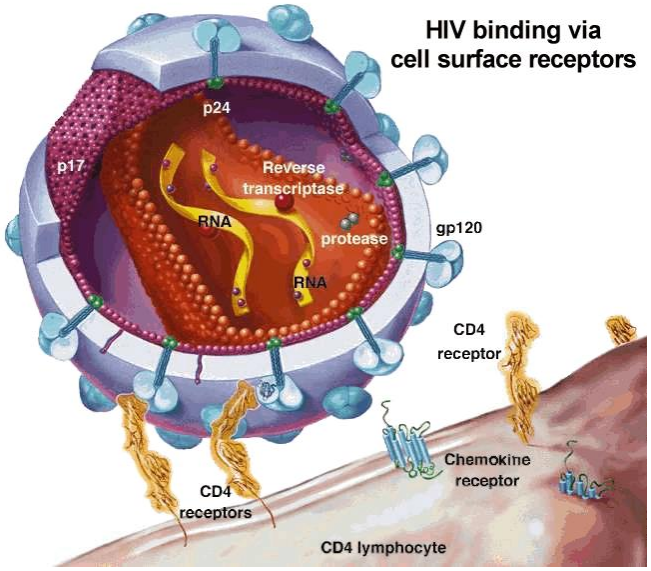
One hand technique

No recapping



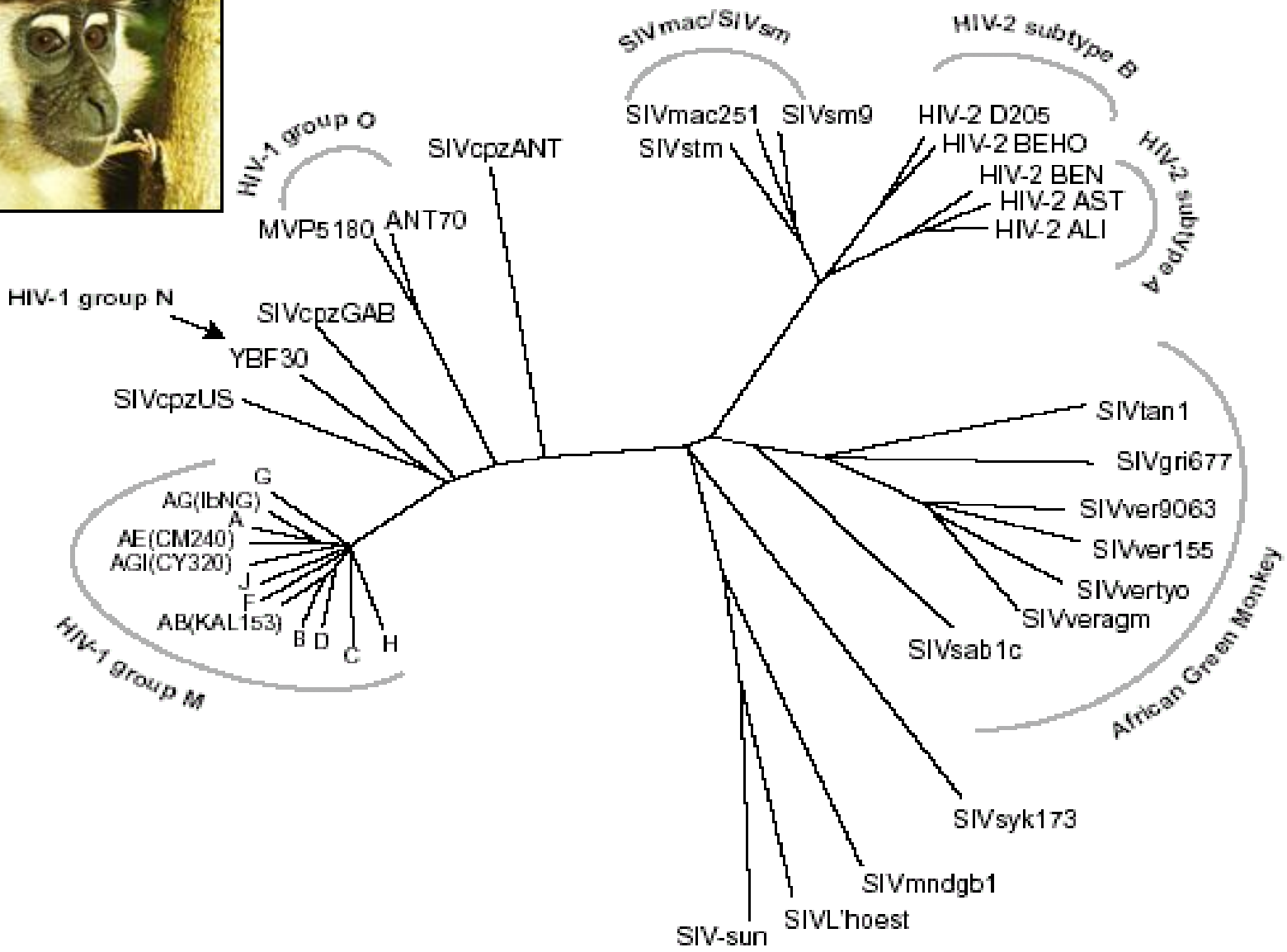
HIV Structure





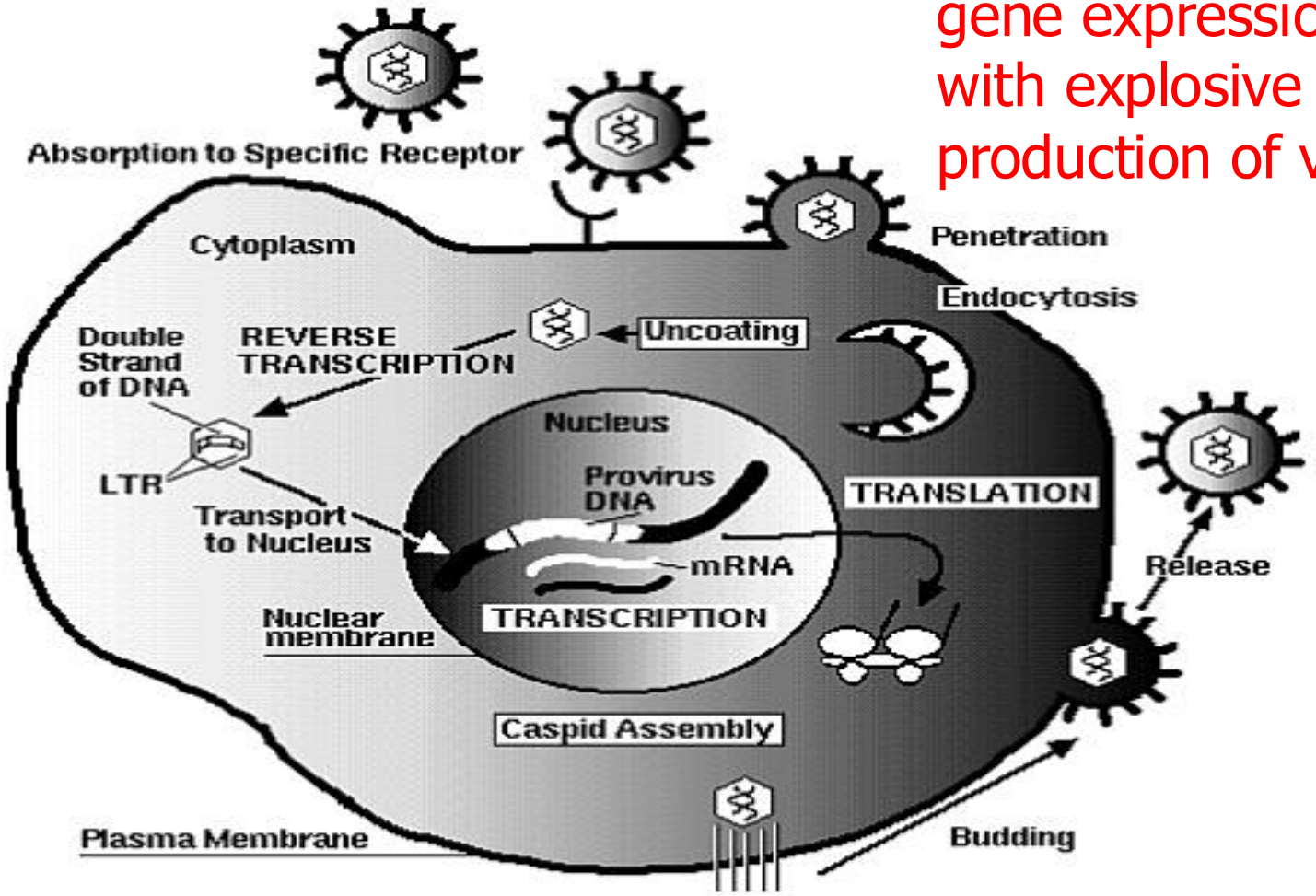
HIV binding via CD4 & chemokine receptor

Phylogenetic tree

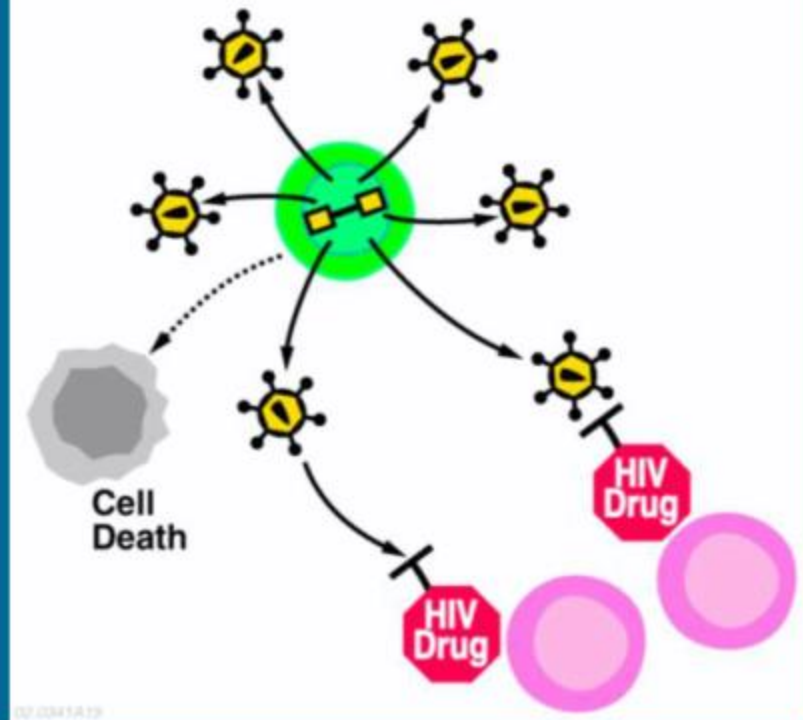


Life cycle of HIV

- Transcriptionally latent
- High levels of gene expression with explosive production of virus

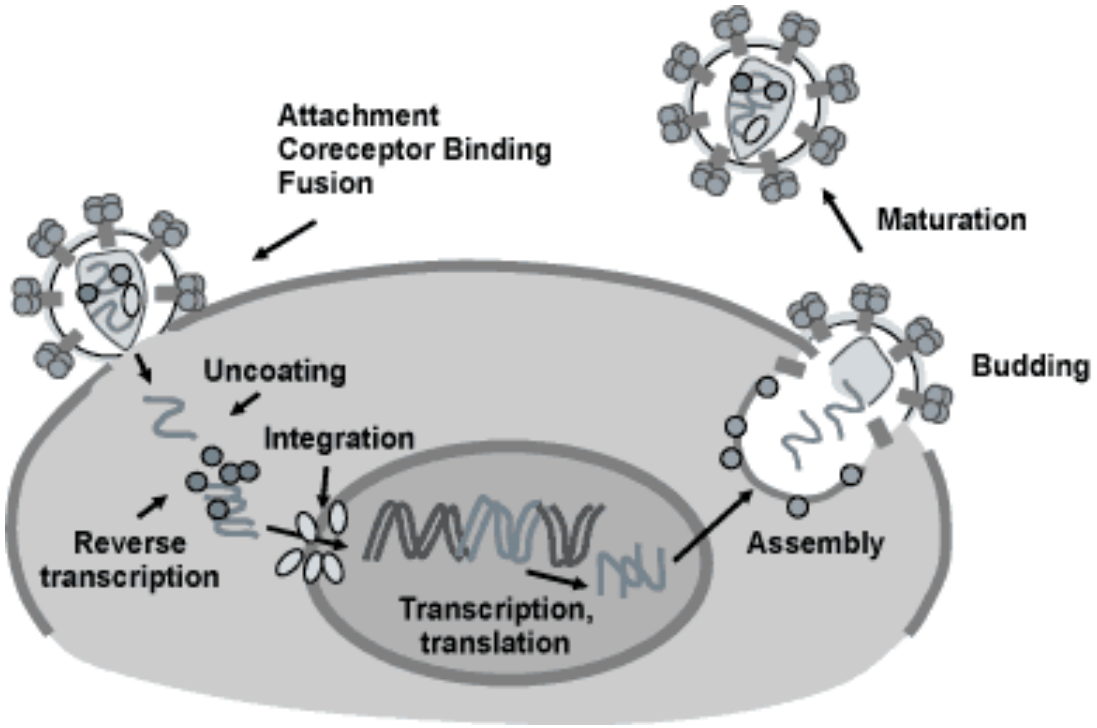


Productively Infected Cells

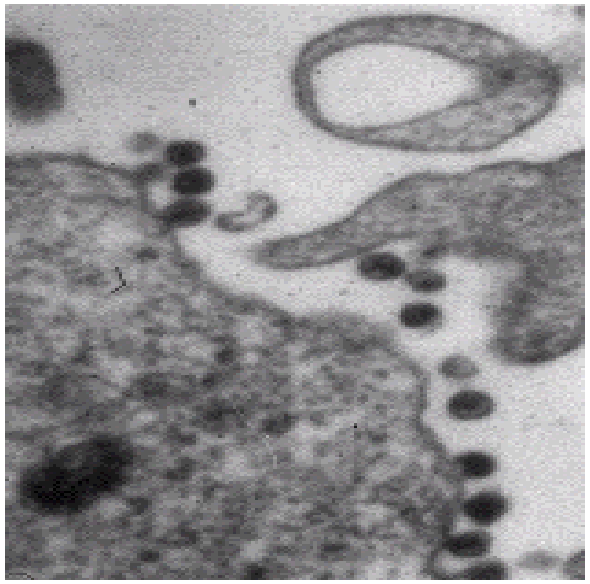


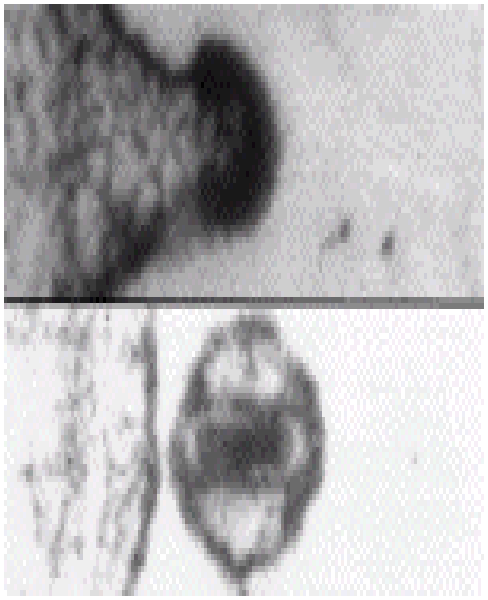
Latently Infected Cells

1. Attachment
2. Coreceptor binding
3. Fusion
4. Uncoating
5. Reverse transcription
6. Integration
7. Transcription
8. Translation
9. Assembly
10. Budding
11. Maturation

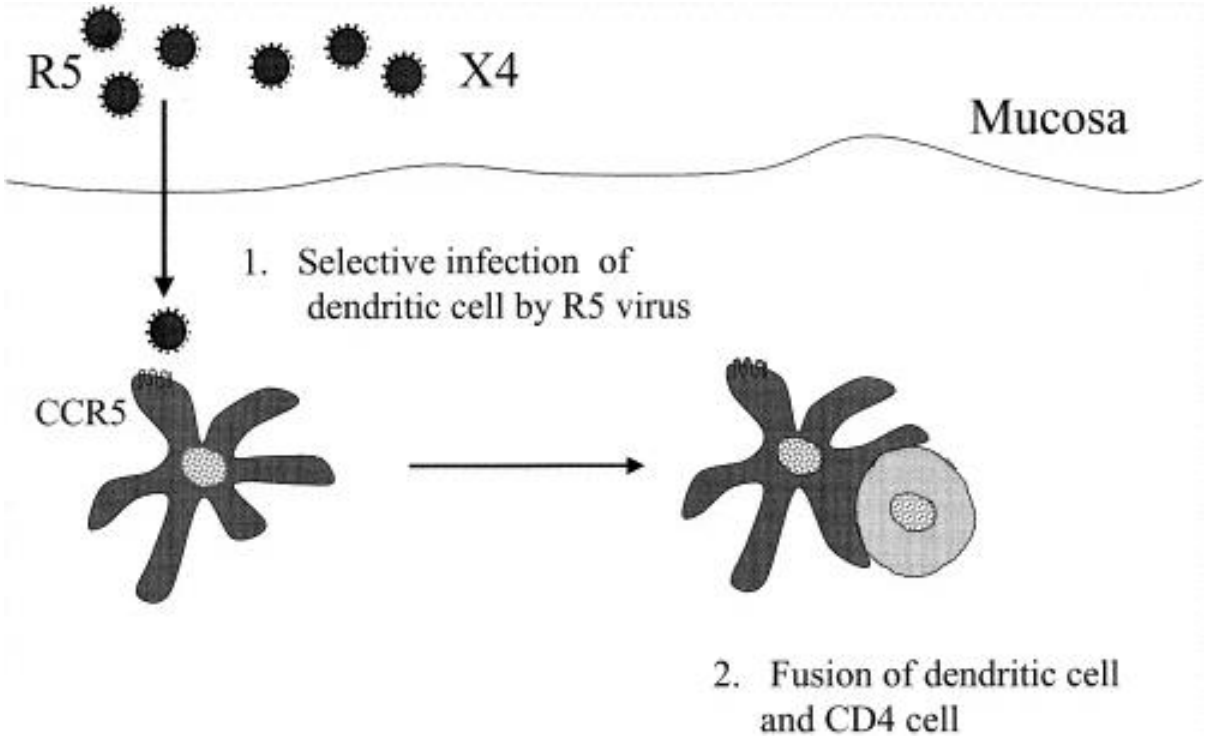


HIV budding

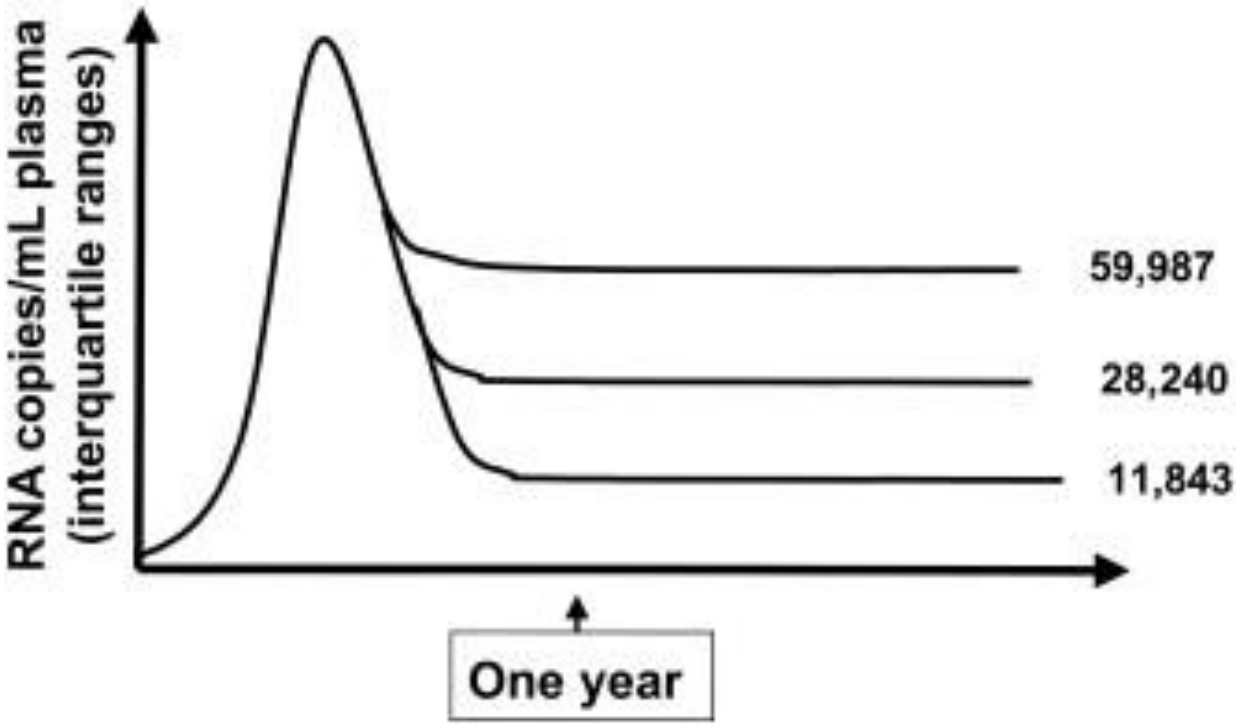




Transmission

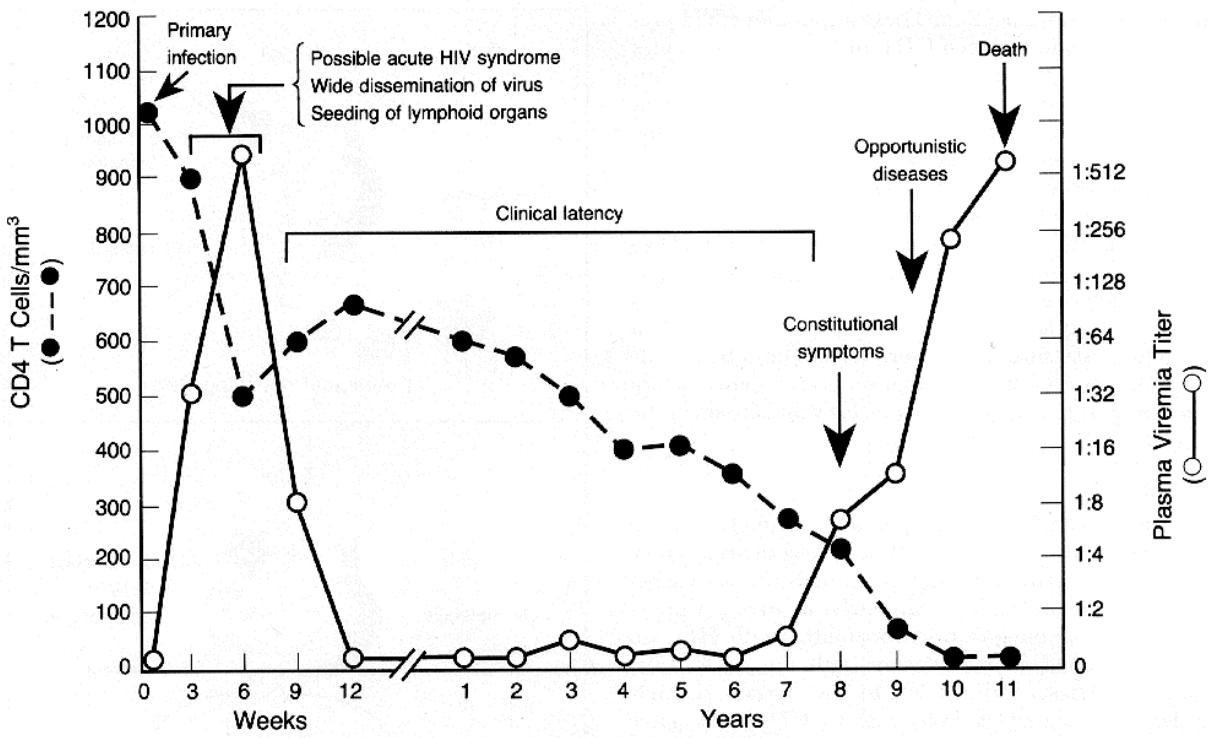


Viral steady state



CID, 2001

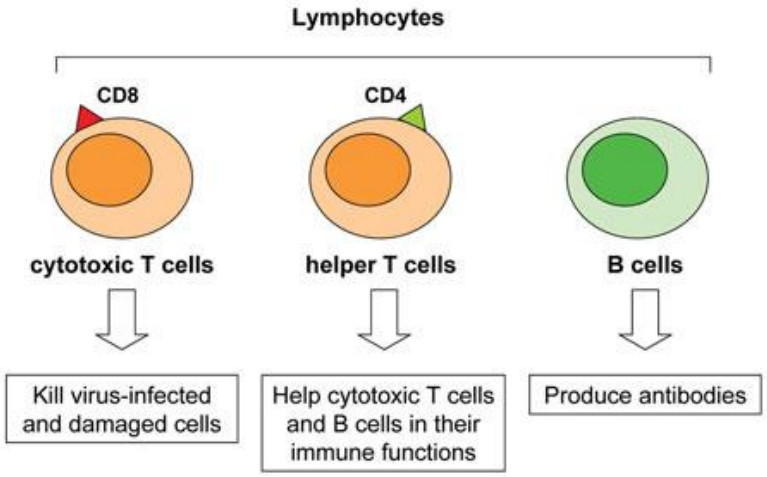
Course of HIV infection



NEJM, 1993

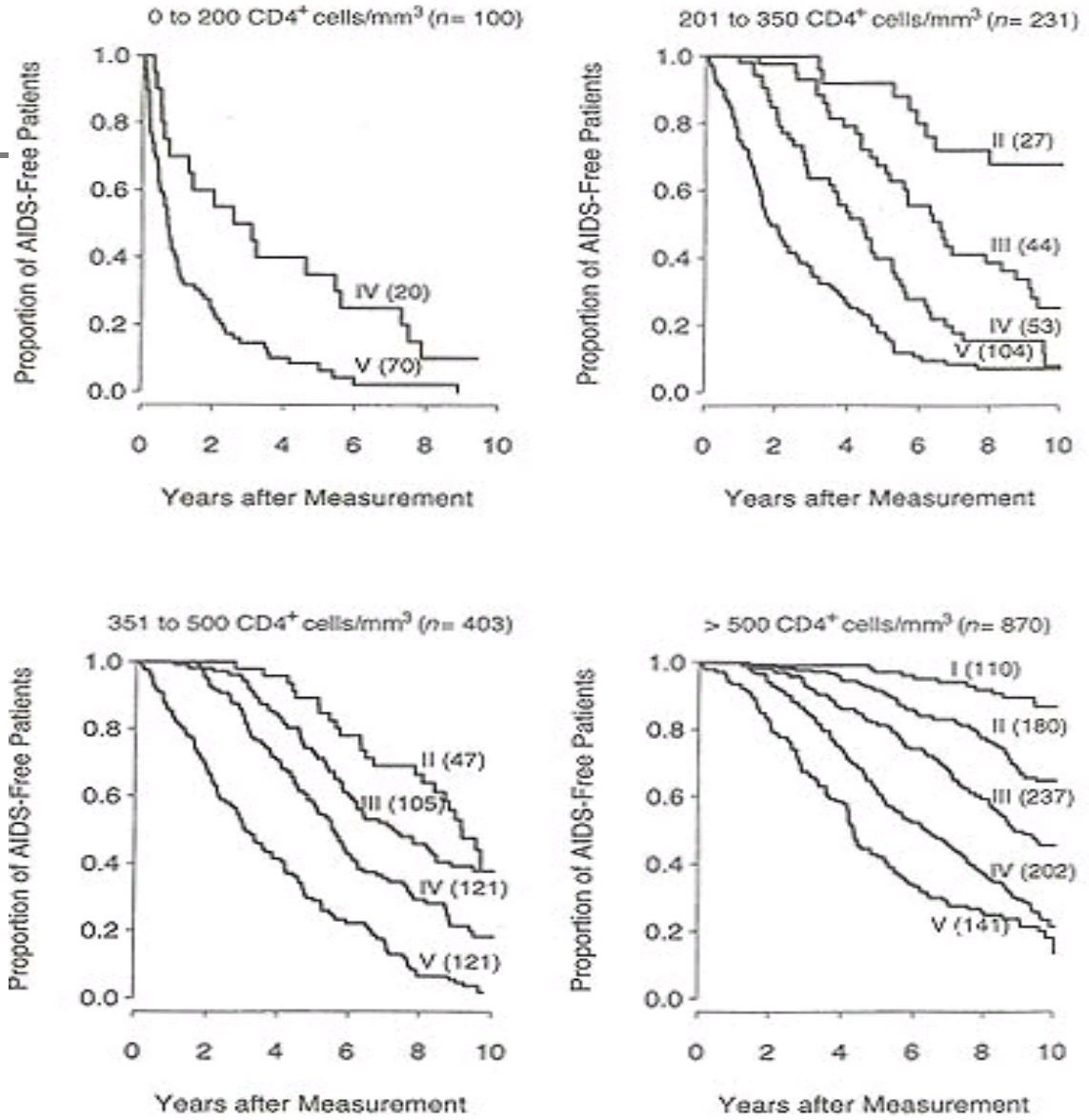
CD4 count

- CD4 count (normal): 430 – 1690 cells/ml
- Above 500 there is no additional benefit to having a higher CD4 count



https://www.open.edu/openlearncreate/mod/oucontent/view.php?id=105&section=1.4.3

Viral load & CD4 as predictors for progression



I, 500 copies/mL or less

II, 501 to 3000 copies/mL

III, 3001 to 10,000 copies/mL

IV, 10,001 to 30,000 copies/mL

V, more than 30,000 copies/mL

AIM, 1997

Acute HIV infection

- Mononucleosis like picture
  - remember secondary syphilis, EBV
- > 70 % of pts present with symptoms,
  - 2 weeks after acquiring HIV but can present as early as 5 days or as late as 3 months after initial infection
- High viremia ≈ 10^{8} copies/ml
- Highly infectious
- Dx by PCR followed by serology
  - 4^{th} gneration Ag/Ab test (10-14 days)

Signs and Symptoms of Acute HIV
occur: 2 weeks – 3 months

- Fever
- Fatigue/Malaise
- Pharyngitis
- Lymphadenopathy
- Myalgia
- Joint Pain
- Rash
- Diarrhea
- Weight Loss
- Headache
- Vomiting
- Oral or genital ulcer

- **Rare presentation**

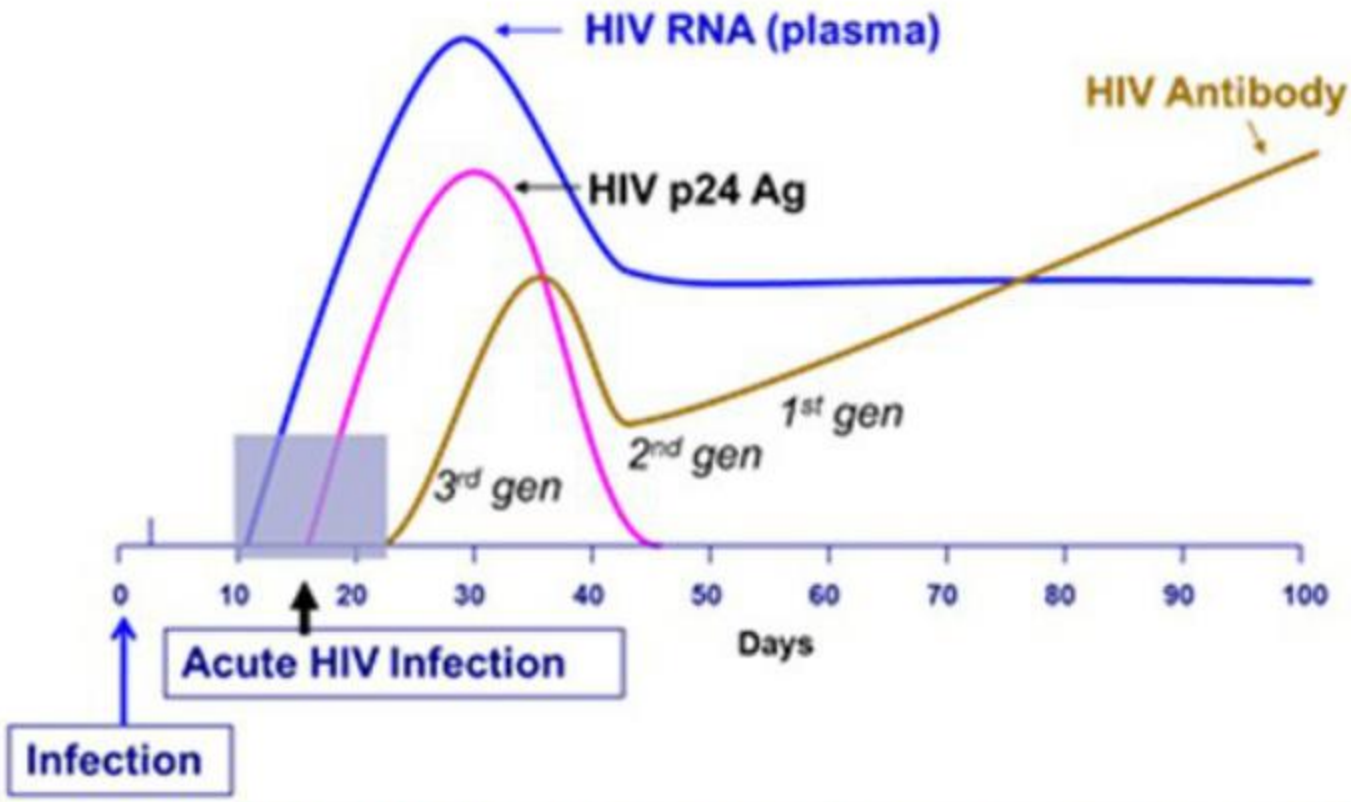
- Guillain-Barré Syndrome
- aseptic meningitis
- hepatitis

- completely asymptomatic

RNA test and DX of acute HIV

- Although acute HIV infection with HIV RNA <10,000 copies/mL has been described, such results could also represent false positive tests
  - further lab tests should be performed (eg, additional antibody testing or repeat HIV RNA or both) to confirm cases in which HIV RNA levels lower than 10,000 copies/mL are noted

Window Period and HIV Infection

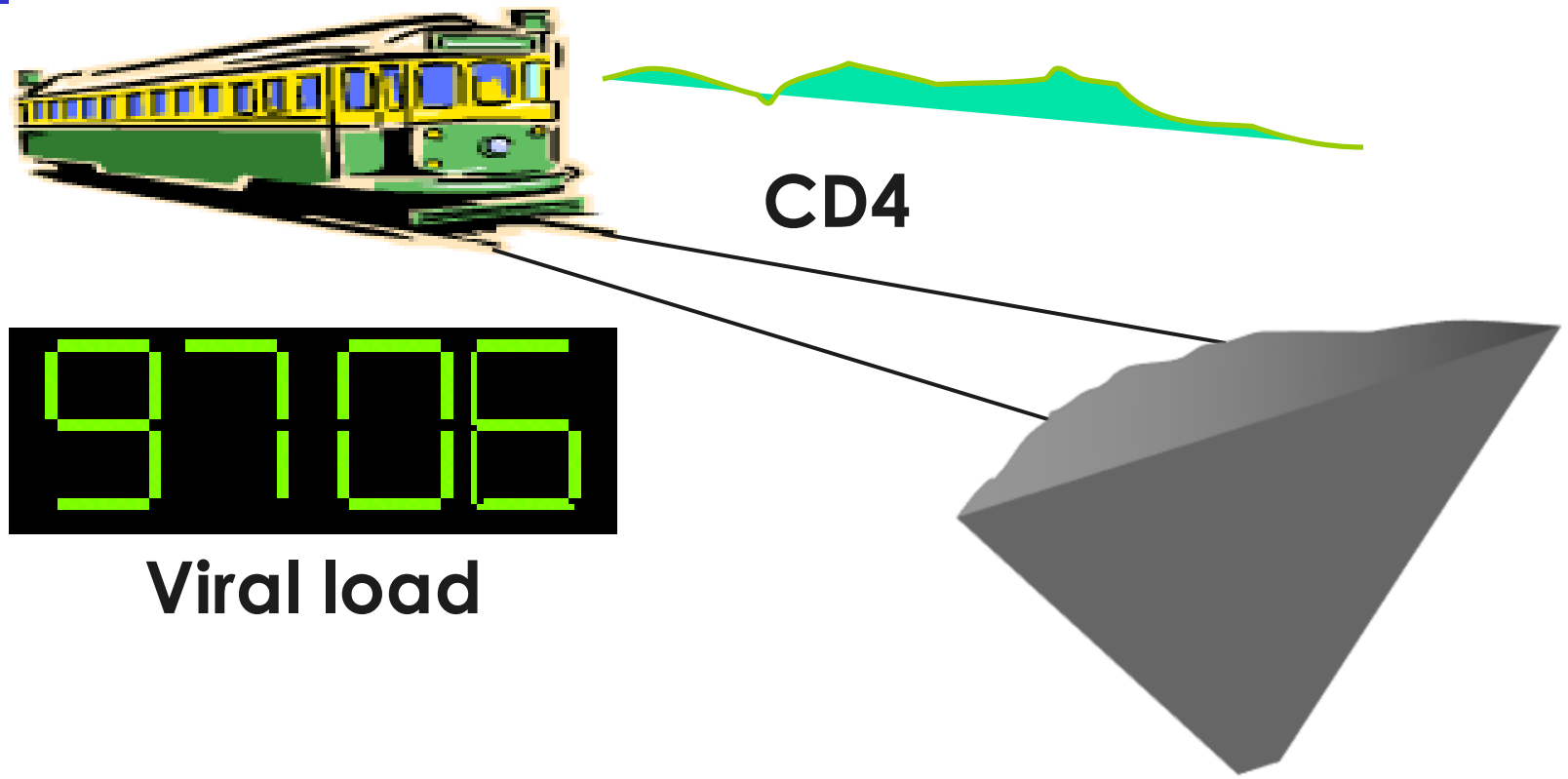


Busch MP, et al. *Am J Med* 1997; 102(5B):117-124. Modified diagram based on first iteration in stated source and updated using several publications since 1997.

Persons recommended for evaluation of acute HIV infection with available appropriate tests

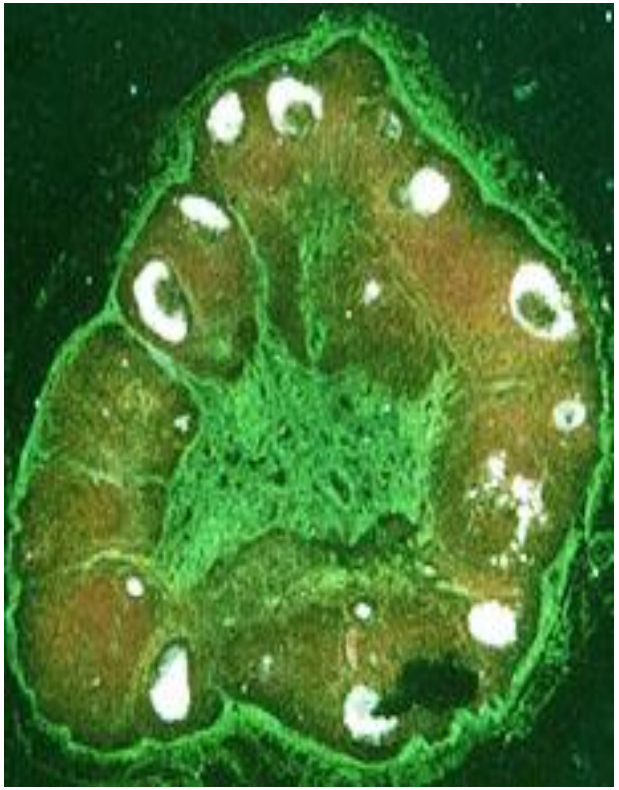
- All of the following risk groups, ESPECIALLY with **history of an illness with clinical features compatible with acute HIV ("mono" or "flu-like" illness, regardless of severity):**
- recent sexual or needle-sharing exposure with a known HIV-infected partner or a partner of unknown serostatus in the past **2-6** weeks
- Men who report unsafe sexual practices with other men
- A newly diagnosed STD
- Aseptic meningitis
- Requesting HIV testing
- Pregnant and breastfeeding women

Viral Load (V.L) & CD4 count



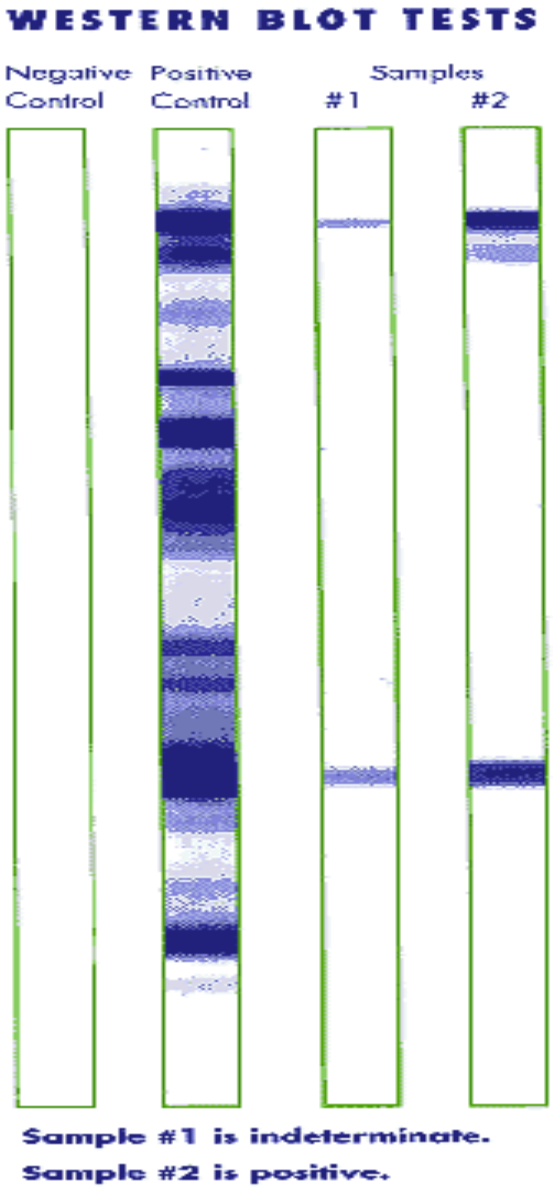
HIV = destruction of immunity

- Destruction of CD4 cells
- Evasion of immune response
- Lymph node pathology
- Exhaustion of immunity



HIV Diagnosis

- Viral load (PCR)
  - as early as 7-10 days
- ELISA
- Western blot



CDC Classification (1993)

CD4	A Asymptomatic, acute or PGL	B Symptomatic, not A or C	C AIDS indicator
≥500	A1	B1	C1
200-499	A2	B2	C2
<200	A3	B3	C3

CDC classification

Bacillary Angiomatosis
Oral thrush
Persistent vulvovaginitis
Fever or diarrhea > 1 month
Hairy leukoplakia
VZV
ITP
PID
Peripheral neuropathy

B Symptomatic, not A or C
B1
B2
B3

CDC AIDS defining diseases (CD4 < 200 cells/ml)

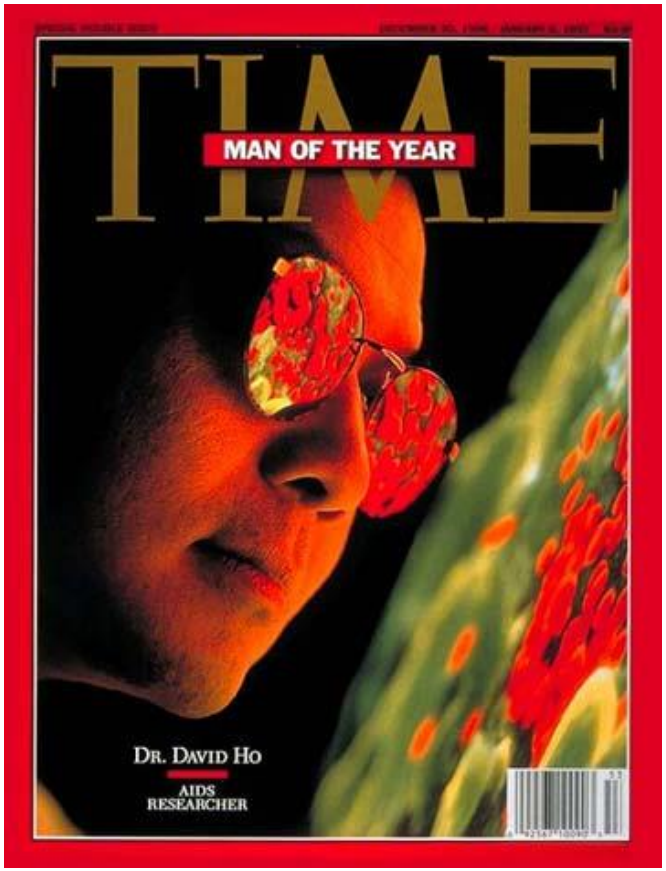
1) Candidiasis
2) Cervical cancer
3) Coccidioidomycosis
4) Cryptococcosis
5) CMV
6) Encephalopathy
7) HSV
8) Histoplasmosis
9) TB
10) Cryptosporidiosis
11) Lymphoma
12) PCP
13) Recurrent pneumonia
14) MAC
15) PML
16) Salmonellosis
17) Brain Toxoplasmosis
18) Wasting
19) Kaposi's sarcoma
20) Isosporiasis

Highly Active Anti-Retroviral Therapy (HAART) "Cocktail", "ART"

2 NRTI + PI

- Aim:
  - Suppress viral load
  - Increase CD4

- Disadvantages:
  - Toxicity
  - Cost

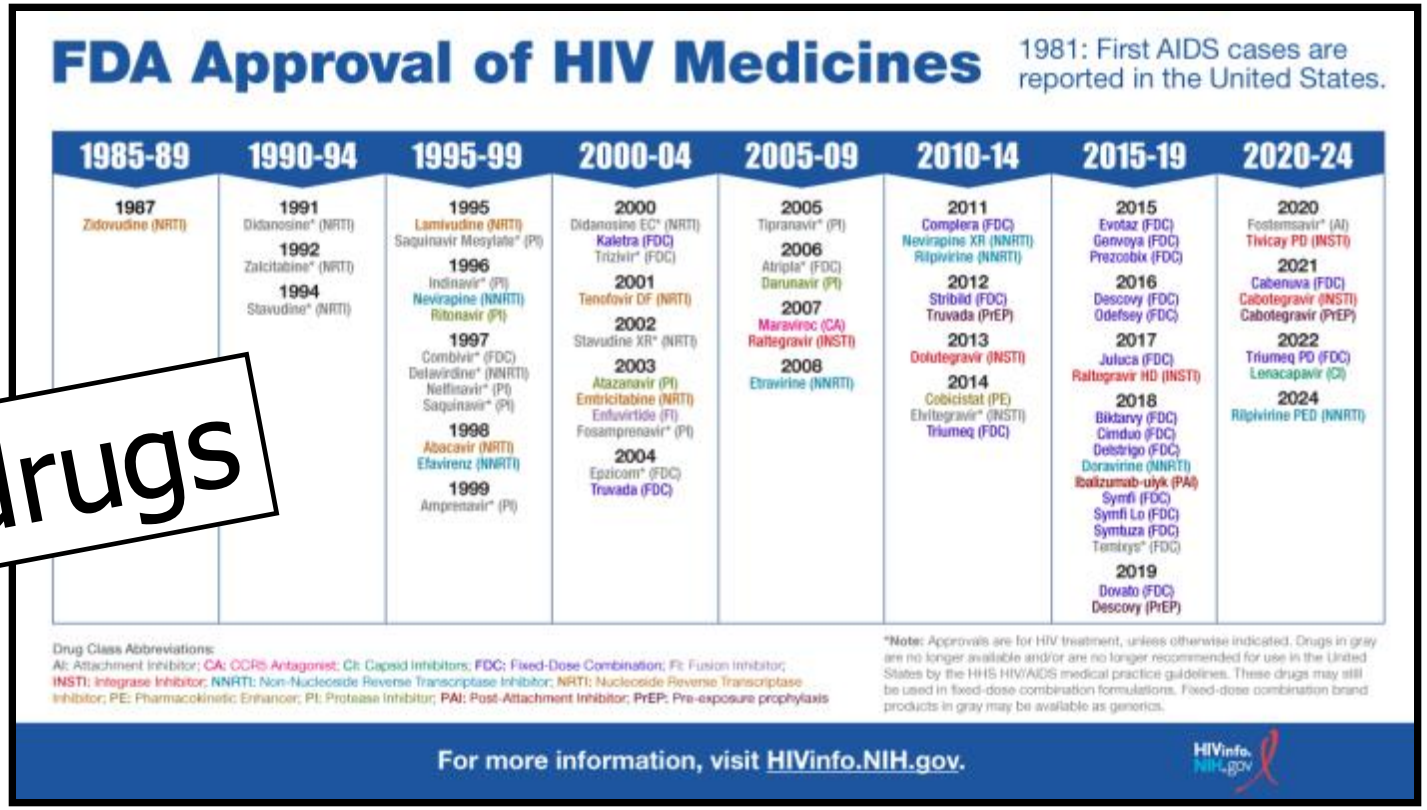


Classes - Anti HIV drugs

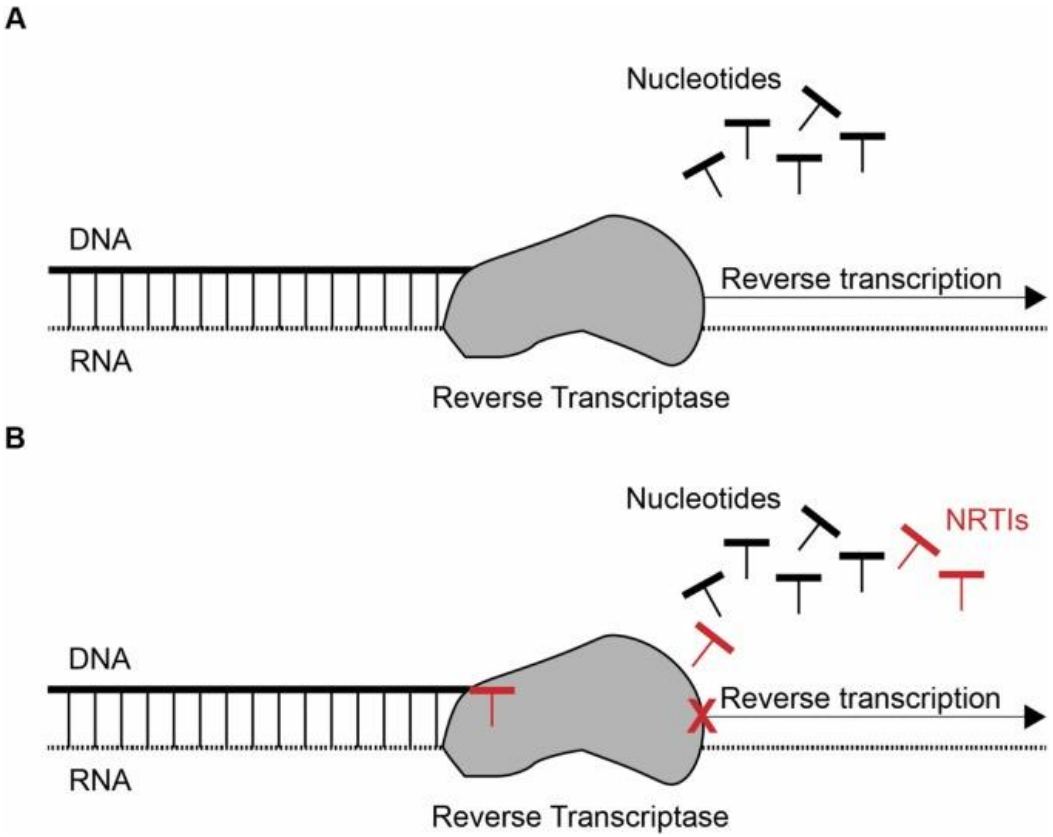
1) Nucleoside reverse transcriptase inhibitors (NRTIs)
2) Non-nucleoside reverse transcriptase inhibitors (NNRTIs)
3) Protease inhibitors (PIs)
4) Fusion inhibitors
5) Integrase strand transfer inhibitors (INSTIs)
6) CCR5 antagonists
7) Attachment inhibitors
8) Post-attachment inhibitors

Anti HIV meds

30 drugs

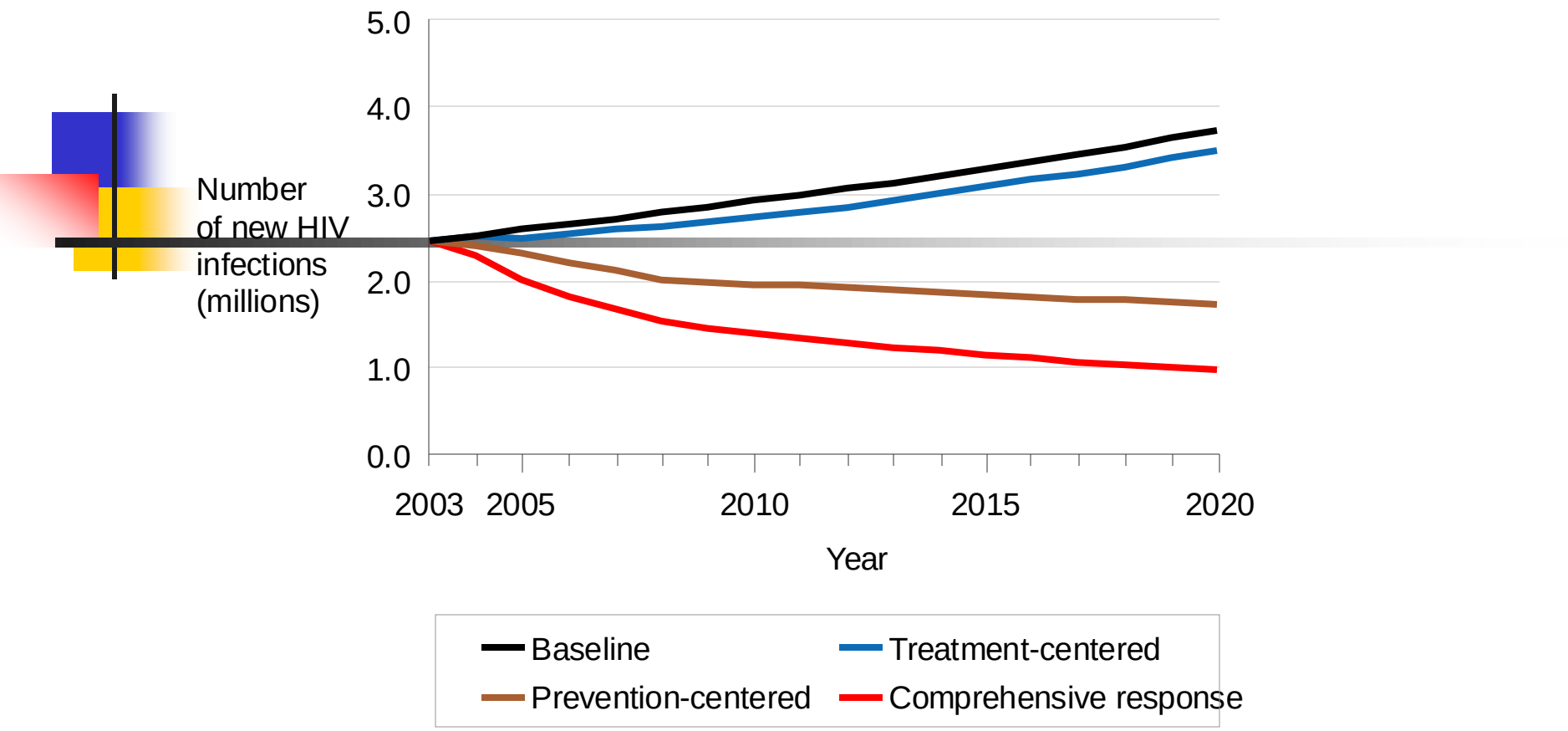


NRTI mechanism of action



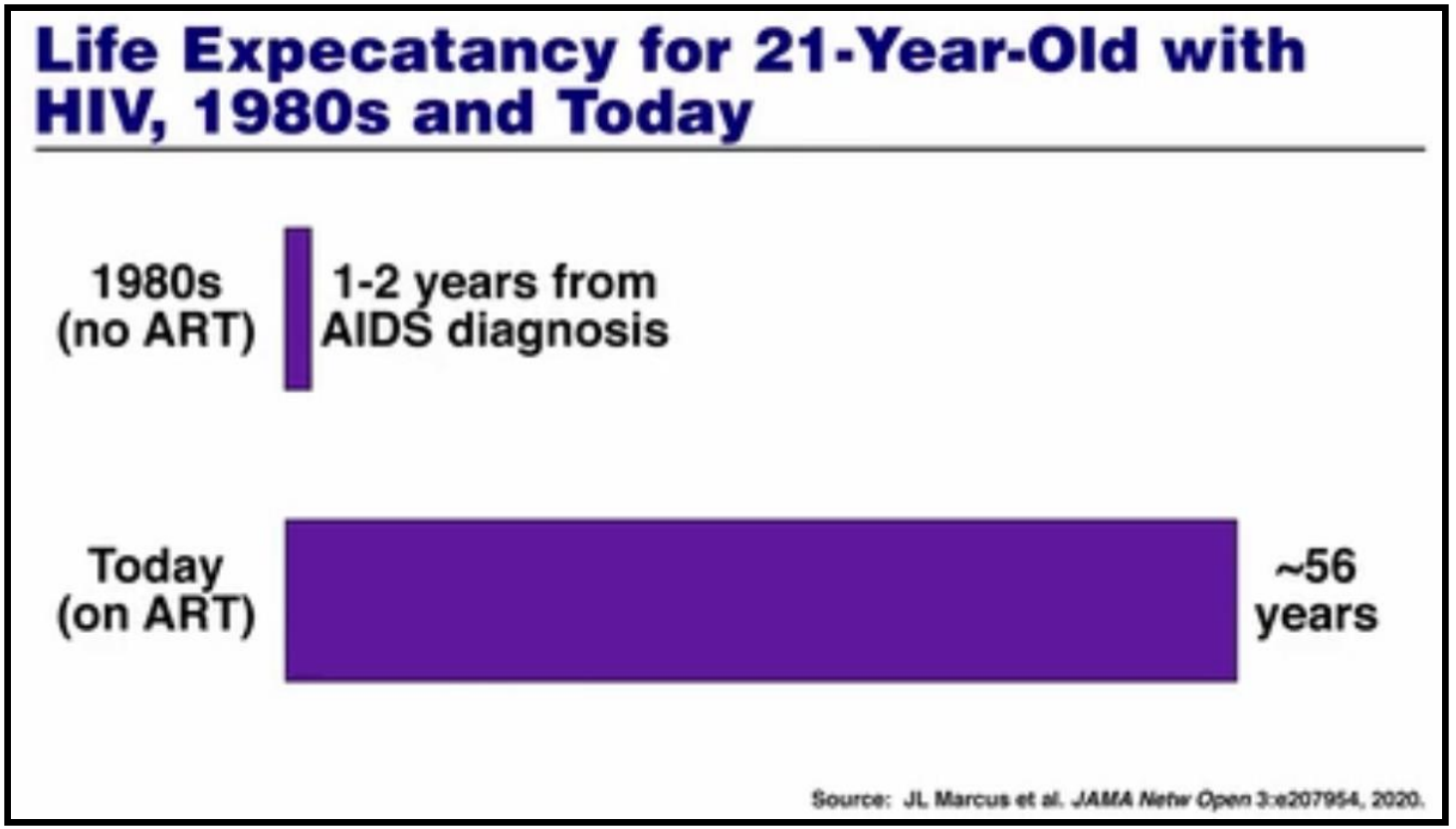
Brochard et al. Ageing Research Reviews 2023

Impact of three scenarios on HIV infection in sub-Saharan Africa, 2003–2020



Source: Salomon JA et al. (2005). Integrating HIV prevention and treatment: from slogans to impact

Life expectancy



Conclusions

- Large & serious epidemic
- Transmission modes
- Basic pathogenesis
- AIDS related illnesses
- The importance of CD4 & VL
- HAART
- Viral resistance (as usual)
- When to start therapy