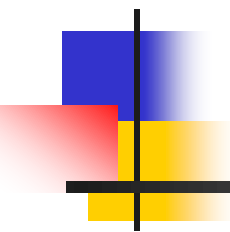


Human immunodeficiency virus (HIV)



Dr Faris Bakri

Jordan University Hospital

2025



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.

*“**Pneumocystis 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.

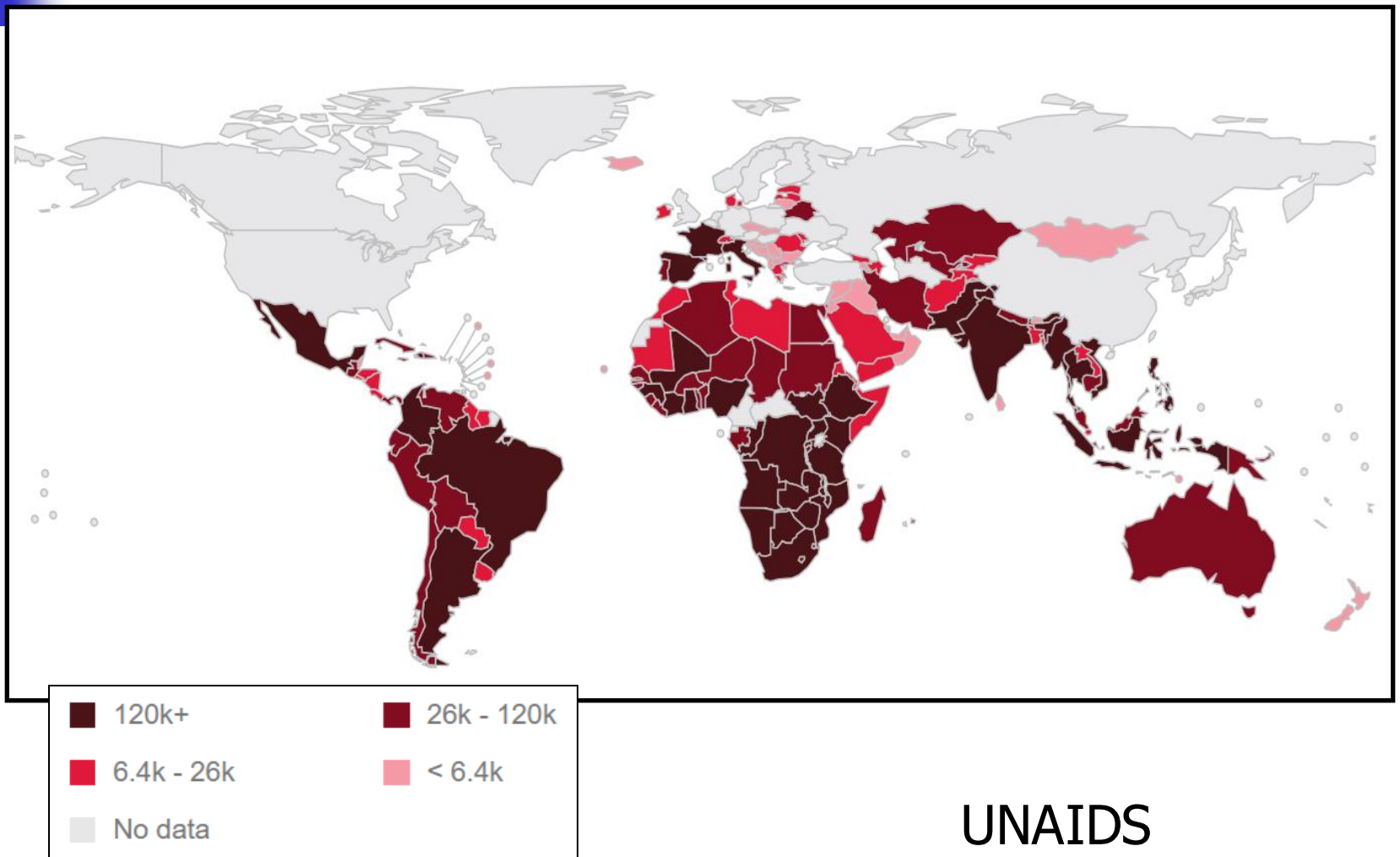


HIV burden (2023)

- **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

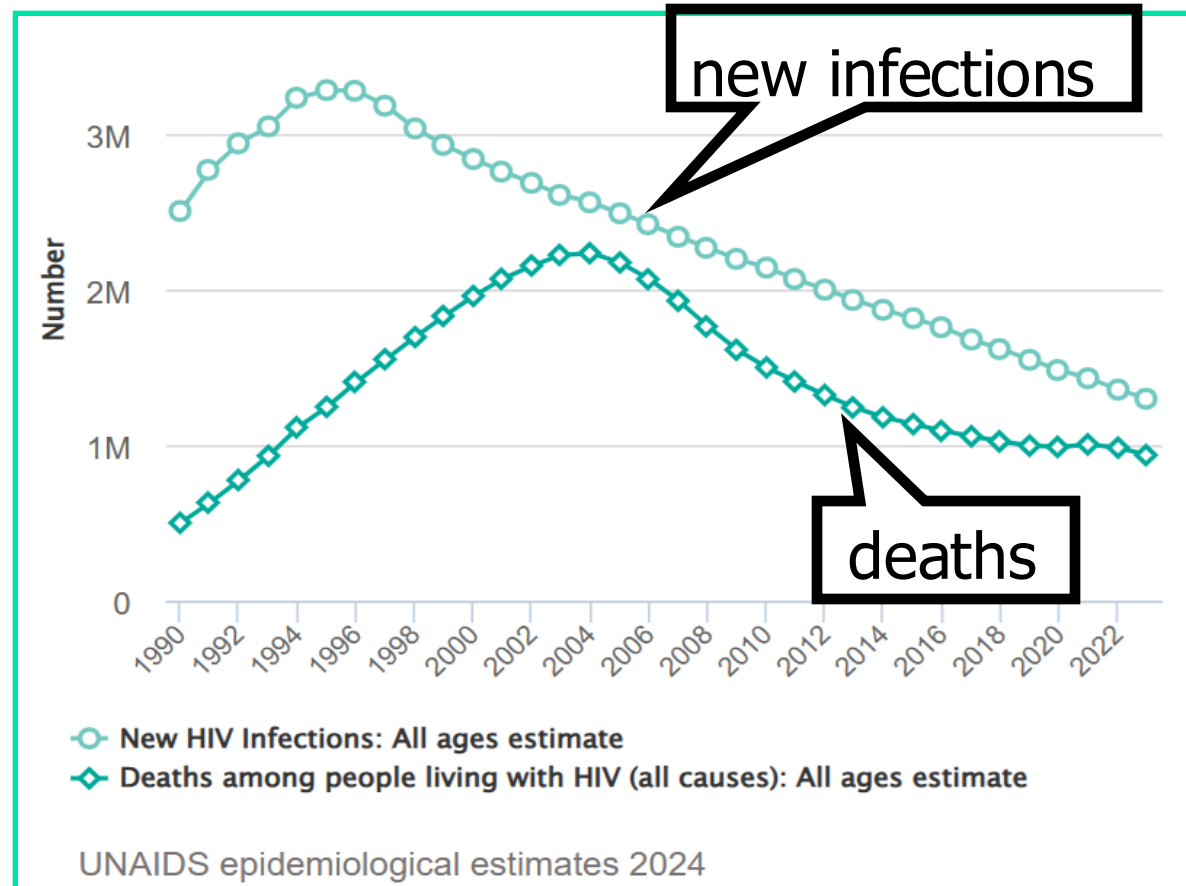
Global HIV & AIDS statistics — Fact sheet
<https://www.unaids.org/en/resources/fact-sheet>

People living with HIV (2023)

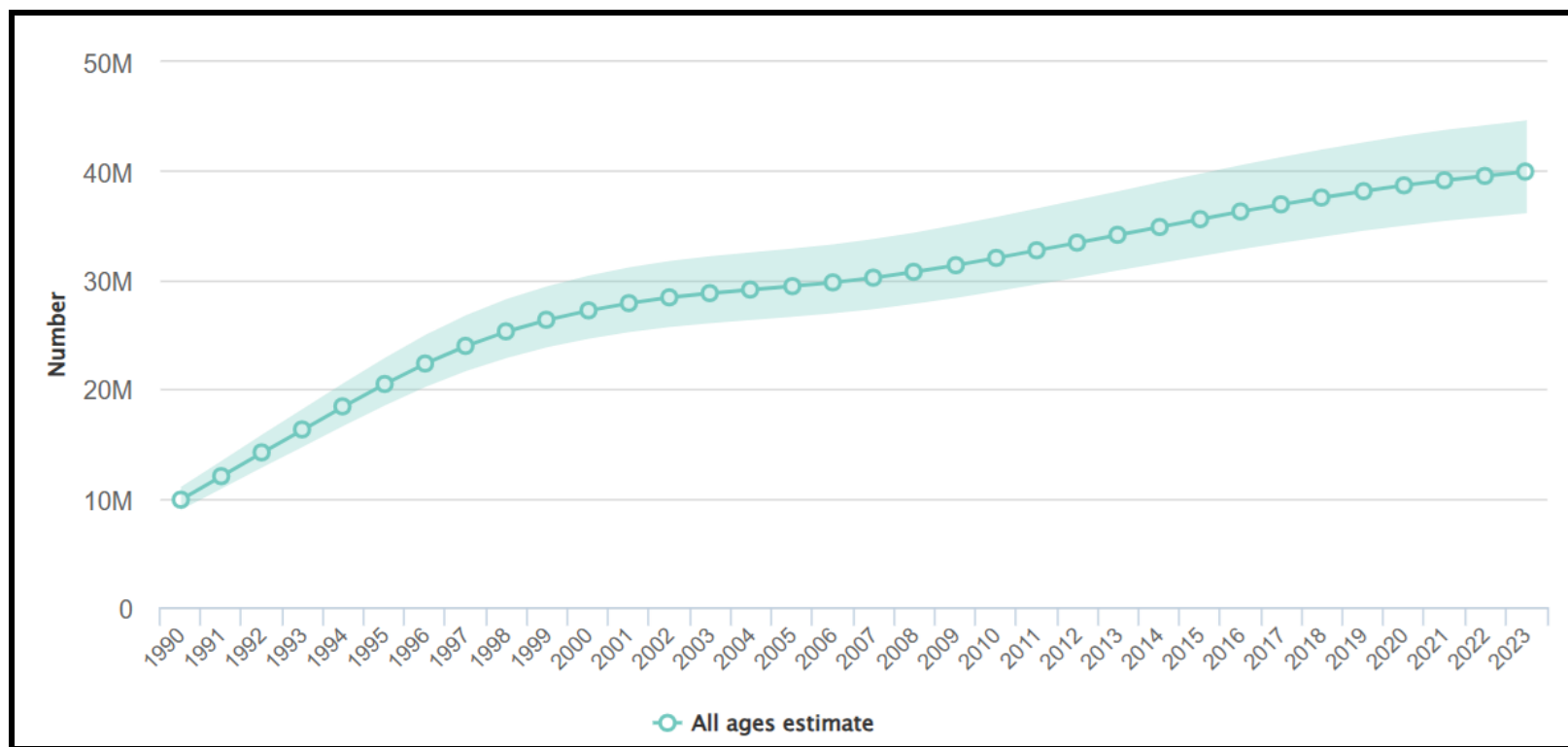


Incidence vs mortality (2023)

Decline in
number of people
acquiring HIV and
HIV deaths

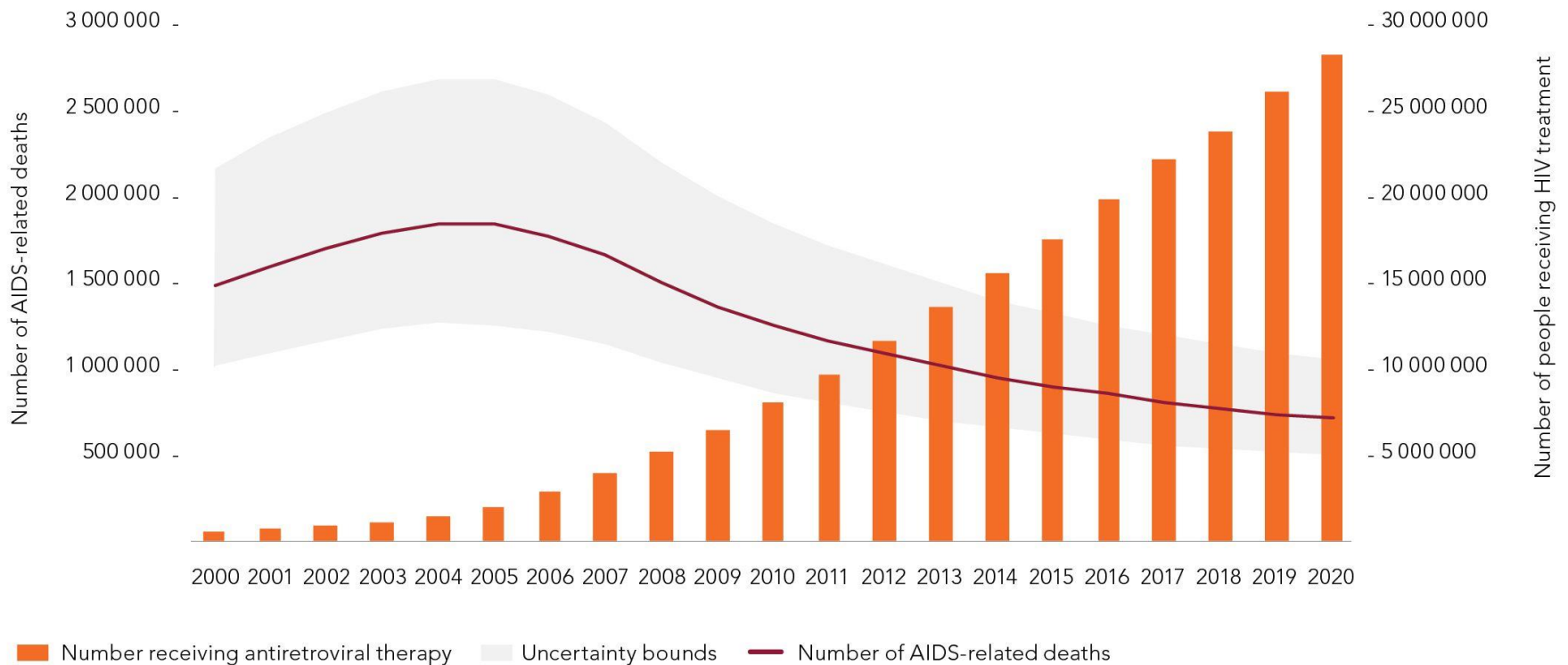


People living with HIV (2024)



HIV treatment and mortality

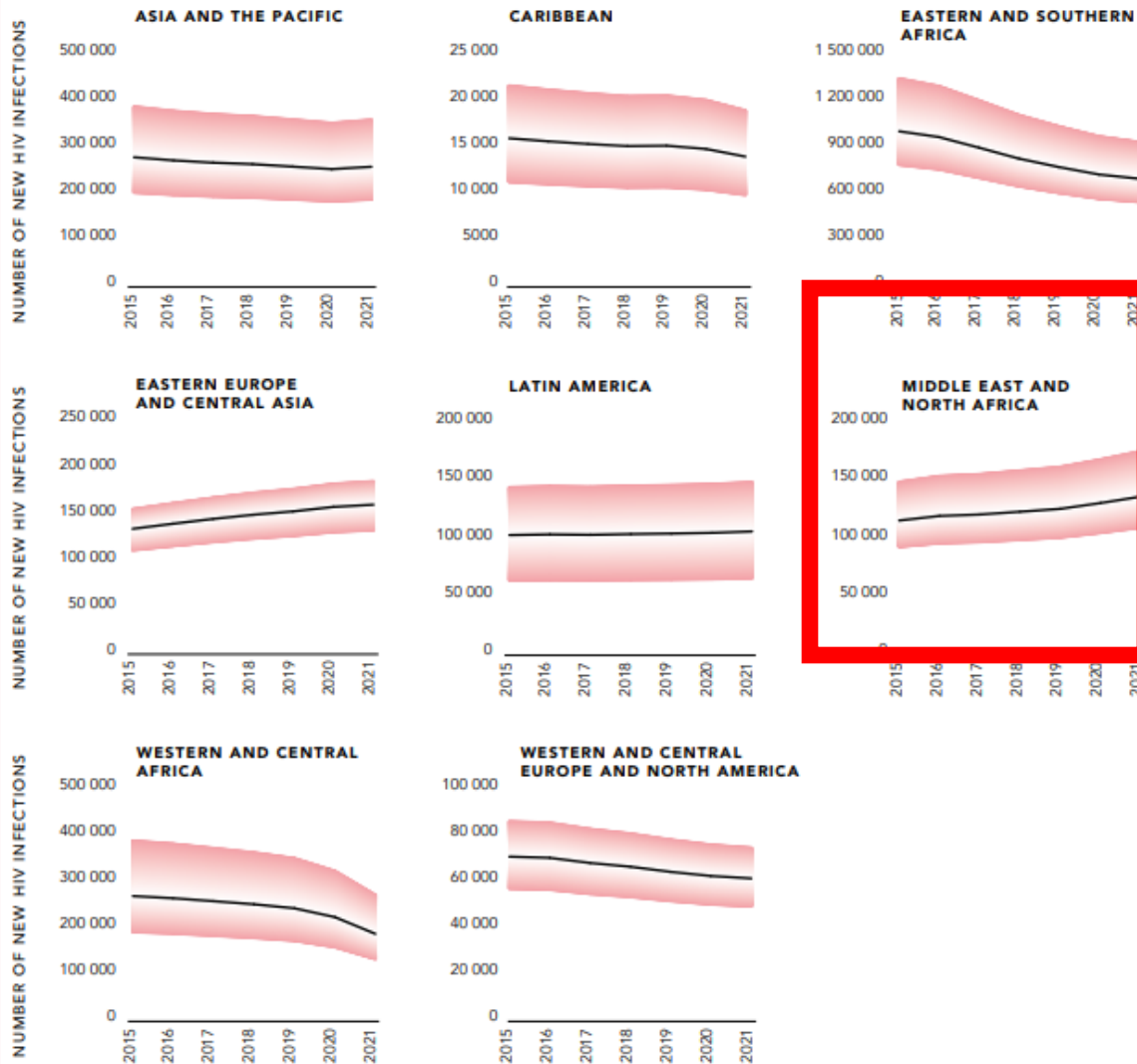
Numbers of AIDS-related deaths and people receiving HIV treatment, global, 2000–2020



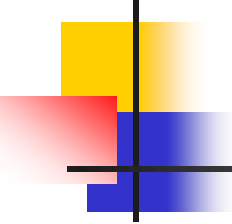
Source: UNAIDS epidemiological estimates, 2021.

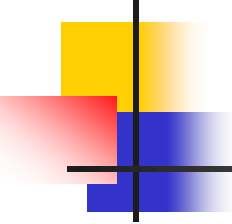
2015-2021 trends

FIGURE 0.1 New HIV infections, by region, 2015–2021



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
 - 14 million orphaned in Africa

Africa and HIV

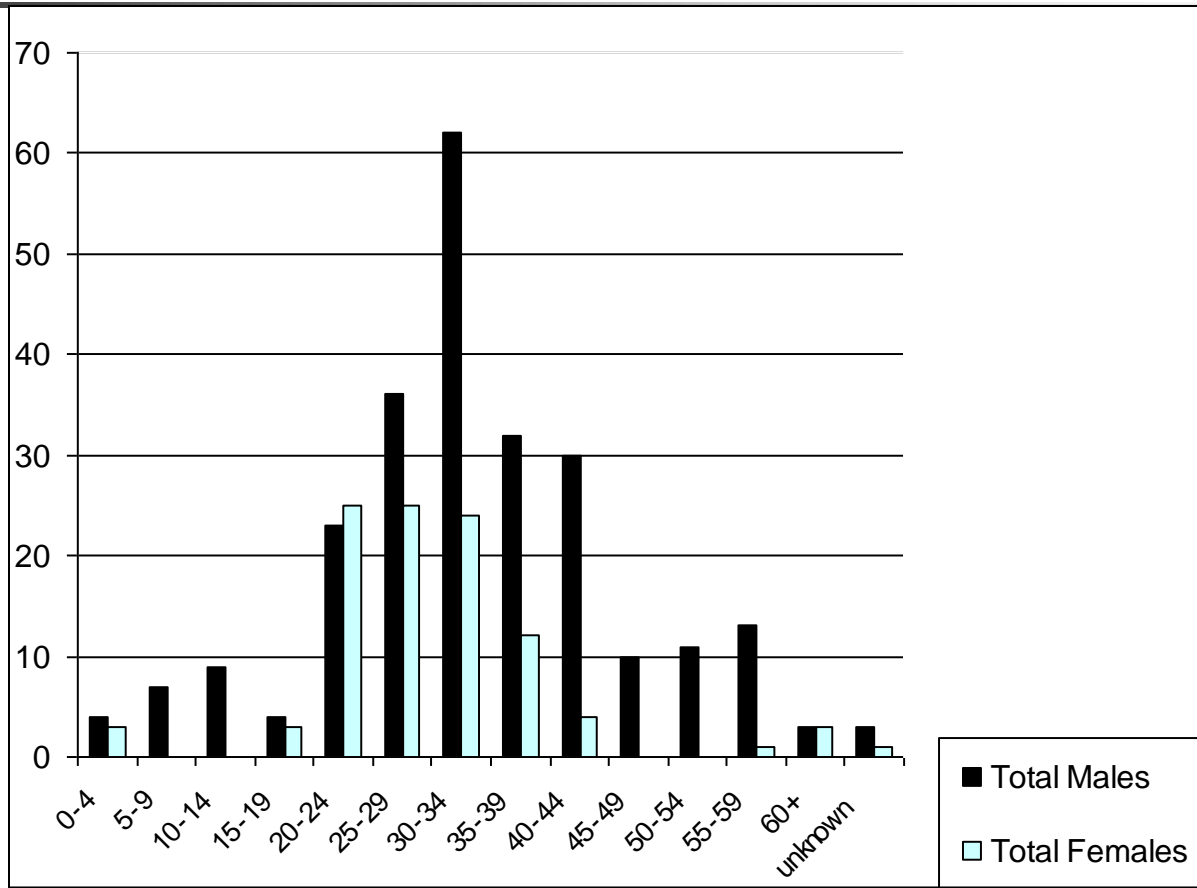
- 8% of adults < 45
- > 80% of prostitutes
- In 2013: **70% of the global total**
- **Life expectancy < 40 years**
- Causes:
 - Multiple sex partners
 - Prostitution
 - STD's
 - Mother to child transmission



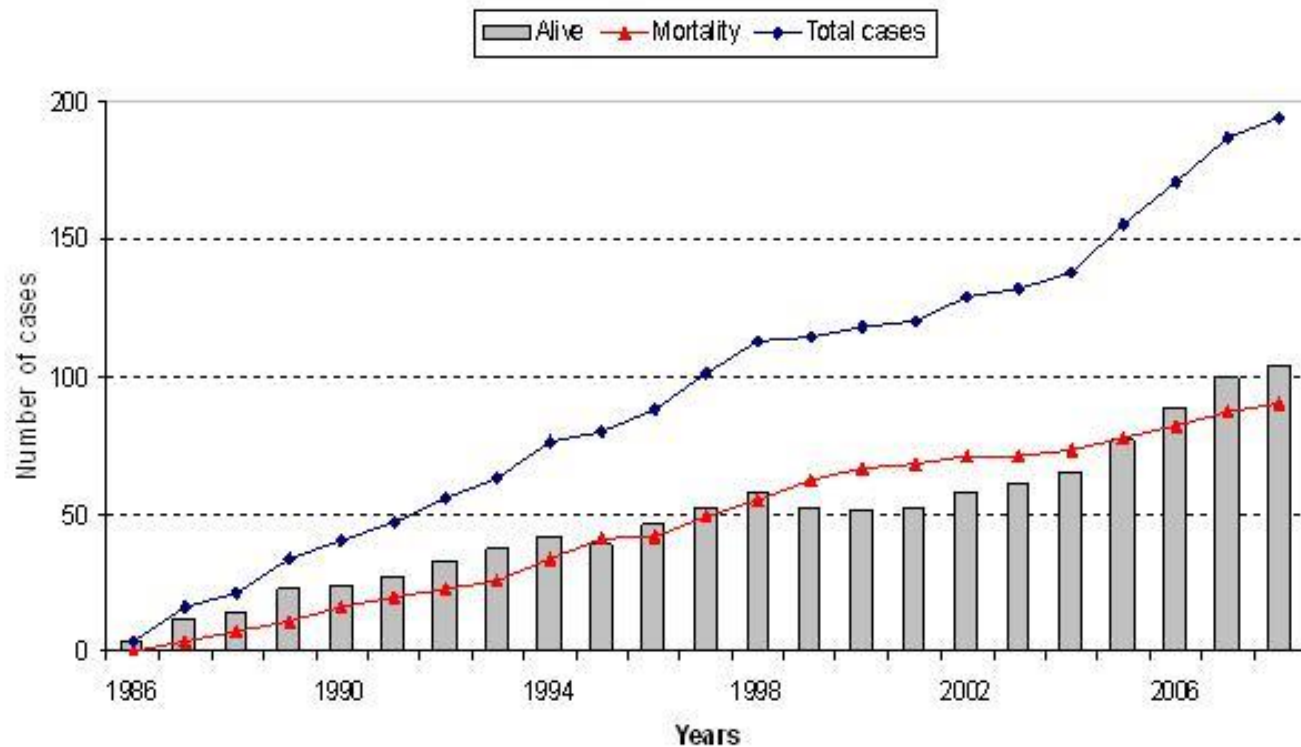
Time cover 2001



HIV in Jordan



HIV – Jordan: mortality



Transmission

- Sexual intercourse
- Mother → child
- IV drug use
- Blood transfusion
- Needlestick injury

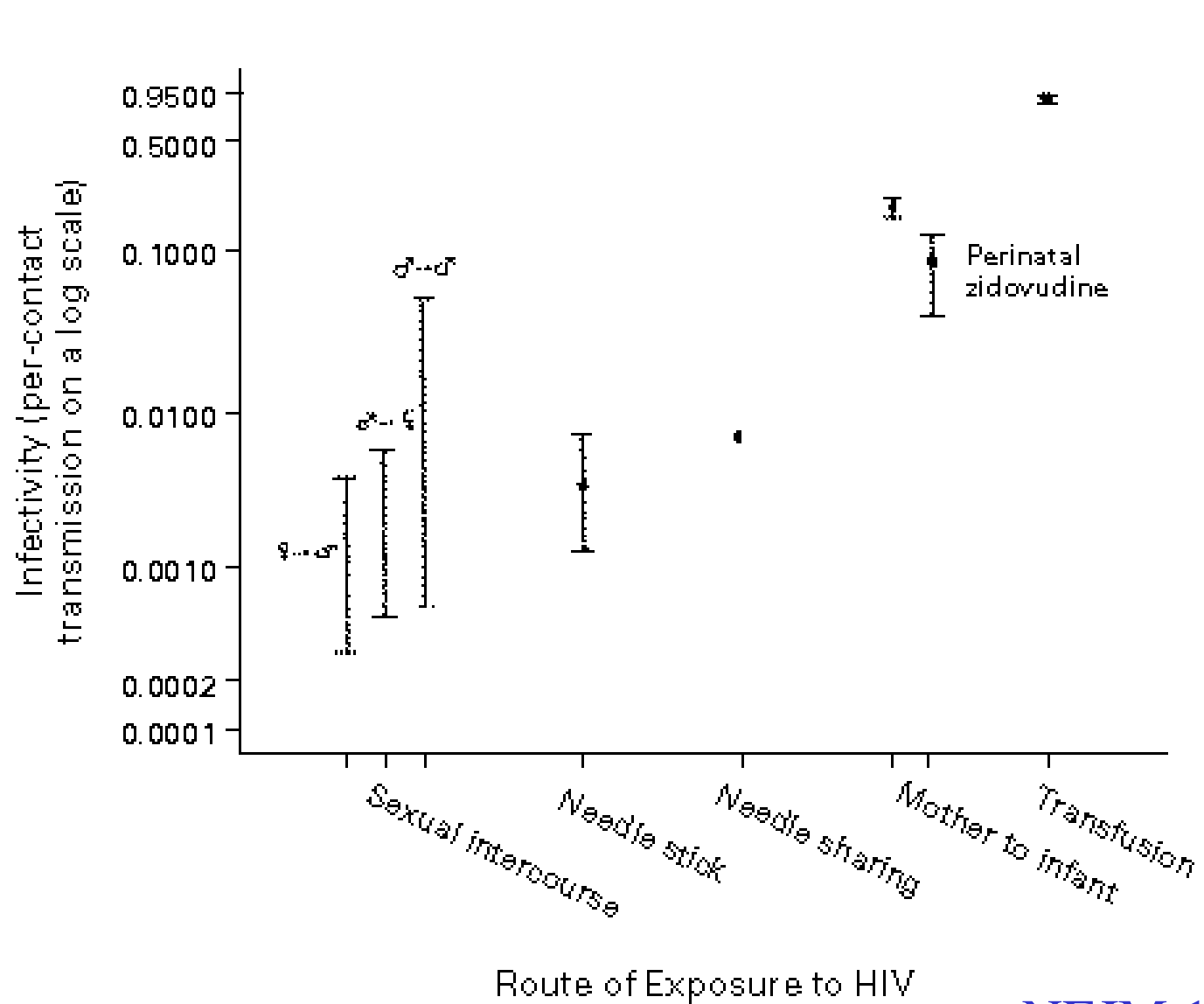




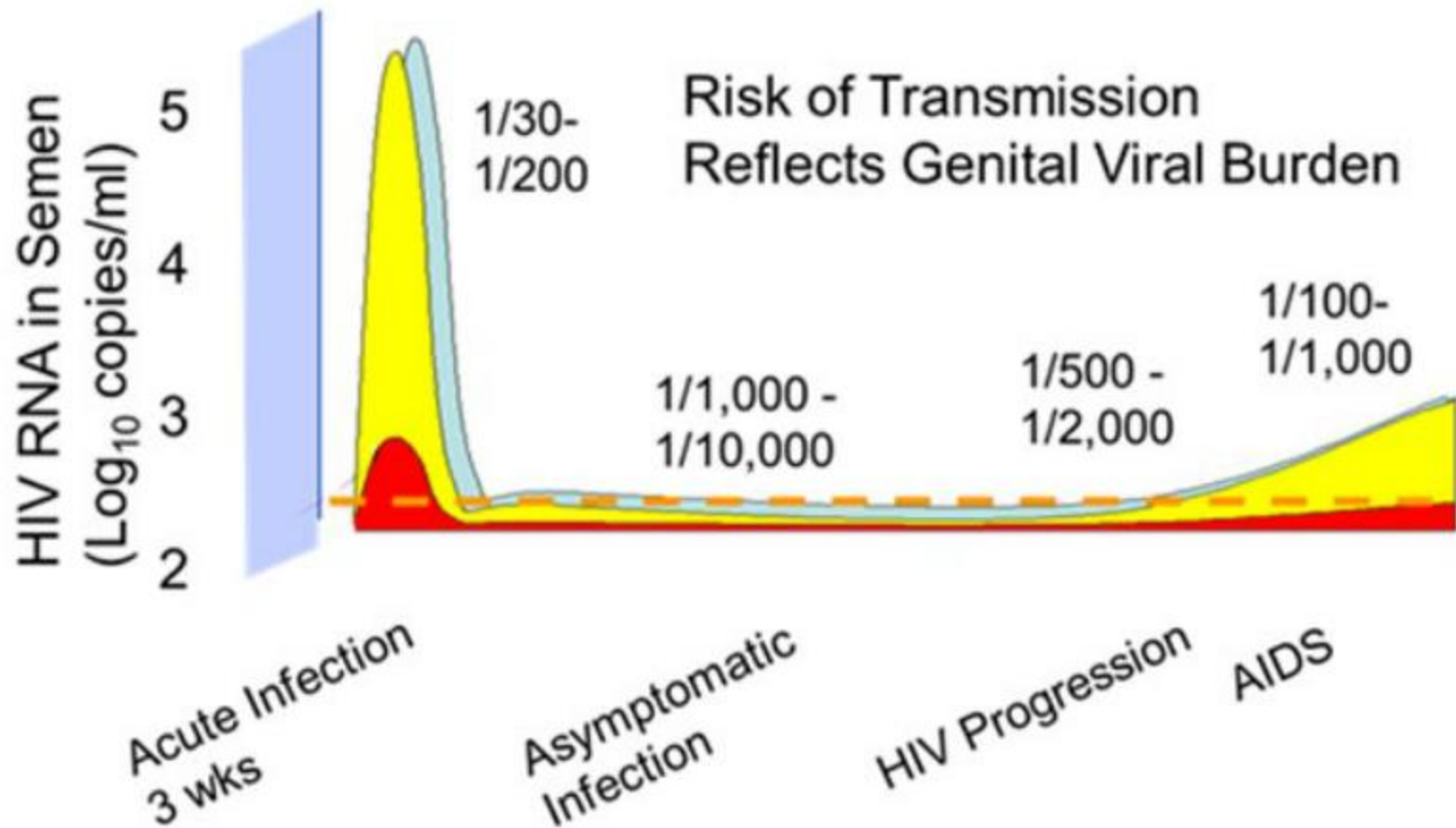
All body fluids...

- 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



Risk of Sexual Transmission of HIV





Healthcare workers

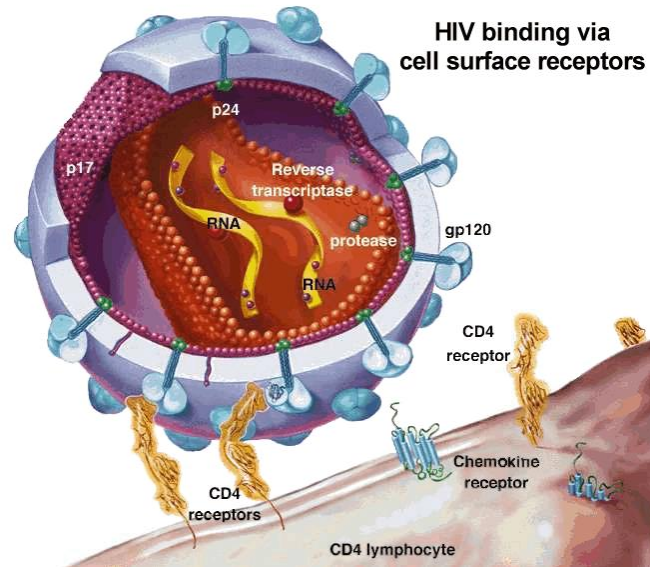
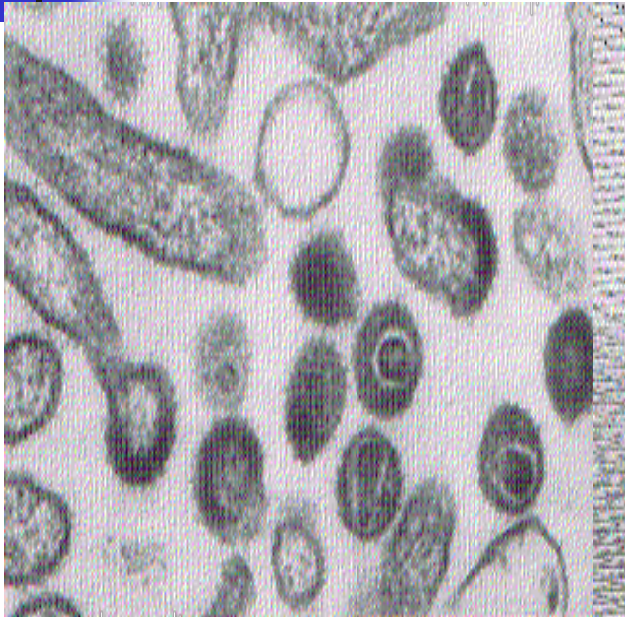
- Low risk
- 0.3%
- Universal precautions *****
 - Hand washing
 - Gloves, gowns, masks
 - Sharps
 - Open lesions...

One hand technique

No recapping



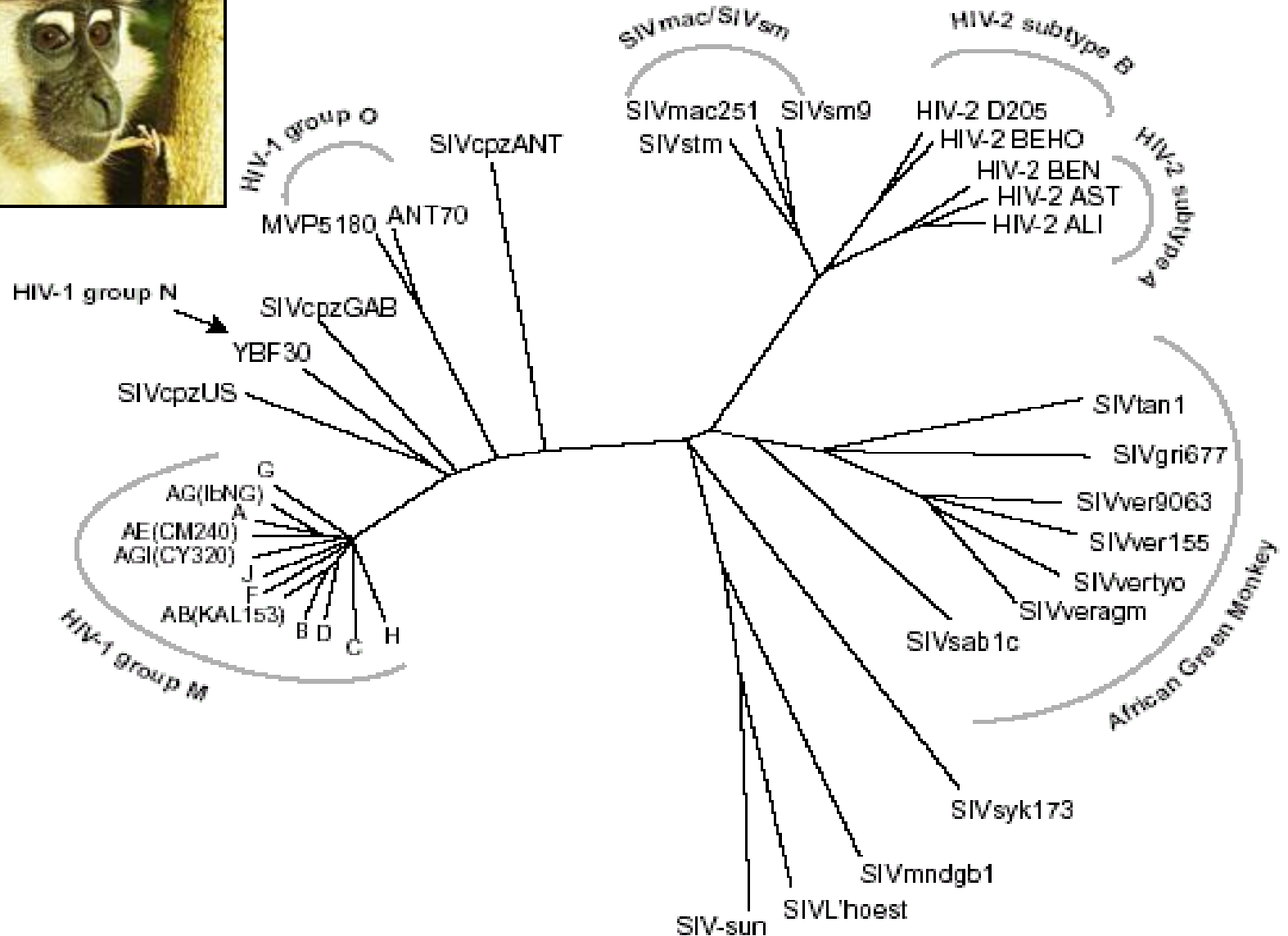
HIV Structure



HIV binding via CD4 & chemokine receptor

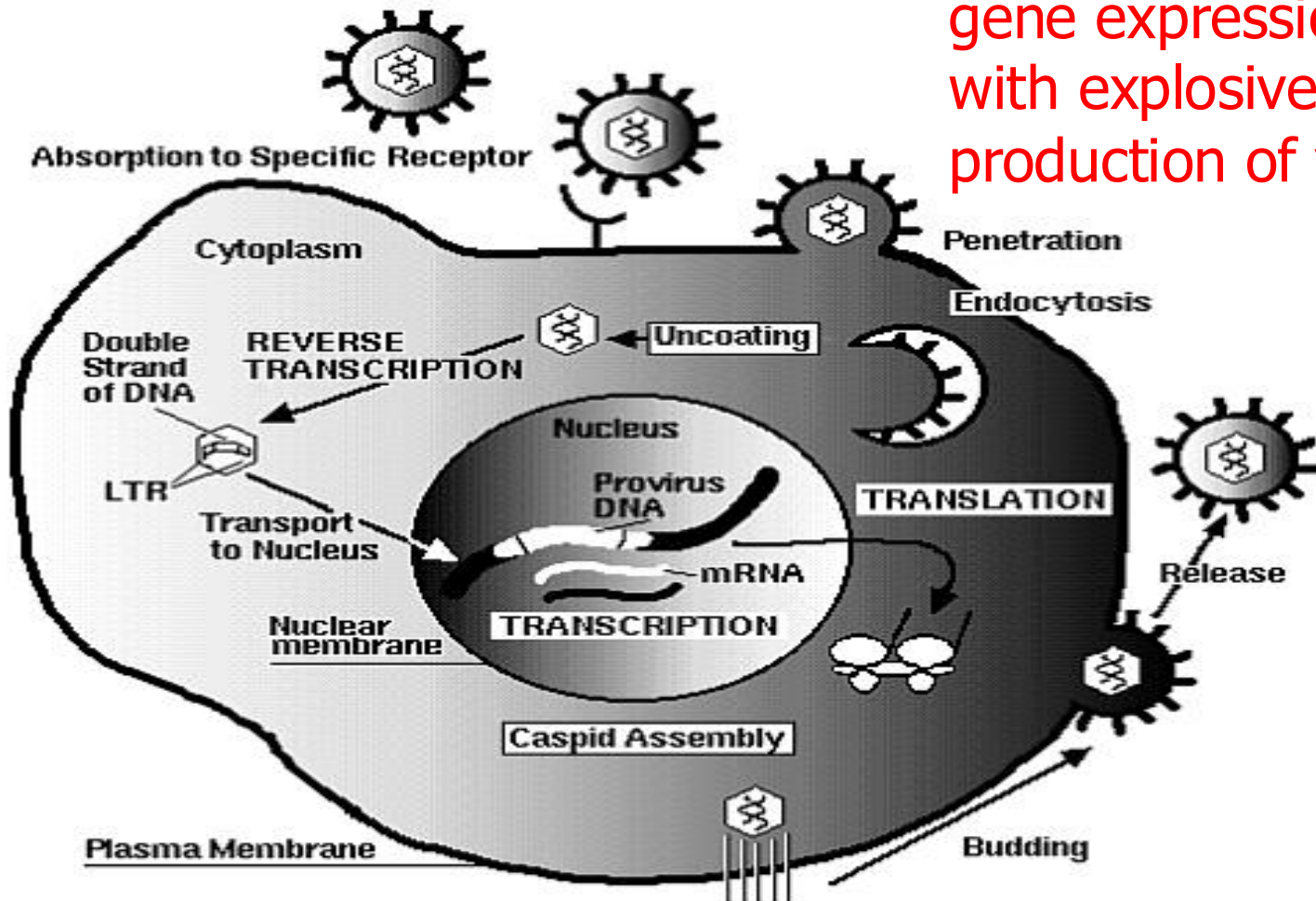


Phylogenetic tree

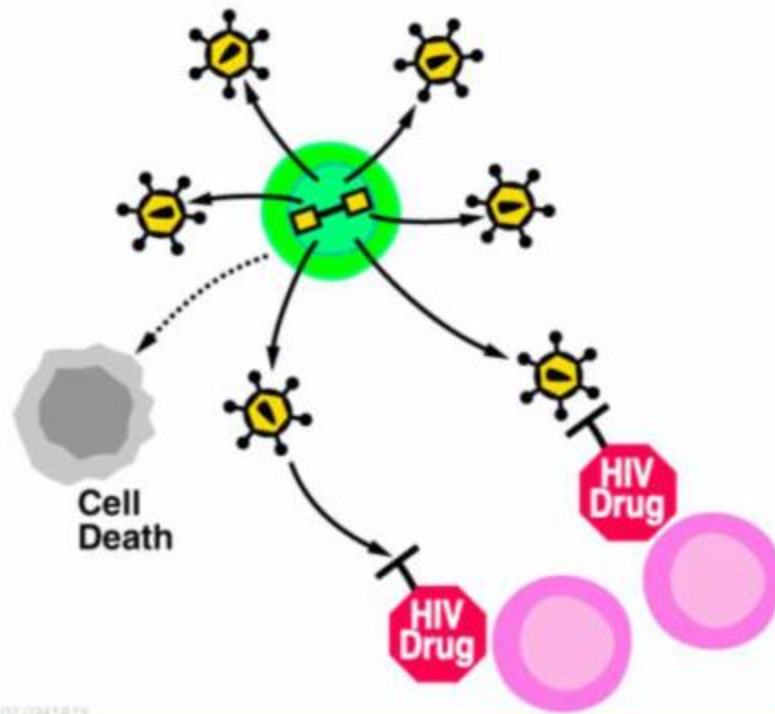


Life cycle of HIV

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



Productively Infected Cells

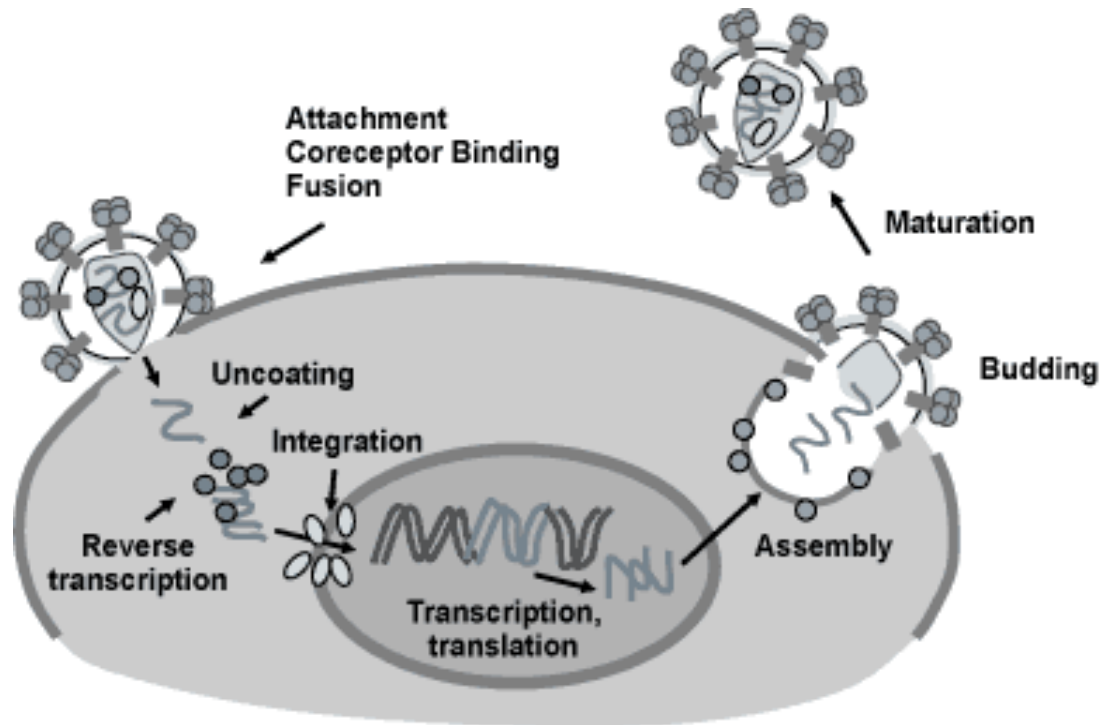


02/03/14 14:19

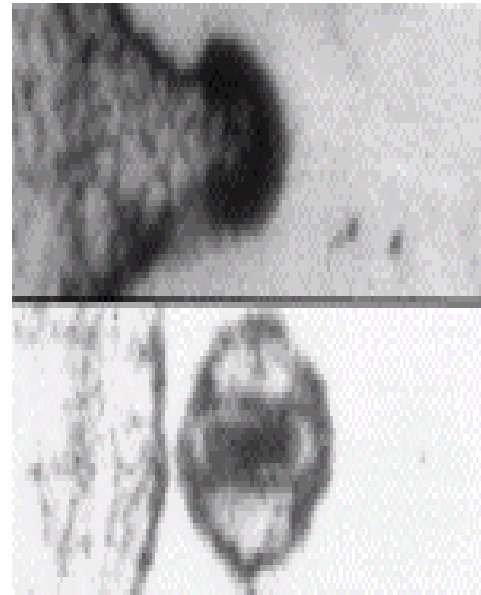
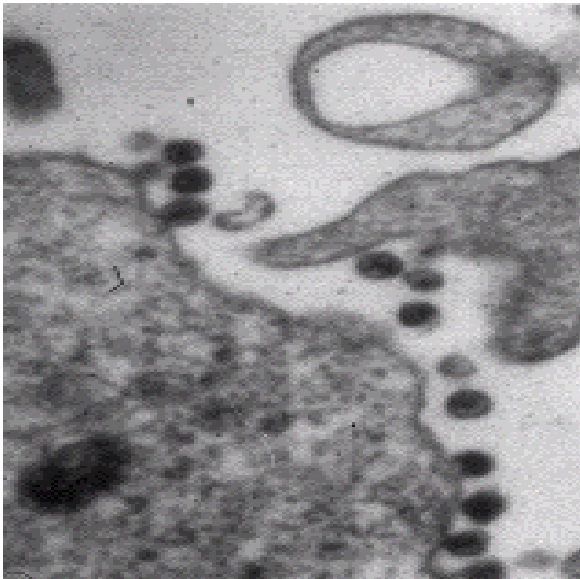
Latently Infected Cells



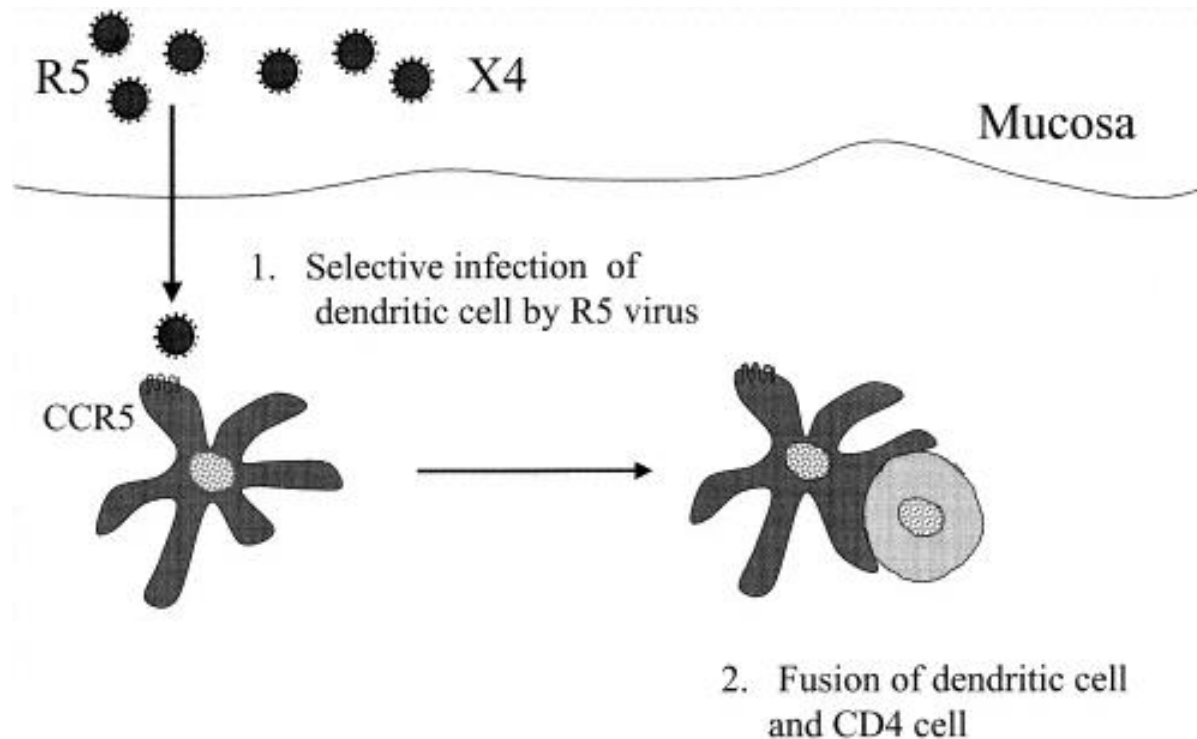
1. Attachment
2. Coreceptor binding
3. Fusion
4. Uncoating
5. Reverse transcription
6. Integration
7. Transcription
8. Translation
9. Assembly
10. Budding
11. Maturation



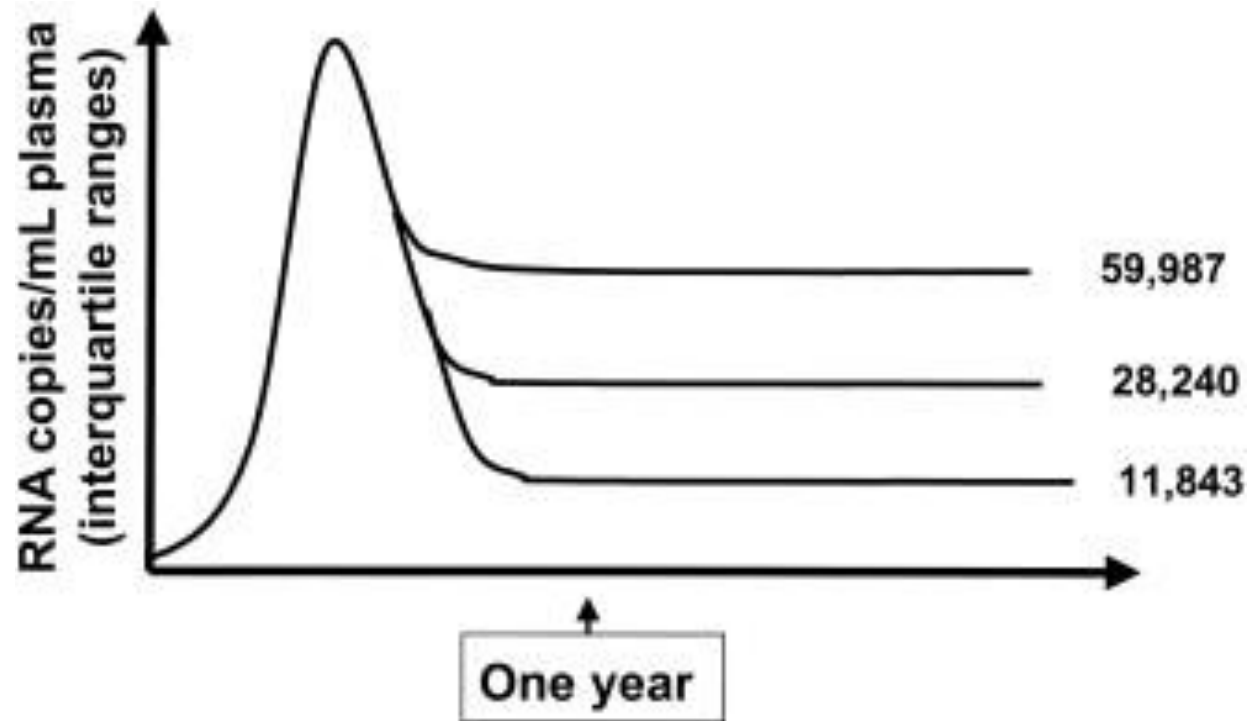
HIV budding



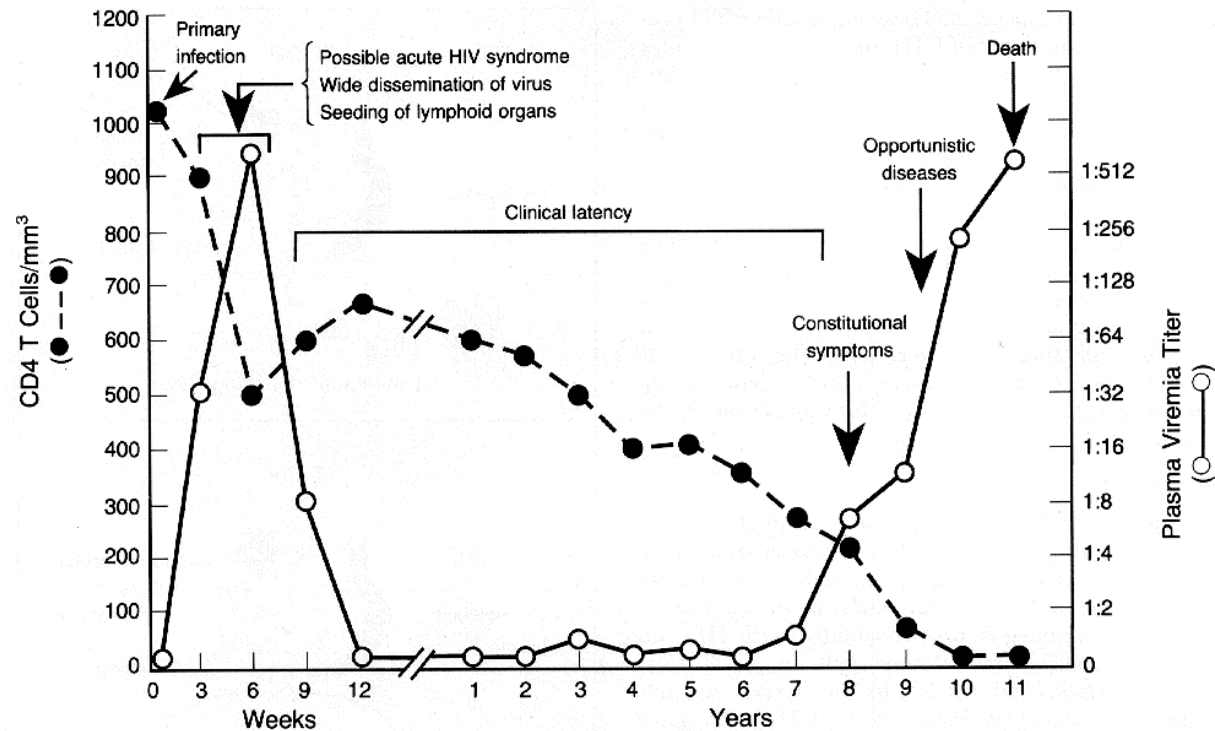
Transmission



Viral steady state

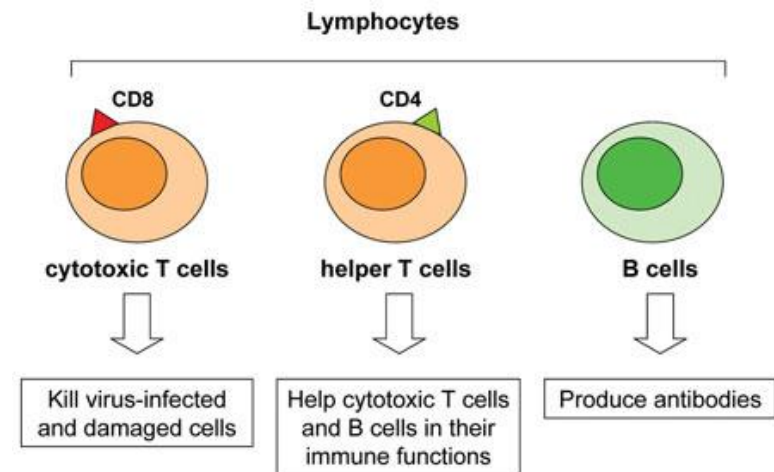


Course of HIV infection

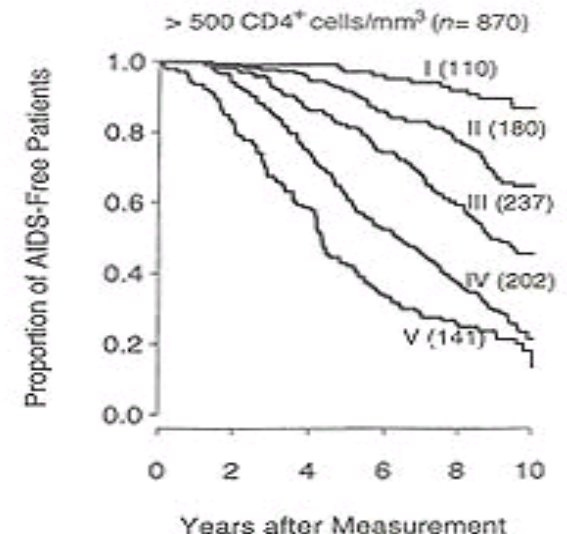
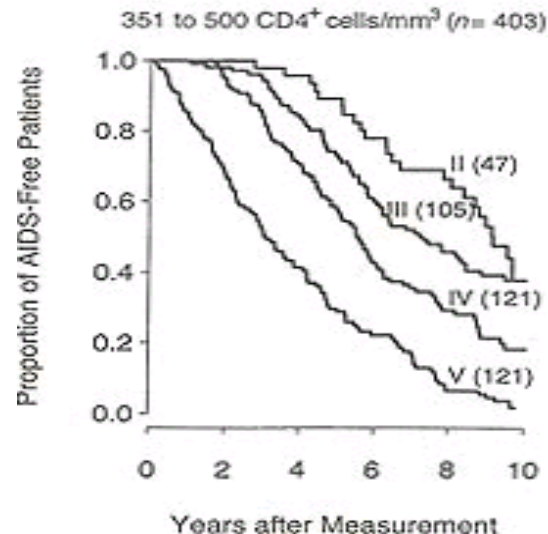
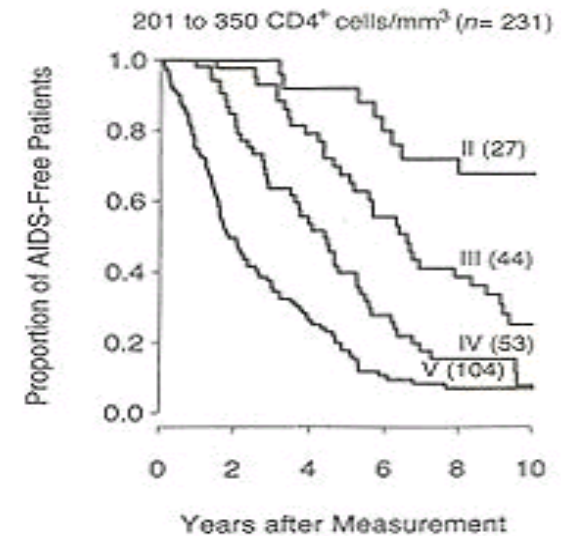
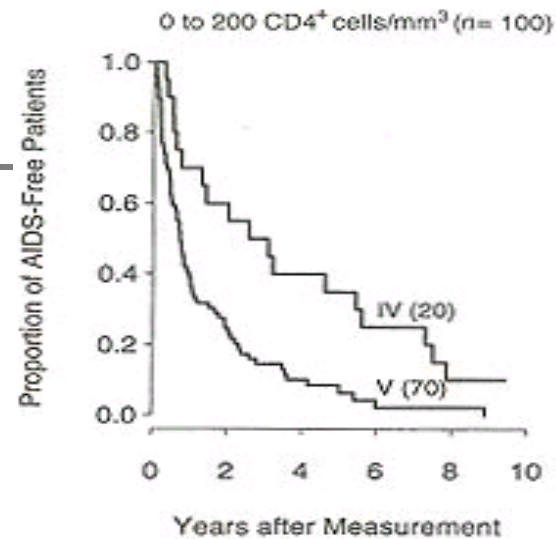
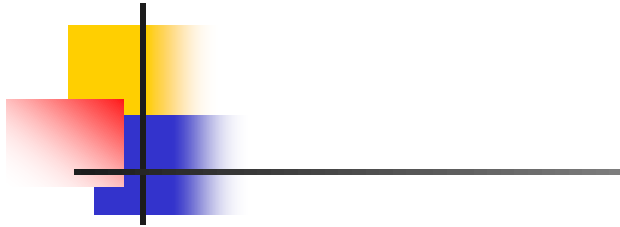


CD4 count

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



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 $\approx 10^8$ copies/ml
- Highly infectious
- Dx by PCR followed by serology
 - 4th generation 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

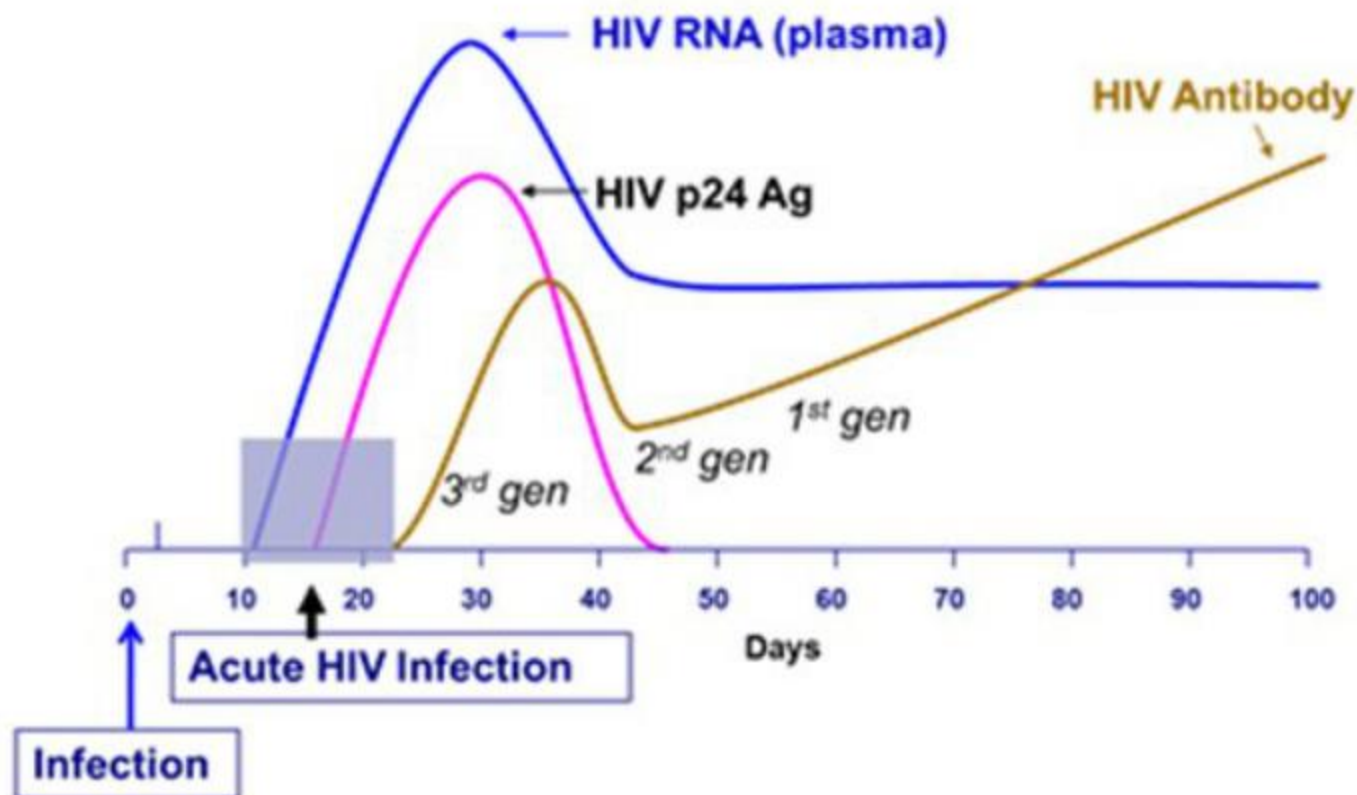
- completely asymptomatic



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



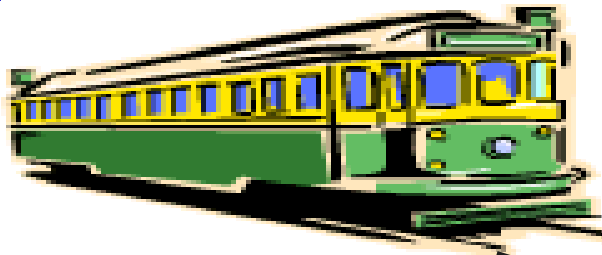
Busch MP, et al. *Am J Med* 1997; 102(5B):117-124. Modified diagram based on first iteration in stated source and updated using several publications since 1997.



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

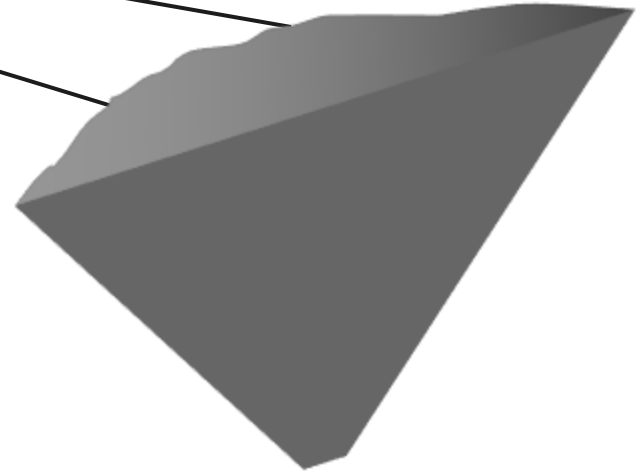
Viral Load (V.L) & CD4 count



CD4

9706

Viral load



HIV = destruction of immunity

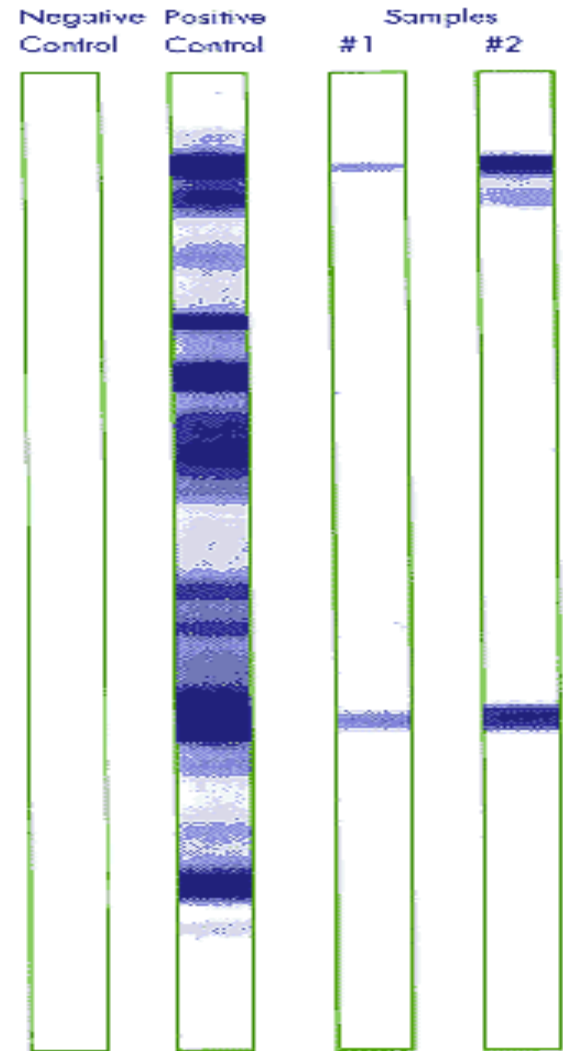
- Destruction of CD4 cells
- Evasion of immune response
- Lymph node pathology
- Exhaustion of immunity



HIV Diagnosis

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

WESTERN BLOT TESTS



Sample #1 is indeterminate.

Sample #2 is positive.



CDC Classification (1993)

	A	B	C
CD4	Asymptomatic, acute or PGL	Symptomatic, not A or 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 | 11) Lymphoma |
| 2) Cervical cancer | 12) PCP |
| 3) Coccidioidomycosis | 13) Recurrent pneumonia |
| 4) Cryptococcosis | 14) MAC |
| 5) CMV | 15) PML |
| 6) Encephalopathy | 16) Salmonellosis |
| 7) HSV | 17) Brain Toxoplasmosis |
| 8) Histoplasmosis | 18) Wasting |
| 9) TB | 19) Kaposi's sarcoma |
| 10) Cryptosporidiosis | 20) Isosporiasis |

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

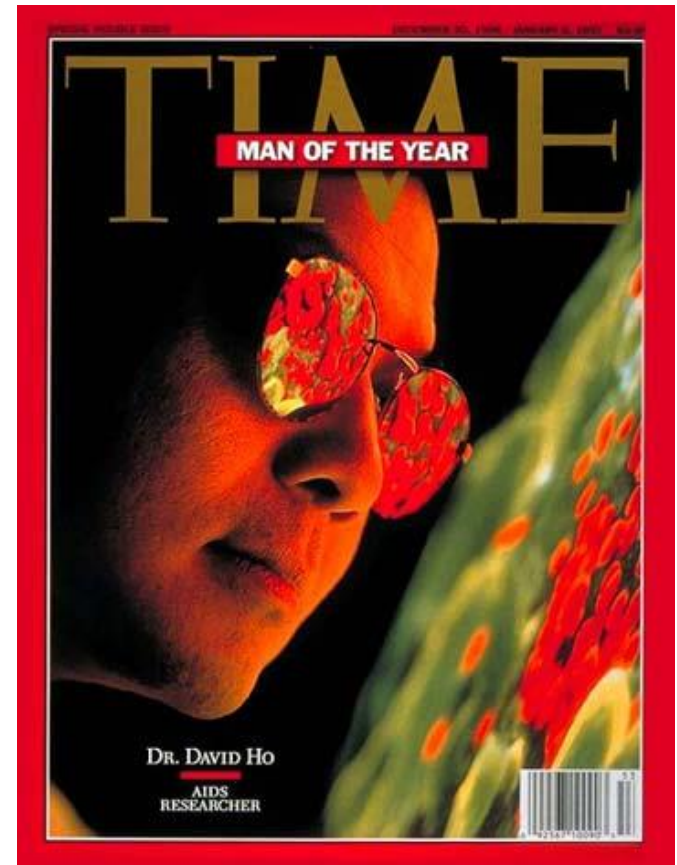
2 NRTI + PI

□ 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

FDA Approval of HIV Medicines

1981: First AIDS cases are reported in the United States.

1985-89	1990-94	1995-99	2000-04	2005-09	2010-14	2015-19	2020-24
1987 Zidovudine (NRTI)	1991 Didanosine* (NRTI) 1992 Zalcitabine* (NRTI) 1994 Stavudine* (NRTI)	1995 Lamivudine (NRTI) Sagunavir Mesylate* (PI) 1996 Indinavir* (PI) Nevirapine (NNRTI) Ritonavir (PI) 1997 Combivir* (FDC) Delavirdine* (NNRTI) Nelfinavir* (PI) Sagunavir* (PI) 1998 Abacavir (NRTI) Efavirenz (NNRTI) 1999 Amprenavir* (PI)	2000 Didanosine EC* (NRTI) Kaletra (FDC) Trizivir* (FDC) 2001 Tenofovir DF (NRTI) 2002 Stavudine XR* (NRTI) 2003 Atazanavir (PI) Emtricitabine (NRTI) Etravirine (NNRTI) Fosamprenavir* (PI) 2004 Epivir* (FDC) Truvada (FDC)	2005 Tipranavir* (PI) 2006 Atriple* (FDC) Darunavir (PI) 2007 Maraviroc (CA) Raltegravir (INSTI) 2008 Etravirine (NNRTI)	2011 Complera (FDC) Nevirapine XR (NNRTI) Ralpivirine (NNRTI) 2012 Stribild (FDC) Truvada (PrEP) 2013 Dolutegravir (INSTI) 2014 Cobicistat (PE) Etravirine* (NNRTI) Trimeq (FDC)	2015 Evotaz (FDC) Genvoya (FDC) Prezobix (FDC) 2016 Descovy (FDC) Odefsey (FDC) 2017 Juluca (FDC) Raltegravir HD (INSTI) 2018 Bikavir (FDC) Cimduo (FDC) Delstrigo (FDC) Doravirine (NNRTI) Ibalizumab-uiyk (PAI) Symfi (FDC) Symfi Lo (FDC) Symtuza (FDC) Tenukeys* (FDC) 2019 Dovato (FDC) Descovy (PrEP)	2020 Fostemsavir* (AI) Tivicay PD (INSTI) 2021 Cabenuva (FDC) Cabotegravir (INSTI) Cabotegravir (PrEP) 2022 Triumeq PD (FDC) Lenacapavir (CI) 2024 Ralpivirine PED (NNRTI)

30 drugs

Drug Class Abbreviations:

AI: Attachment Inhibitor; CA: CCR5 Antagonist; CI: Capsid Inhibitors; FDC: Fixed-Dose Combination; FI: Fusion Inhibitor;
INSTI: Integrase Inhibitor; NNRTI: Non-Nucleoside Reverse Transcriptase Inhibitor; NRTI: Nucleoside Reverse Transcriptase
Inhibitor; PE: Pharmacokinetic Enhancer; PI: Protease Inhibitor; PAI: Post-Attachment Inhibitor; PrEP: Pre-exposure prophylaxis

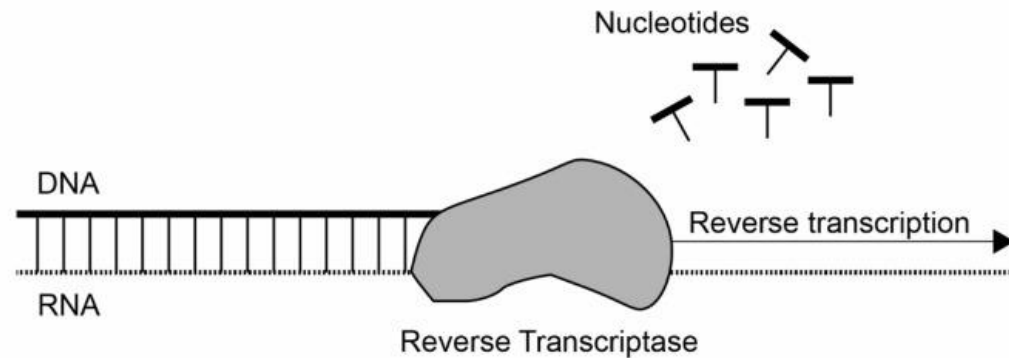
*Note: Approvals are for HIV treatment, unless otherwise indicated. Drugs in gray are no longer available and/or are no longer recommended for use in the United States by the HHS HIV/AIDS medical practice guidelines. These drugs may still be used in fixed-dose combination formulations. Fixed-dose combination brand products in gray may be available as generics.

For more information, visit HIVinfo.NIH.gov.

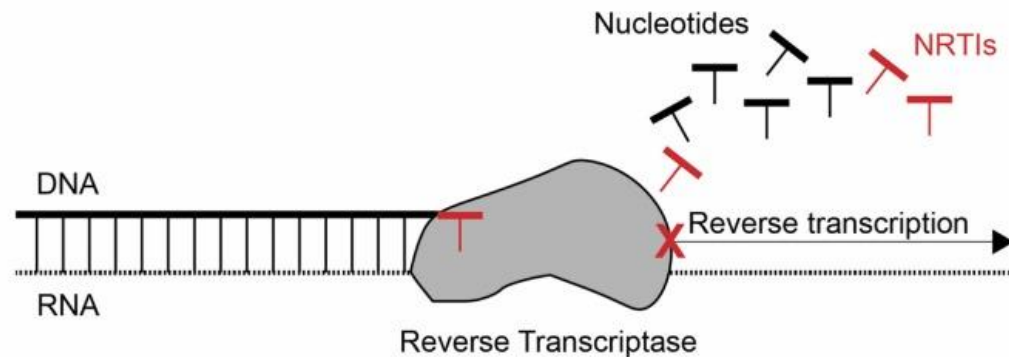


NRTI mechanism of action

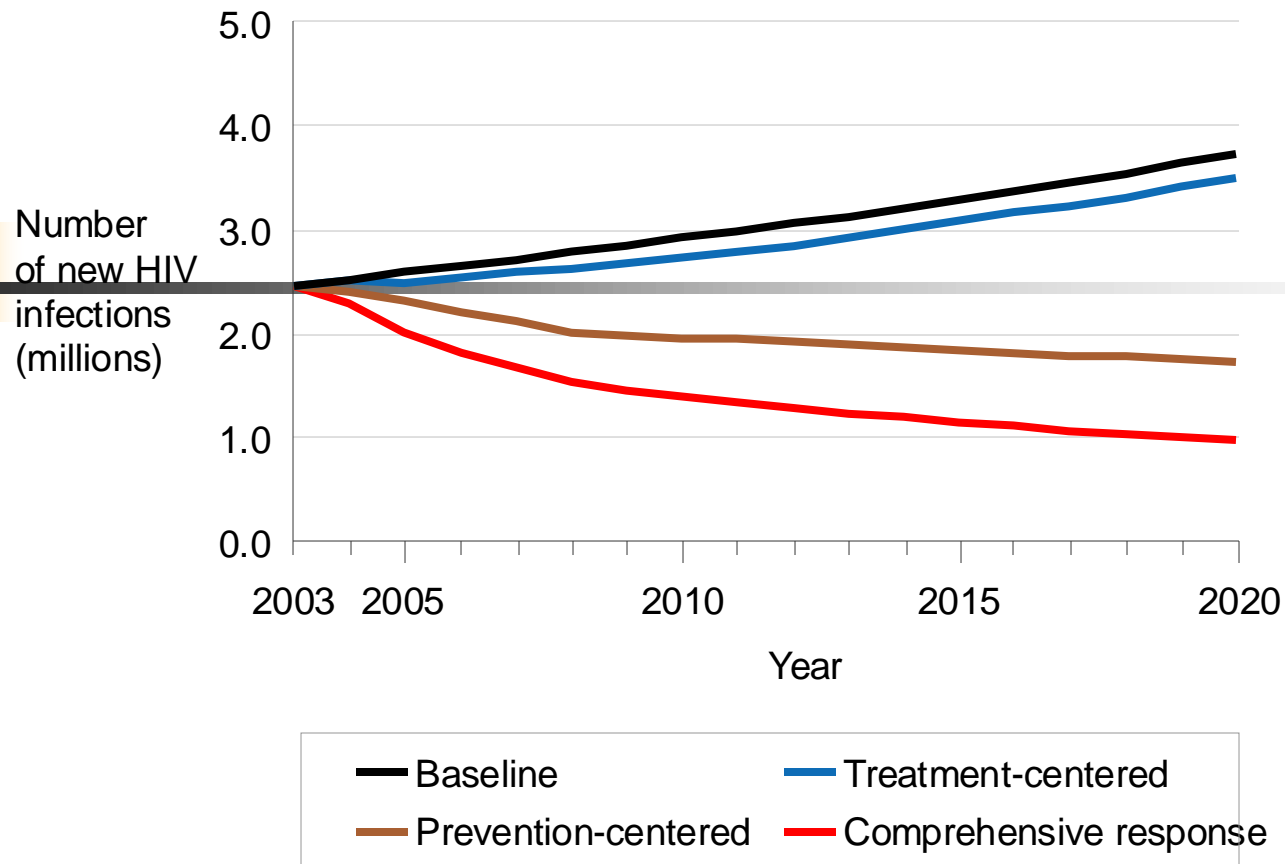
A



B



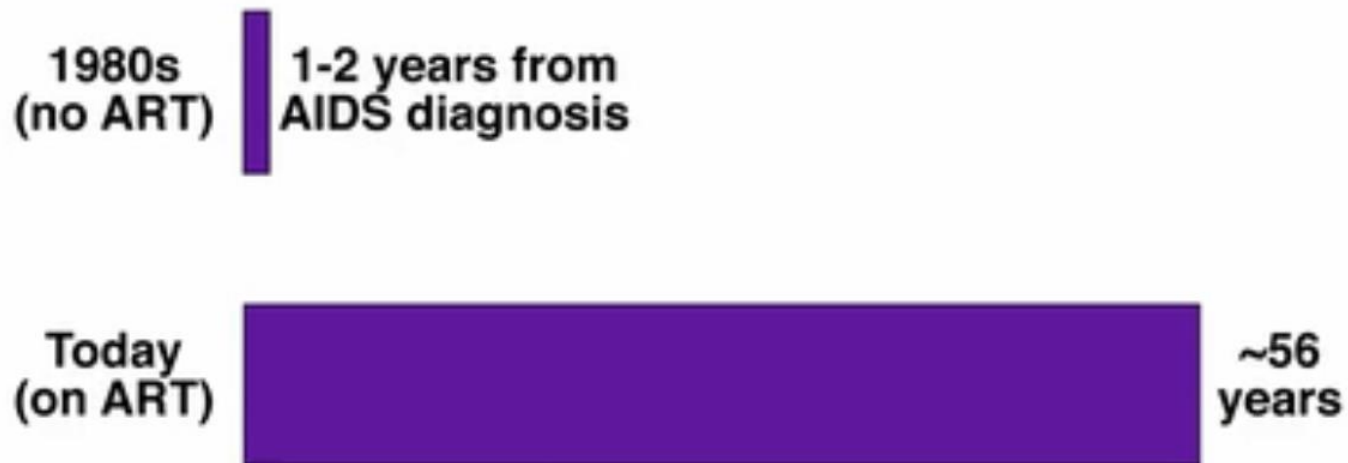
Impact of three scenarios on HIV infection in sub-Saharan Africa, 2003–2020



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

Life expectancy

Life Expectancy for 21-Year-Old with HIV, 1980s and Today



Source: JL Marcus et al. JAMA Netw Open 3:e207954, 2020.



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