

HIV & AIDS



Prof Ranjan Premaratna

HIV

- Human Immunodeficiency Virus

Infects only Human beings

AIDS

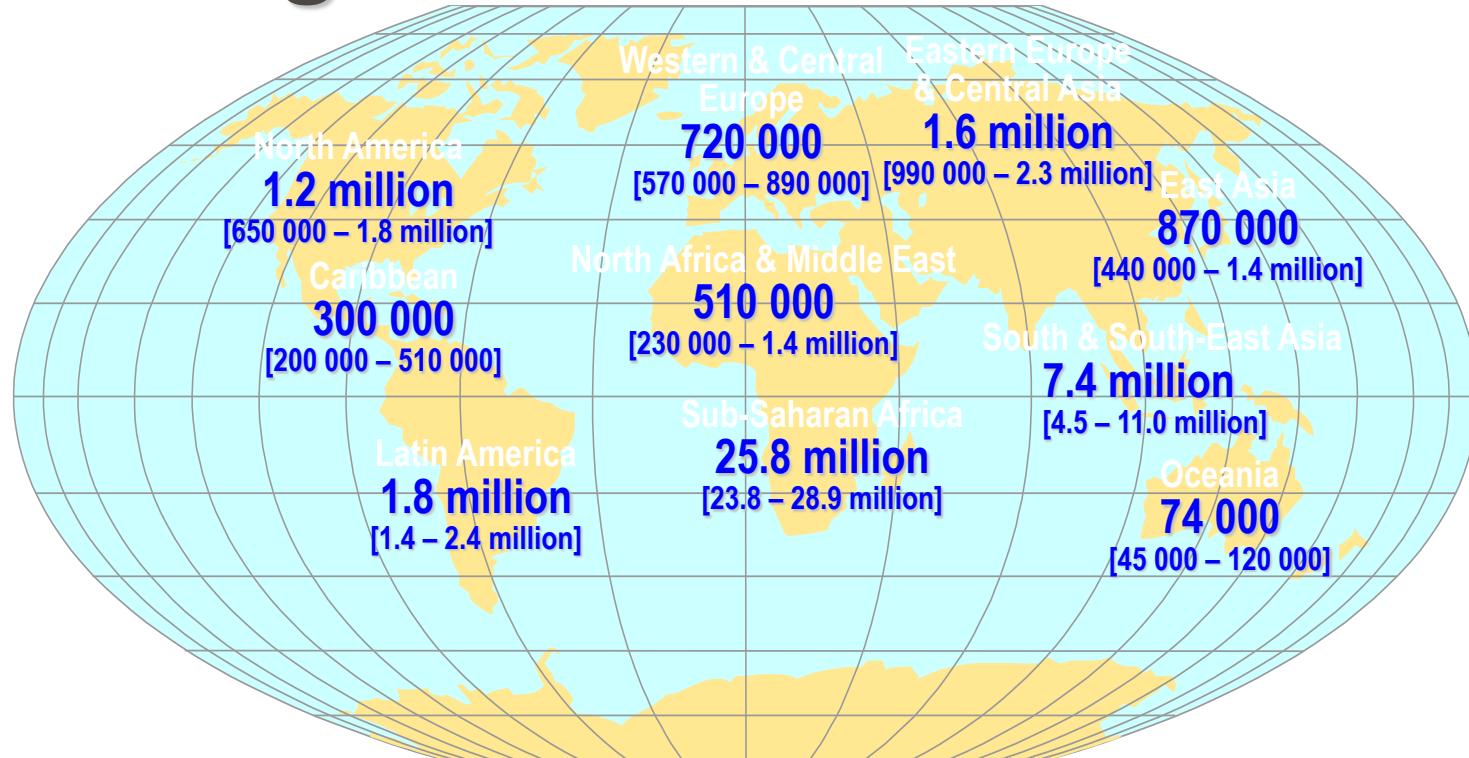
- Acquired Immune Deficiency Syndrome

Acquired (not inherited)
Immune deficiency
Deficiency of CD4+ cells in
the immune system
Syndrome, or a group of illnesses
taking place at the same time

HIV & AIDSEpidemiology

- 1st described: 1981- USA- Gay men & IVDUs
- Since then world wide spread
- HIV 1 & HIV 2

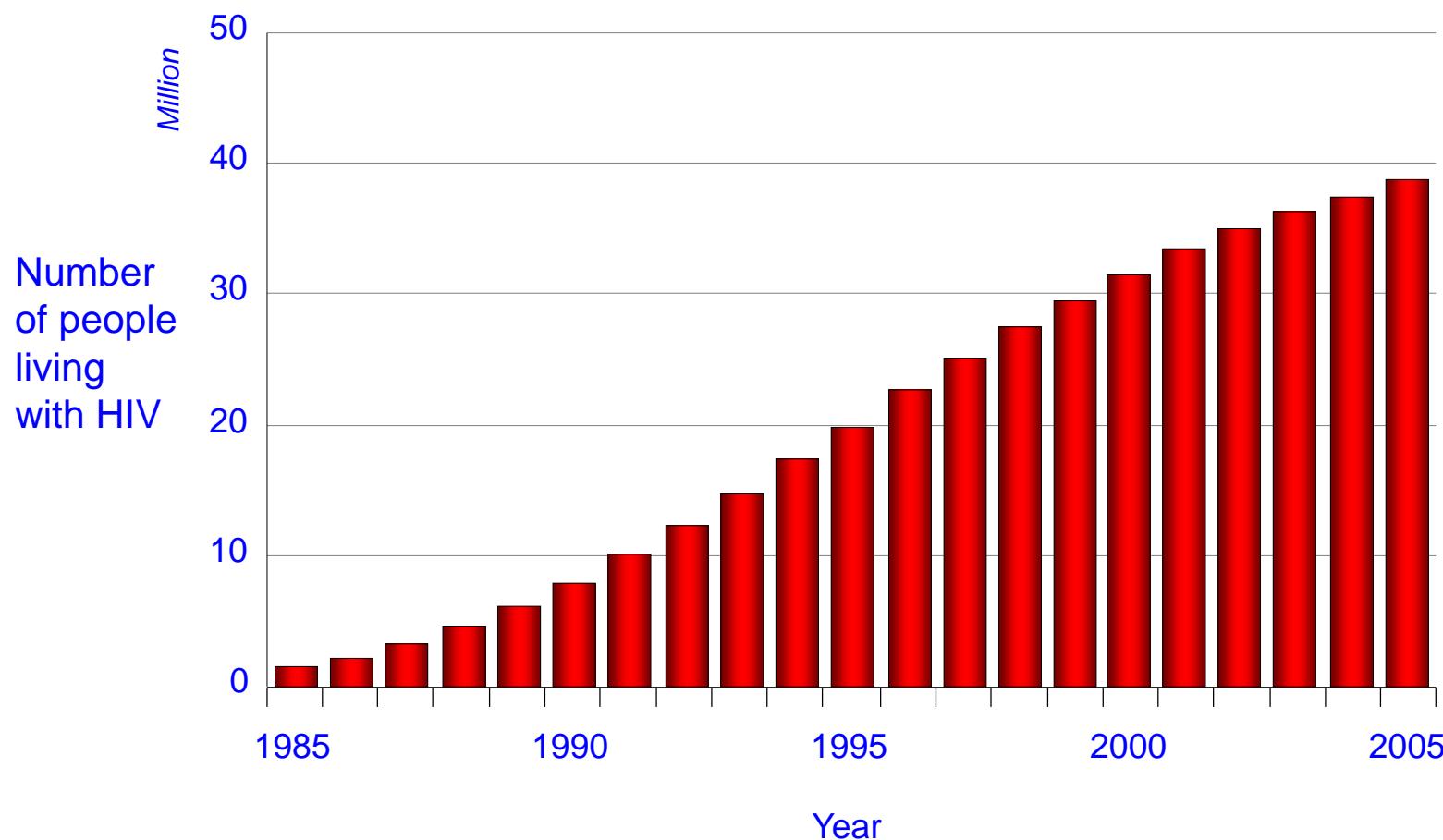
Adults and children estimated to be living with HIV as of end 2005



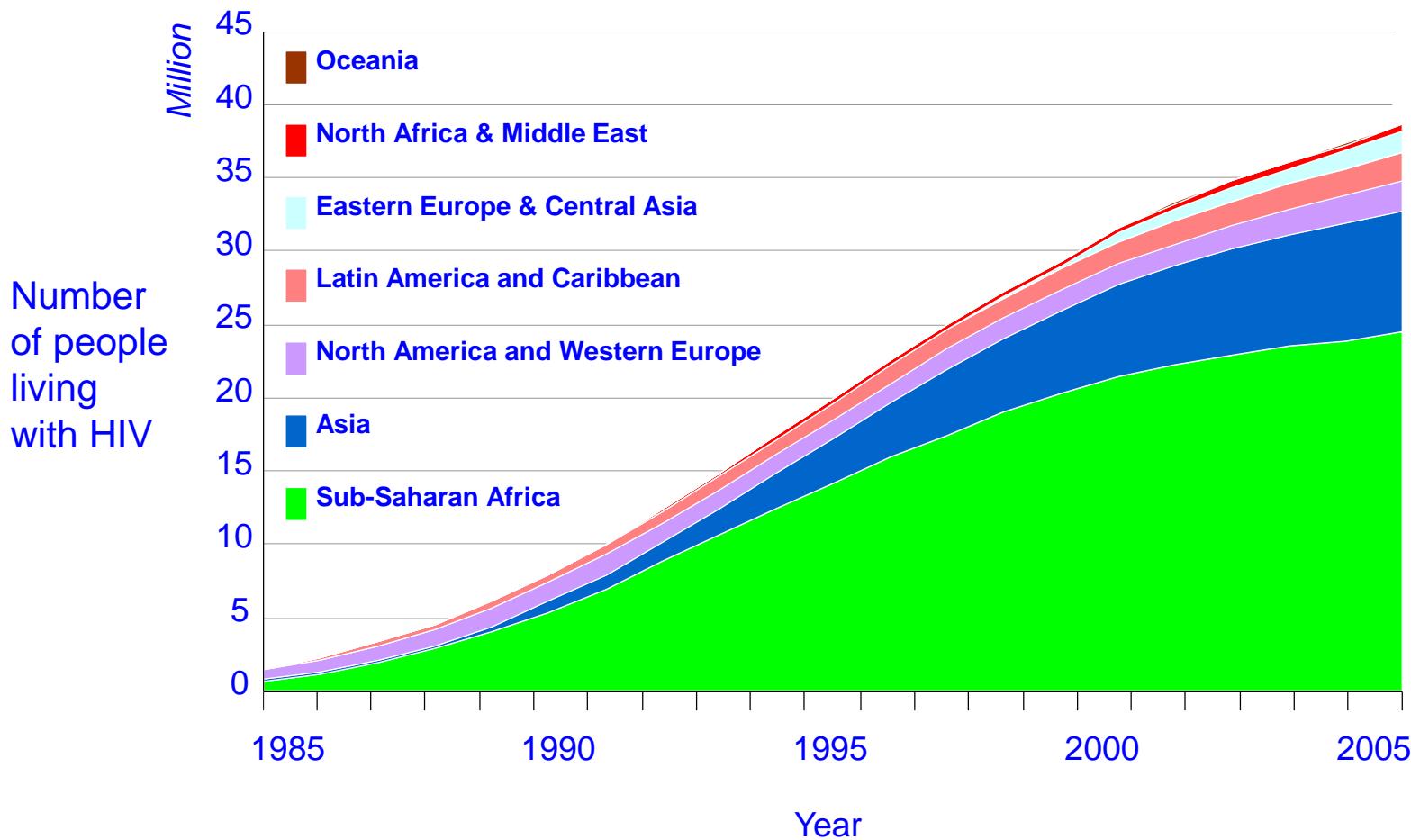
Total: 40.3 (36.7 – 45.3) million

Source: UNAIDS. AIDS Epidemic Update 2005

Estimated number of people living with HIV globally, 1985–2005

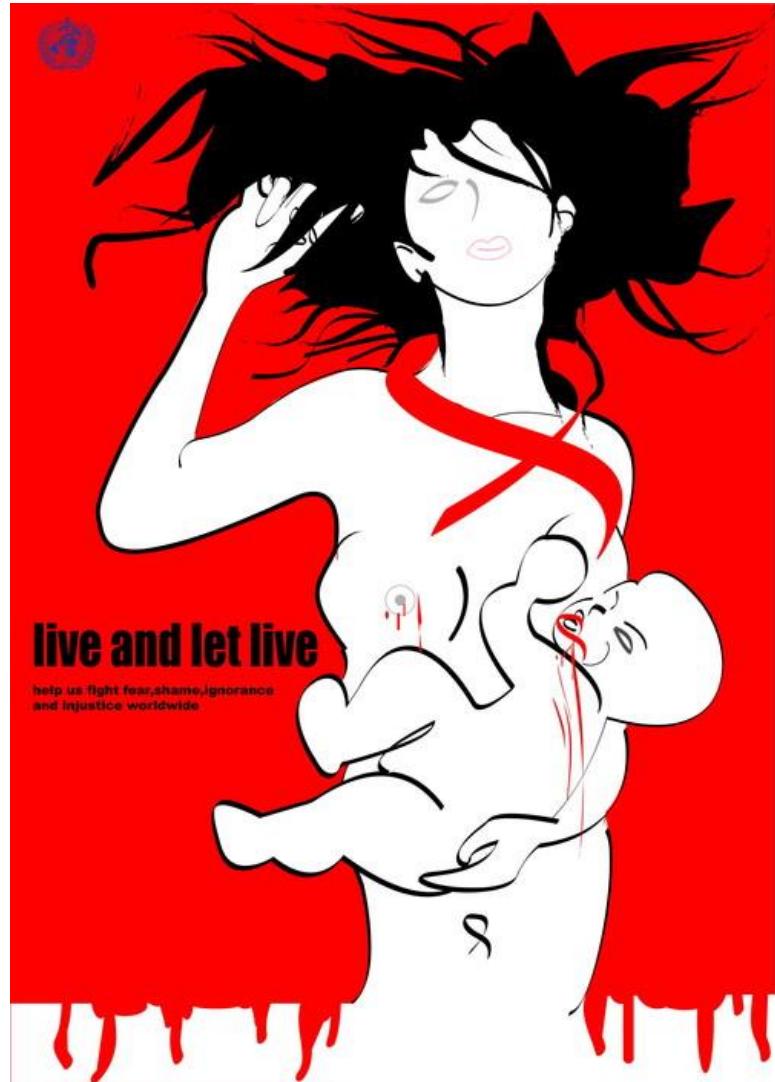


Estimated number of adults and children living with HIV by region, 1986–2005

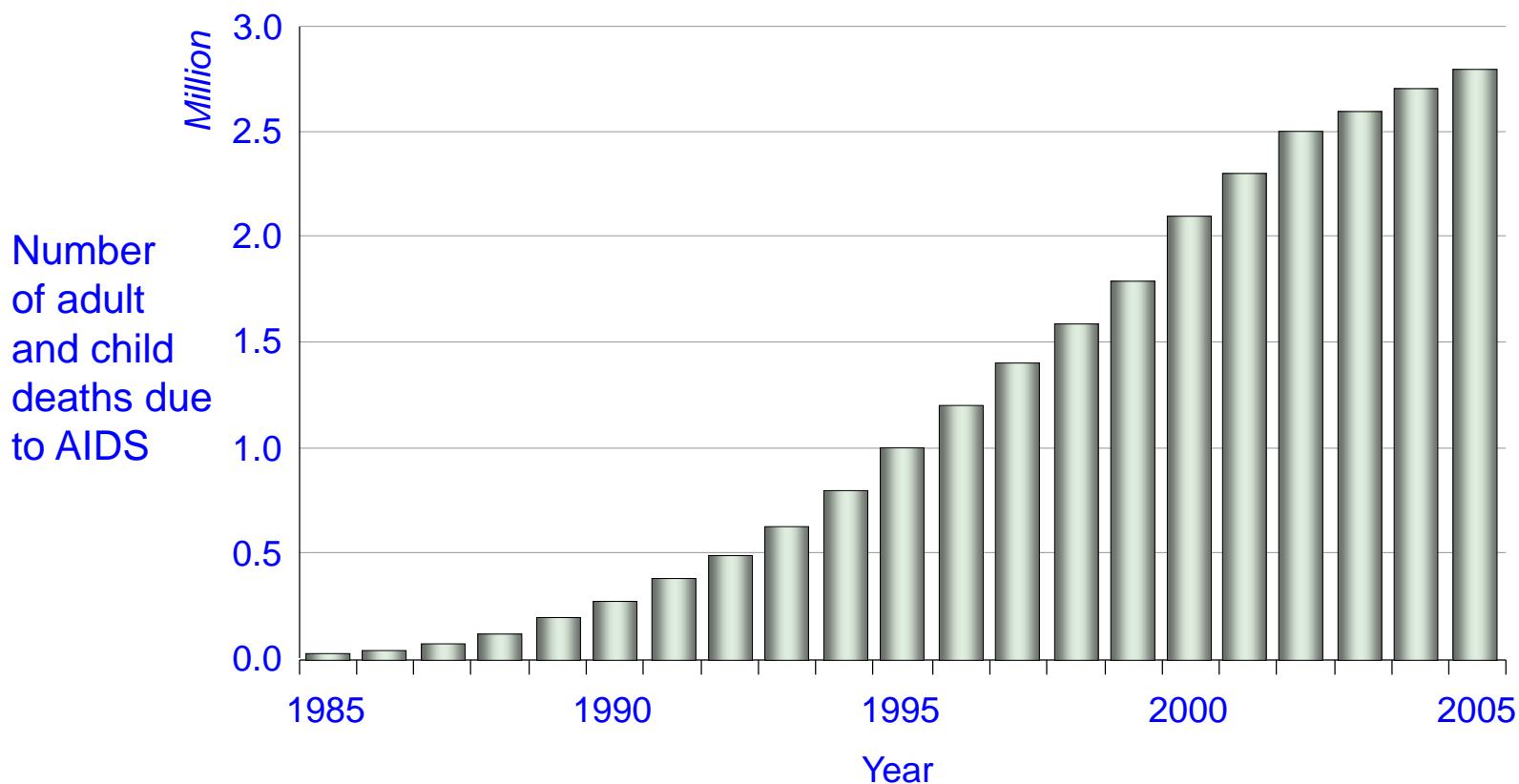


HIV & AIDSEpidemiology

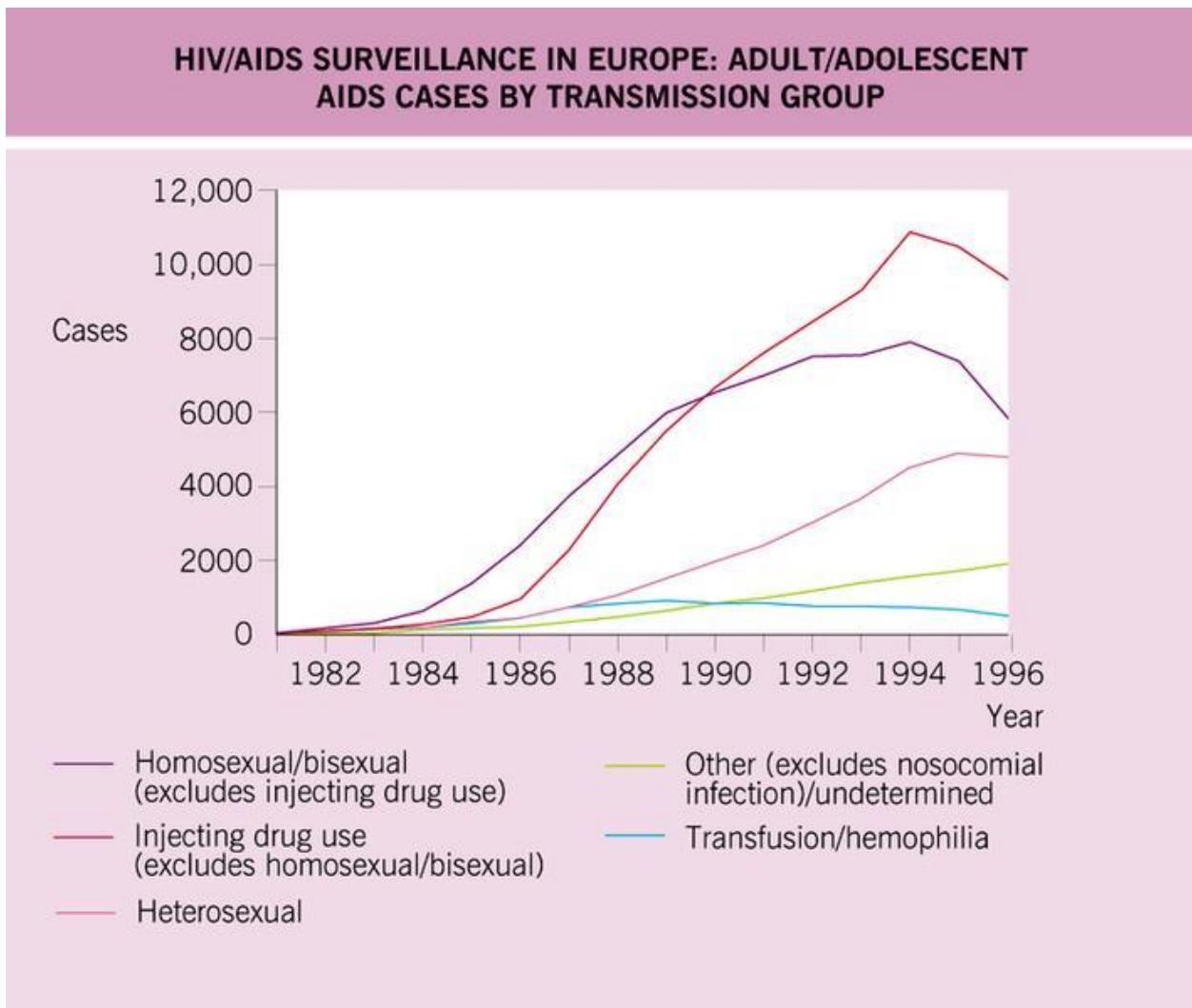
- The developing world accounted for > 75% of all AIDS cases
- 2.7 million cases are paediatric cases due to mother-child transmission



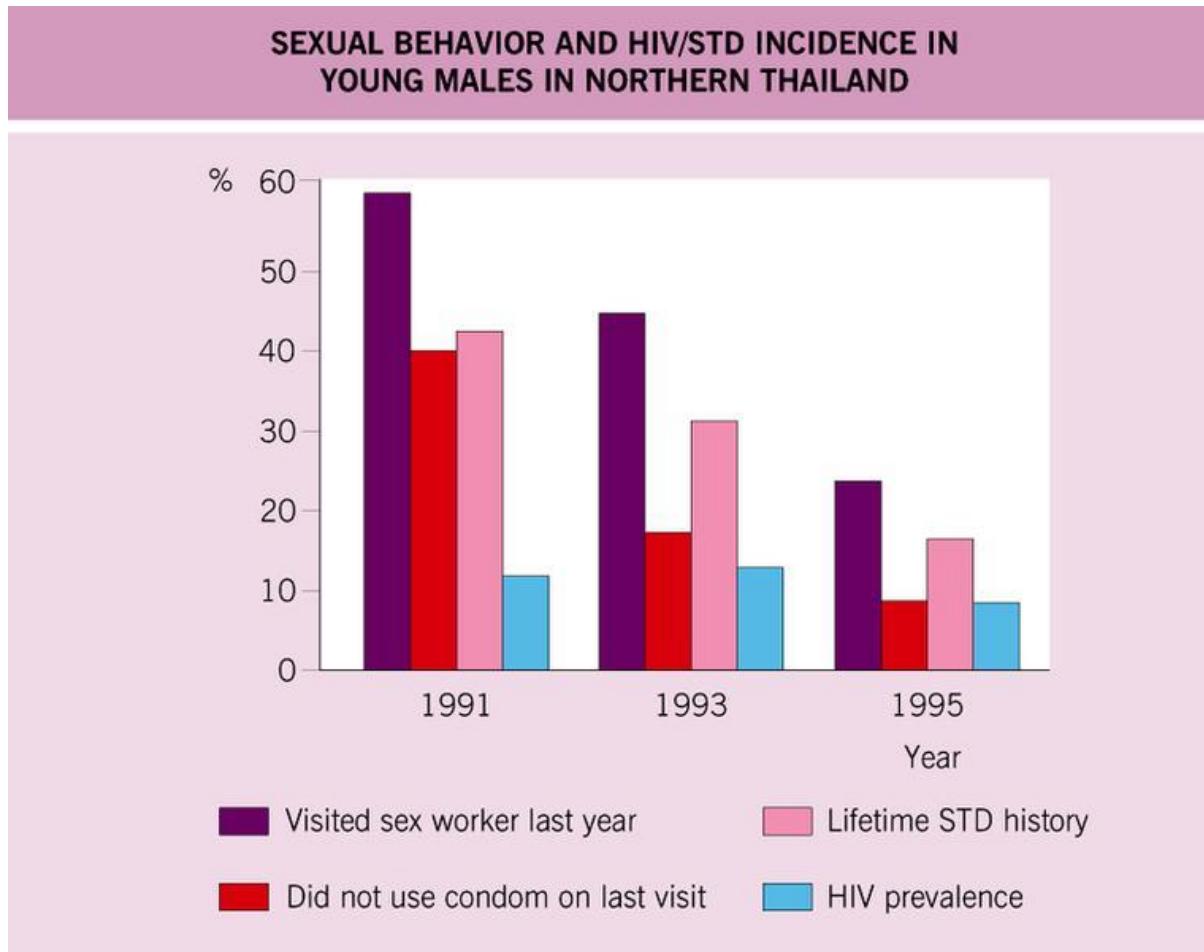
Estimated number of adult and child deaths due to AIDS globally, 1985–2005



HIV & AIDSEpidemiology



HIV & AIDSEpidemiology



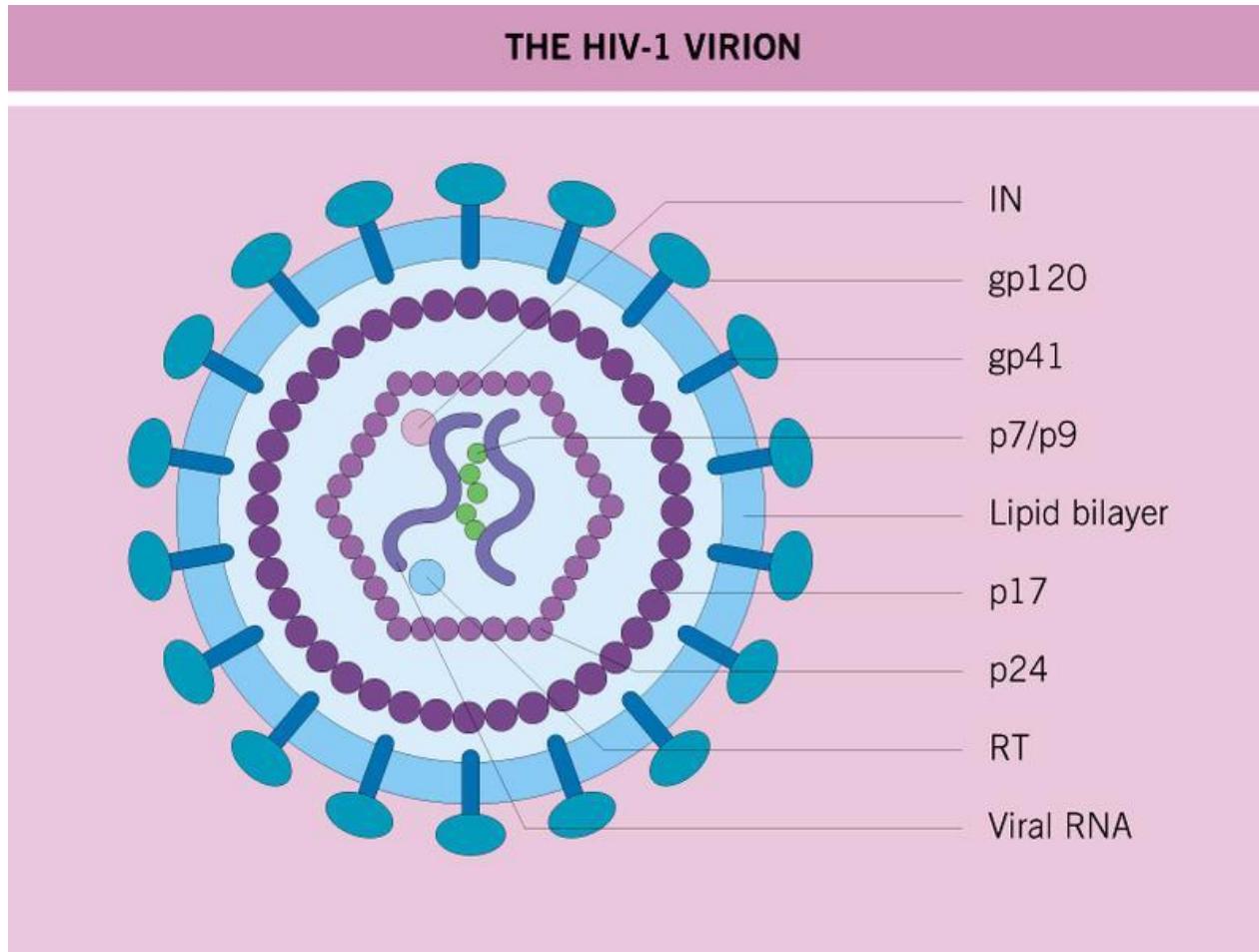
HIV & AIDS

- Caused by HIV 1 & HIV 2
- Retroviruses
- Routes of transmission & risk factors are similar
- Pathogenic effect of HIV 2 < HIV 1
- HIV 2 mainly in West Africa, Mozambique, and Angola

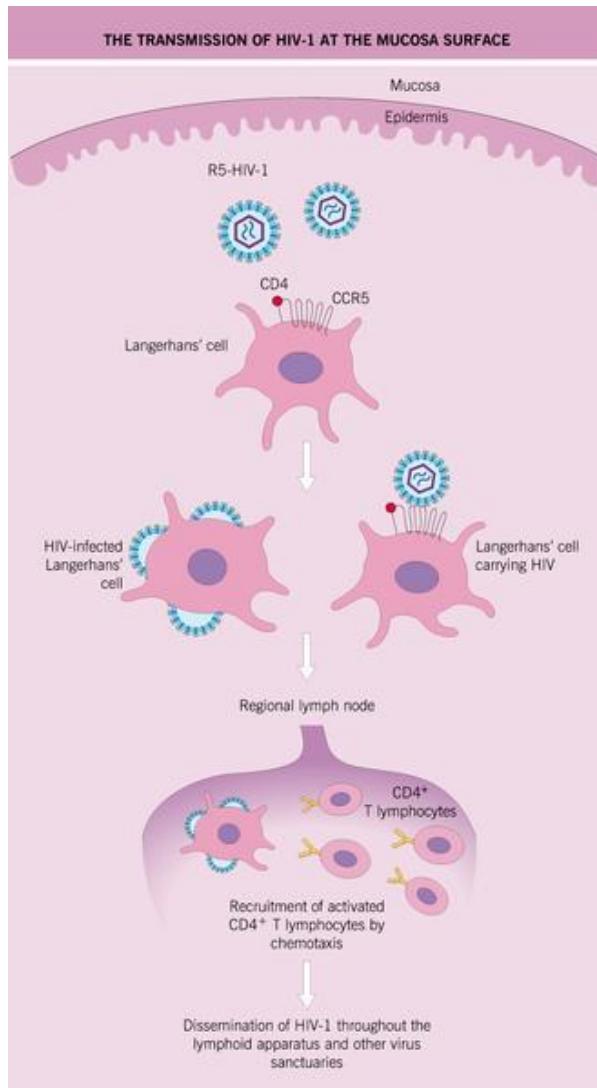
HIV-1 and HIV-2

- HIV-2 is less easily transmitted
- HIV-2 is less pathogenic
- Duration of HIV-2 infection is shorter
- Mother to Child Transmission (MTCT) is relatively rare with HIV-2

HIV & AIDS



HIV infection



Basic concepts in HIV infection

- Infects CD4 T-lymphocytes
- Increase in HIV viral load leads to a reduction in CD4 count & an increase in CD8 T-lymphocytes

HIV & AIDS...immuno-pathogenesis

- Natural history
 - Primary HIV infection
 - Chronic asymptomatic phase
 - Overt AIDS
 - Generally occur over a period of 8 – 12 months

Primary HIV infection

- Transient condition
- Symptomatic illness ~ 40-90%
- Characterised by
 - Rapid rise in viremia > 1 000 000 / ml
 - Decrease in CD4 T-lymphocyte count
 - Large increase in CD8 T-lymphocytes
- Followed by a rapid reduction in viremia & resolution of symptoms
- Appearance of virus specific immune response

Primary HIV infection

- Signs & symptoms ~ 2 – 4 Wks of exposure
- Duration of symptoms ~ few days - > 10 weeks (generally < 2 wks)
- Mimic acute infectious mononucleosis
- (symptoms: non-specific; D by Ixs)
 - H/O exposure
 - p24 Ag +ve
 - Plasma RNA (almost always > 50 000/ml)

Primary HIV infection

- Clinical features
 - Characterised by a maculopapular rash & mucosal ulcerations

Primary HIV infection



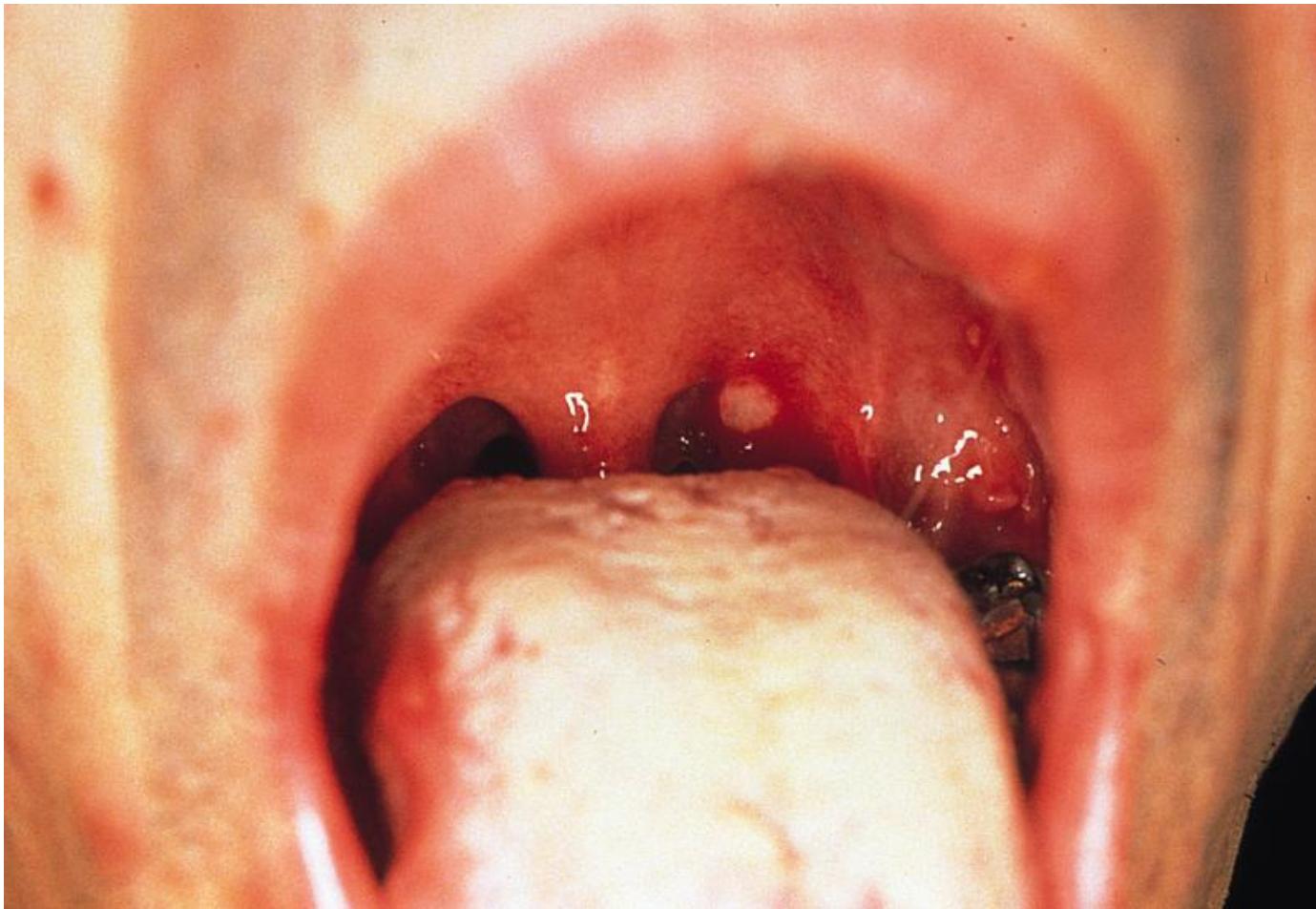
Primary HIV infection



Primary HIV infection



Primary HIV infection



Primary HIV infection

- Other Clinical features
 - Presentation ~ IMN
 - Meningoencephalitis
 - Radiculopathy, facial palsy, Gullian-Barre' syndrome, severe encephalitis & coma



A 22-Year-Old Man with a Flu-Like Illness

- A 22-year-old man
- 3-day history of fever, sore throat, headache, myalgias, and fatigue
- A diffuse maculopapular, erythematous rash
- Anonymous sex with 2 men about 3 weeks ago

Morbilliform Rash

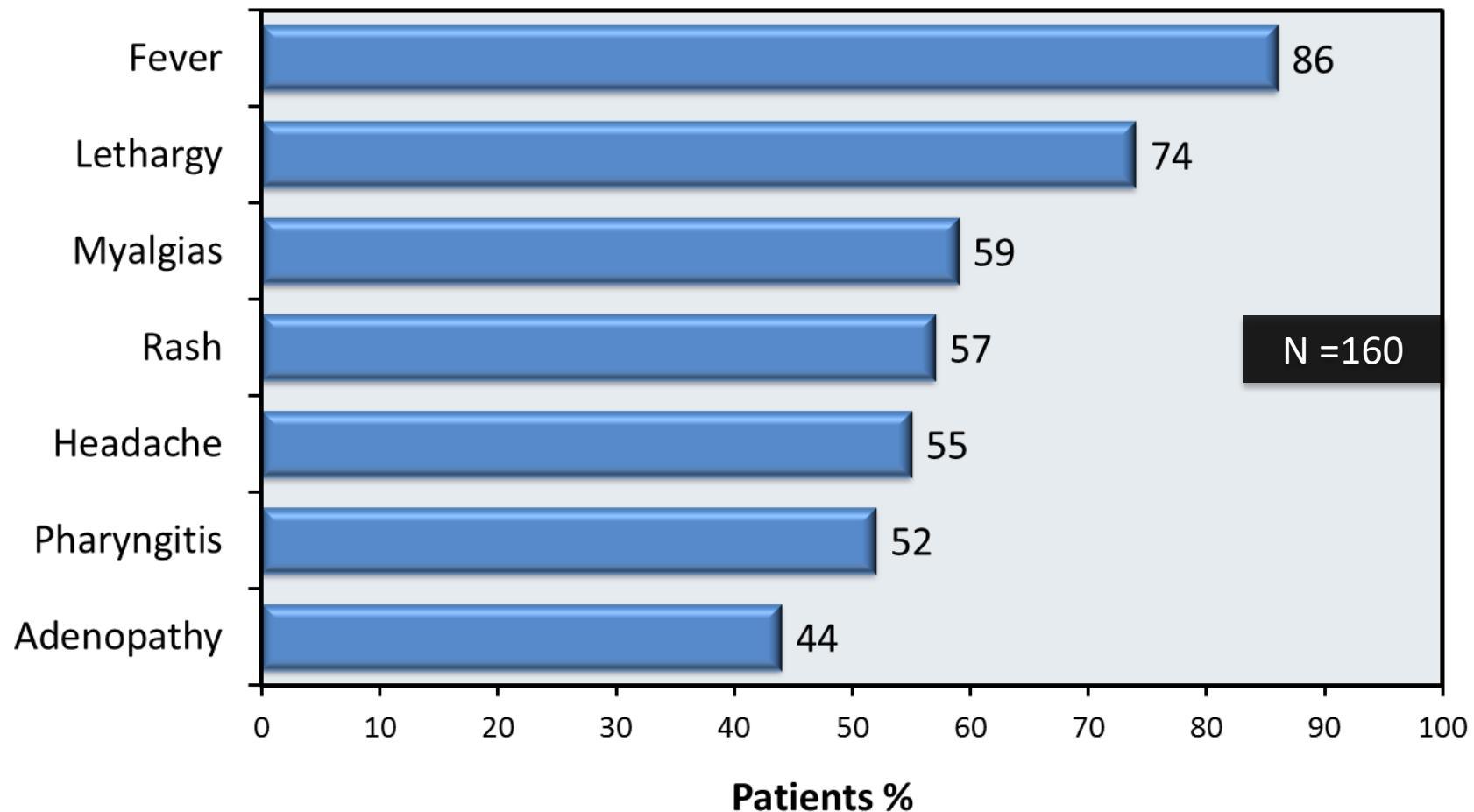




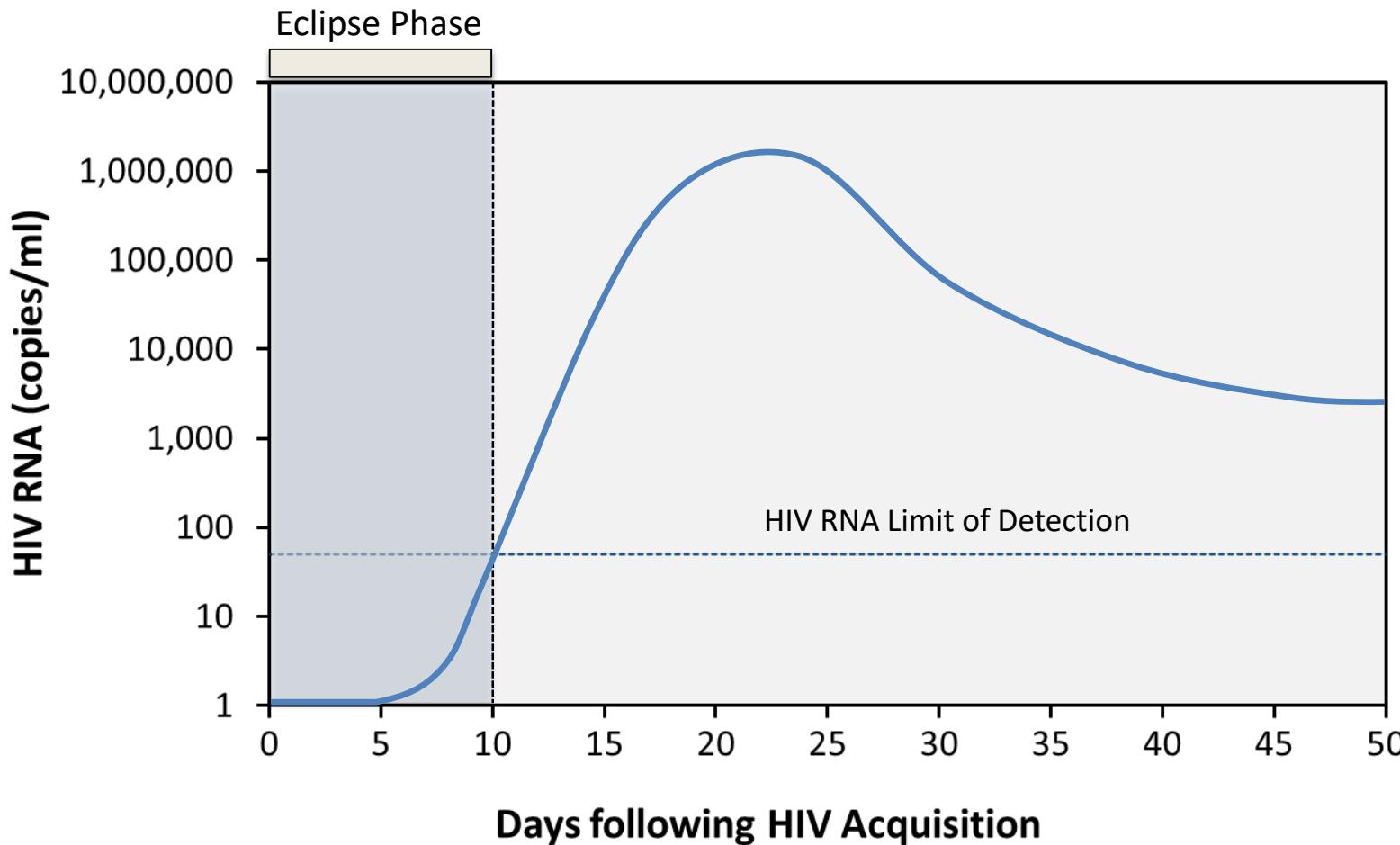
A 22-Year-Old Man with a Flu-Like Illness

- What is in your differential diagnosis?
- What tests would you order?

Clinical Manifestations of Primary HIV Infection

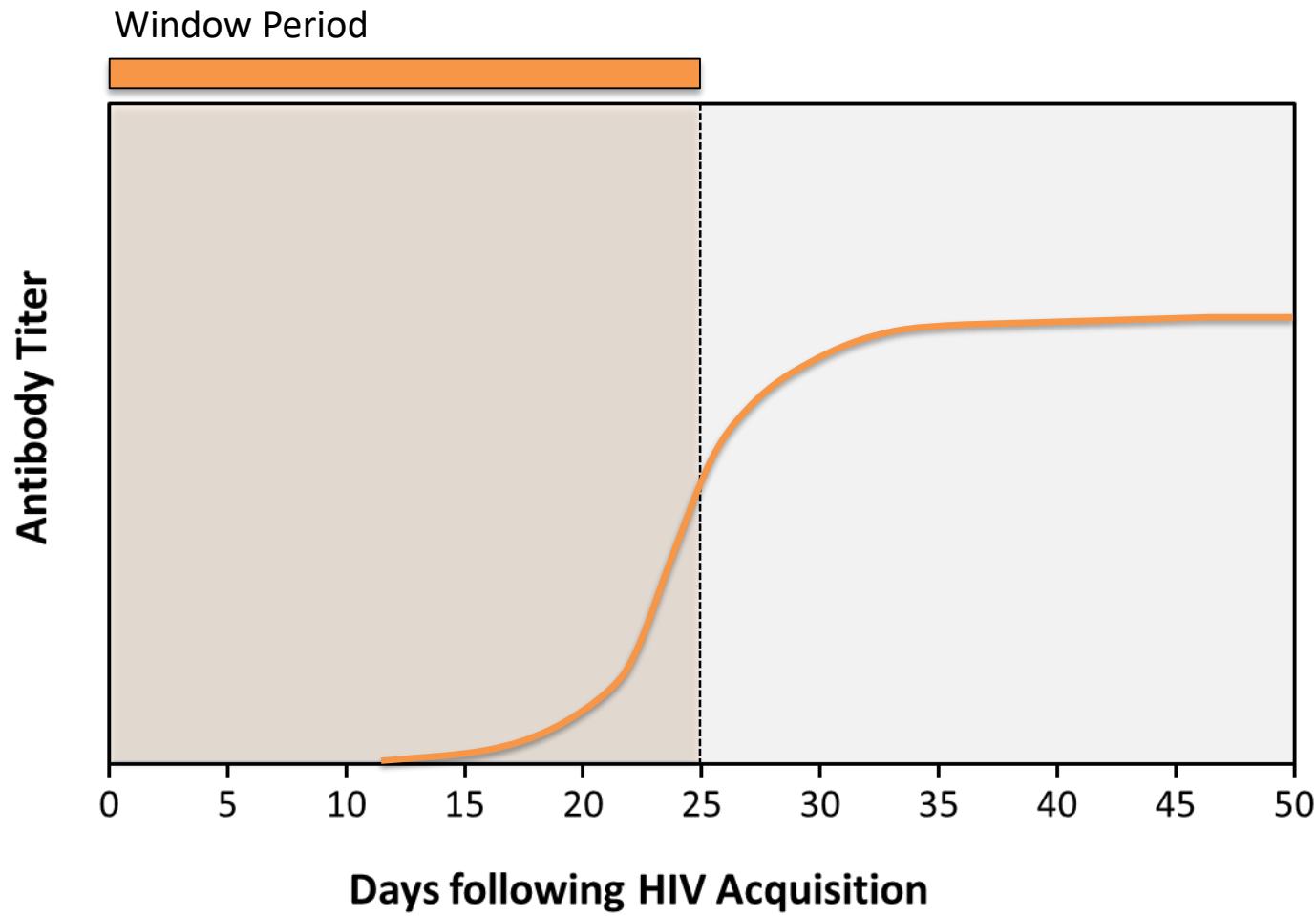


Acute (Primary) HIV: Eclipse Phase



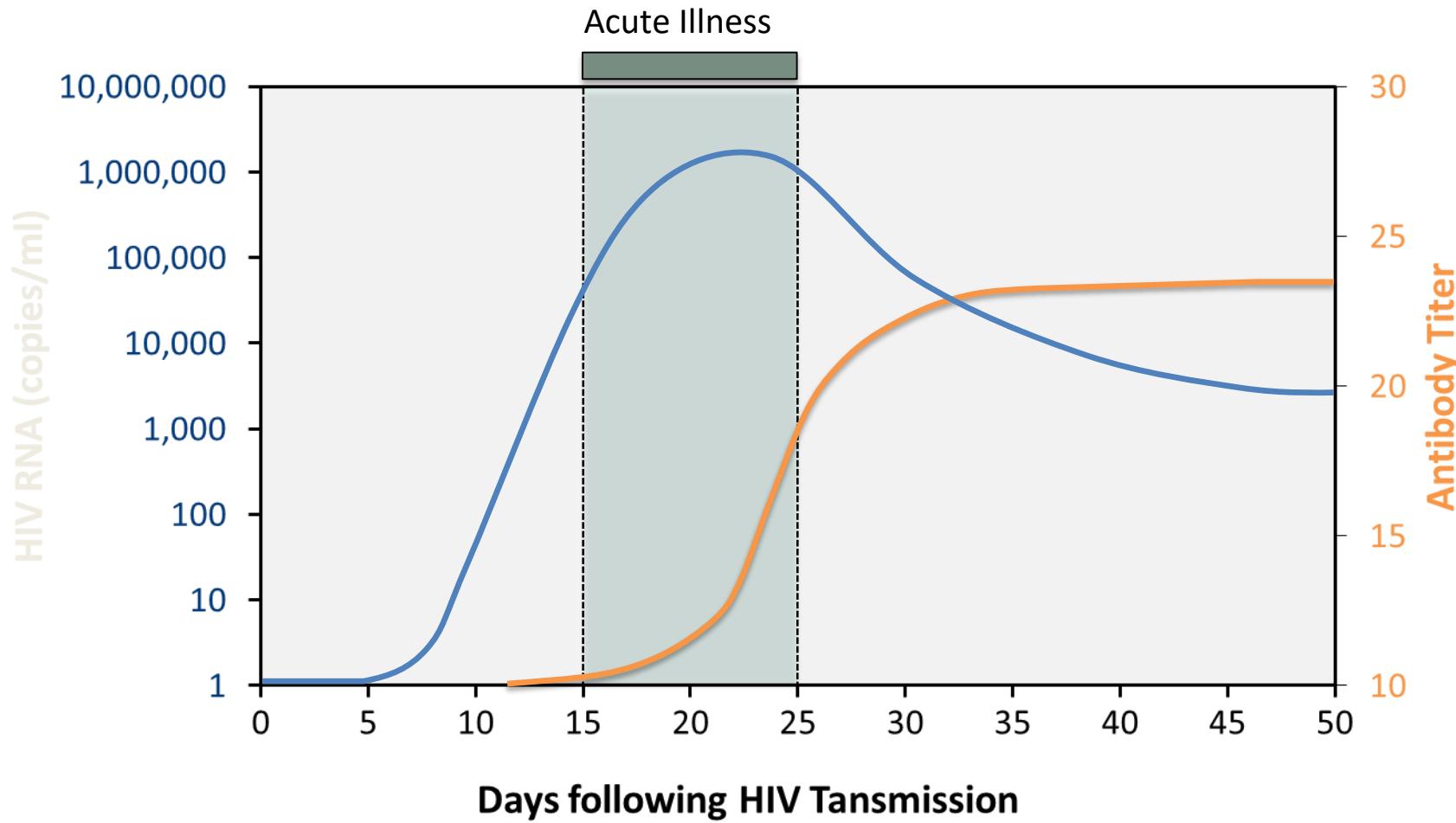
Eclipse Phase = Time between infection and detectable HIV RNA

Acute (Primary) HIV: Window Period



Window Period = Time between infection and detectable HIV antibodies

Acute (Primary) HIV: Symptomatic Disease



Symptomatic Disease Often Precedes Positive Antibody Test

Chronic asymptomatic phase

- Long period of clinical latency (median of 10yrs)
- Characterised by relatively stable viral replication & CD4 counts
- No clinical symptoms / signs

Risk of such individual is Transmission
to others

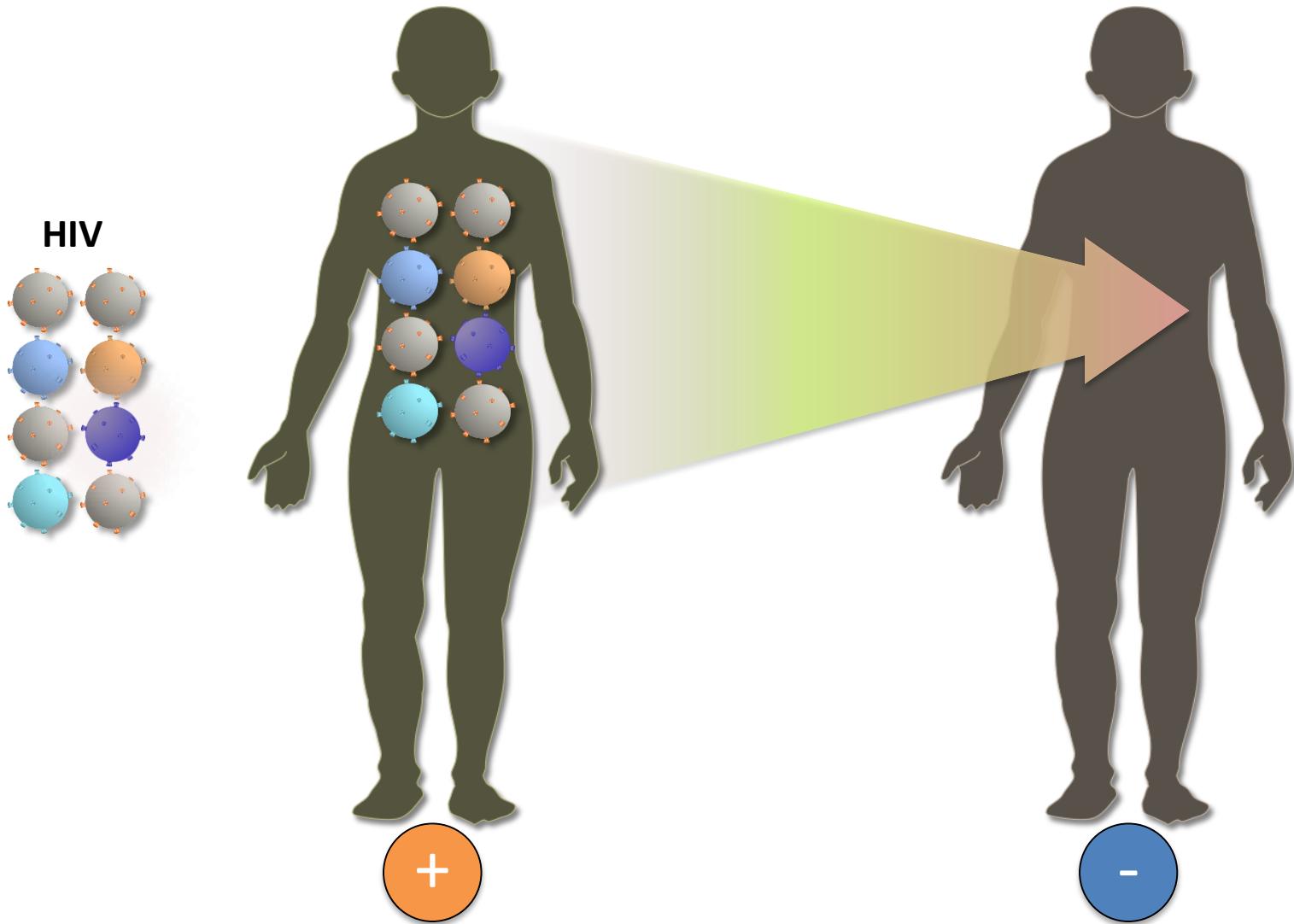
60% of carriers dont know they have **HIV**



Get tested. It only takes one prick.

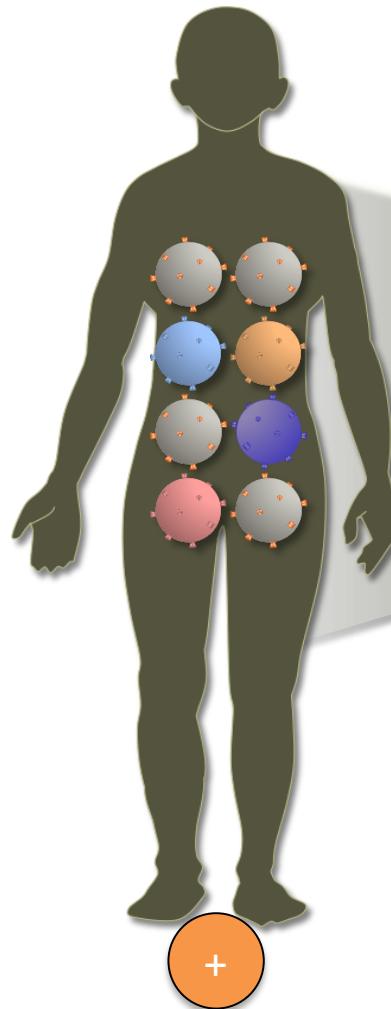


Transmission of HIV

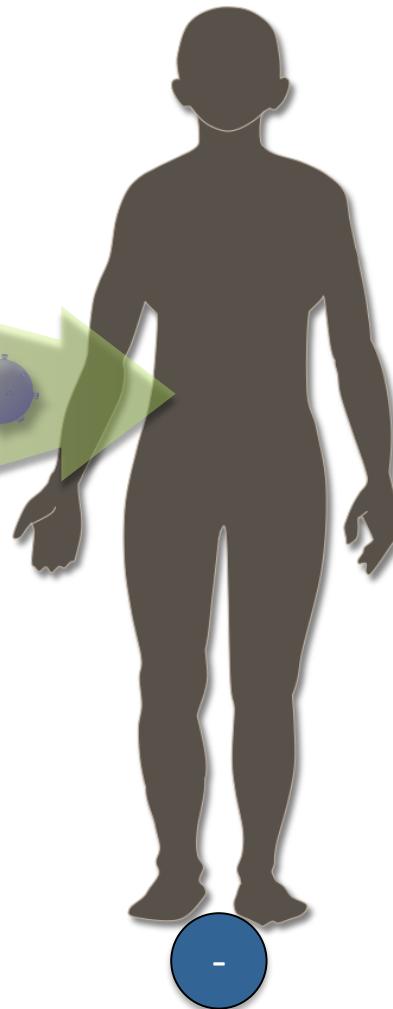


Transmission of HIV

Chronic HIV infection
Quasispecies

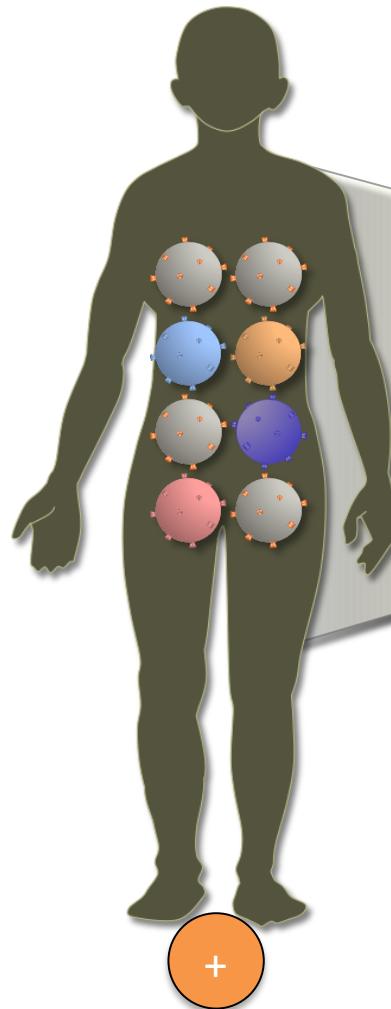


HIV-Negative

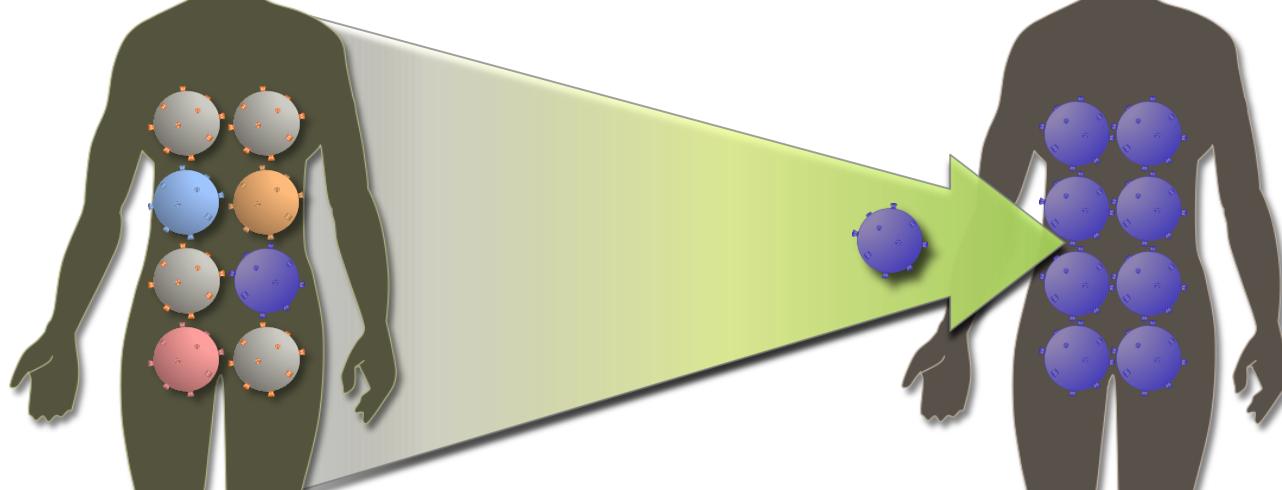
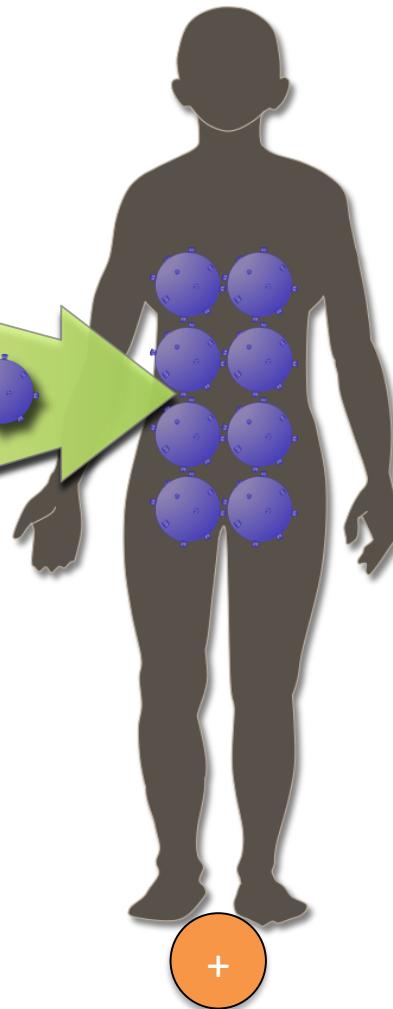


Transmission of HIV: Founder Virus

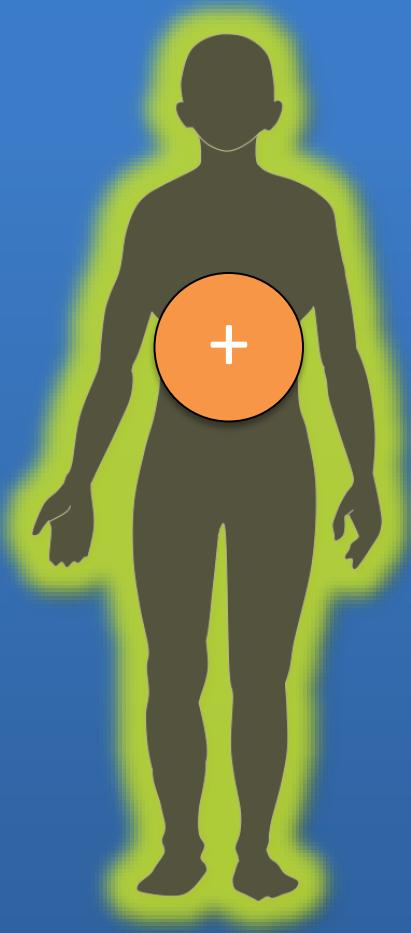
Chronic HIV infection
Quasispecies



New Infected with HIV
Founder Virus



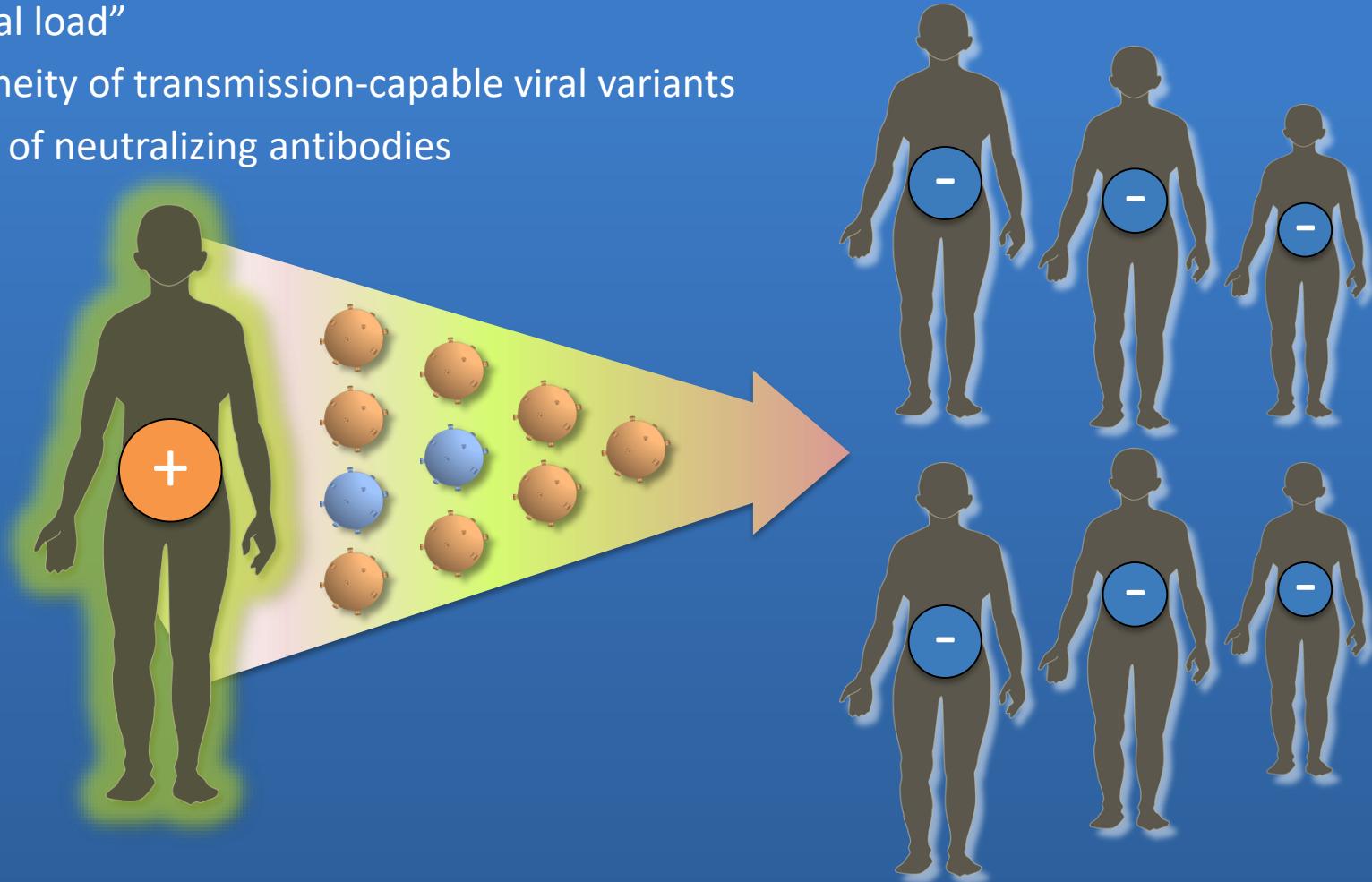
Acute (Primary) HIV High Transmission Risk



Acute (Primary) HIV

Factors Associated with High Transmission Risk

- Unaware of HIV status
- High “viral load”
- Homogeneity of transmission-capable viral variants
- Low titer of neutralizing antibodies

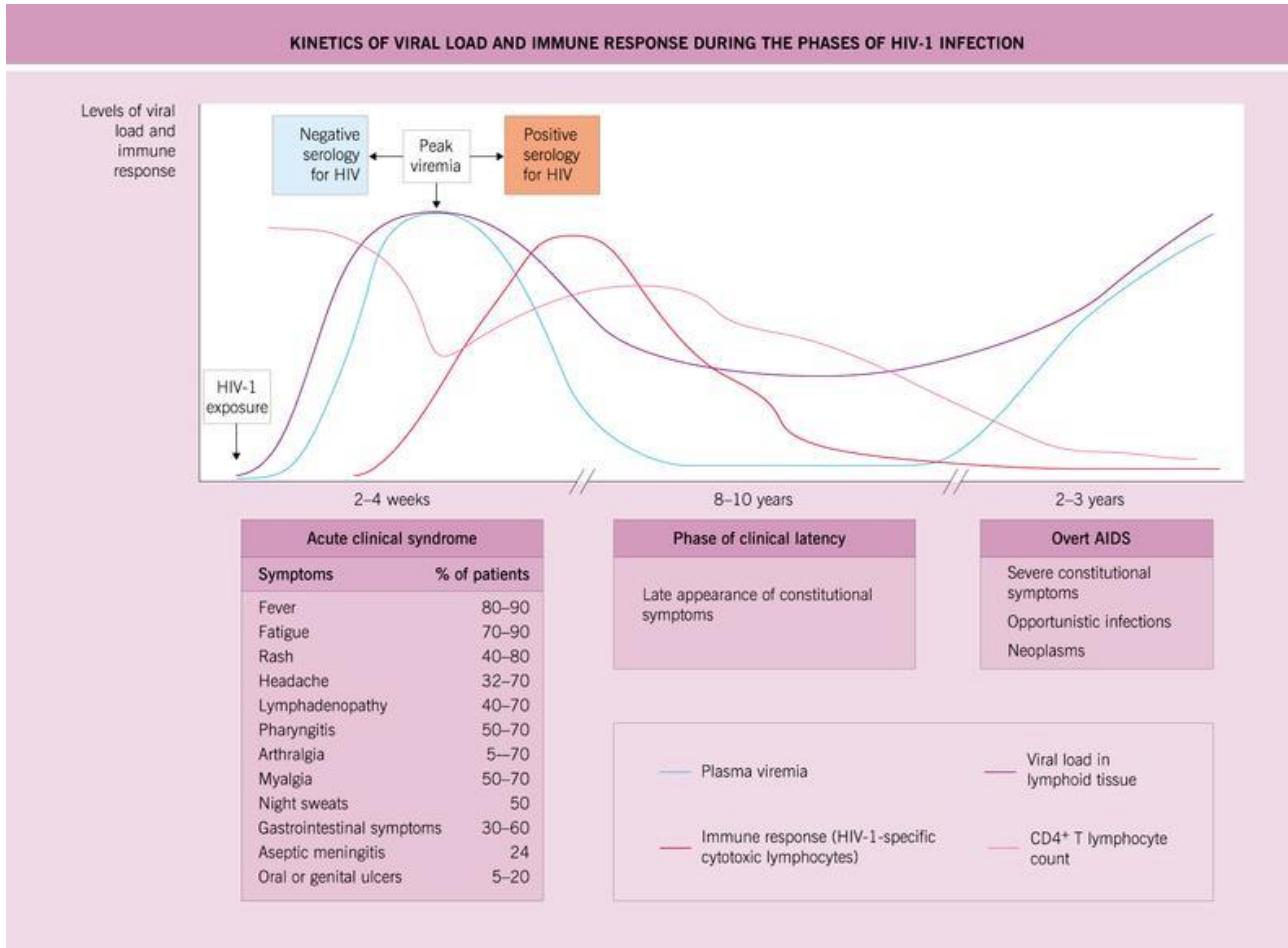


Overt AIDS

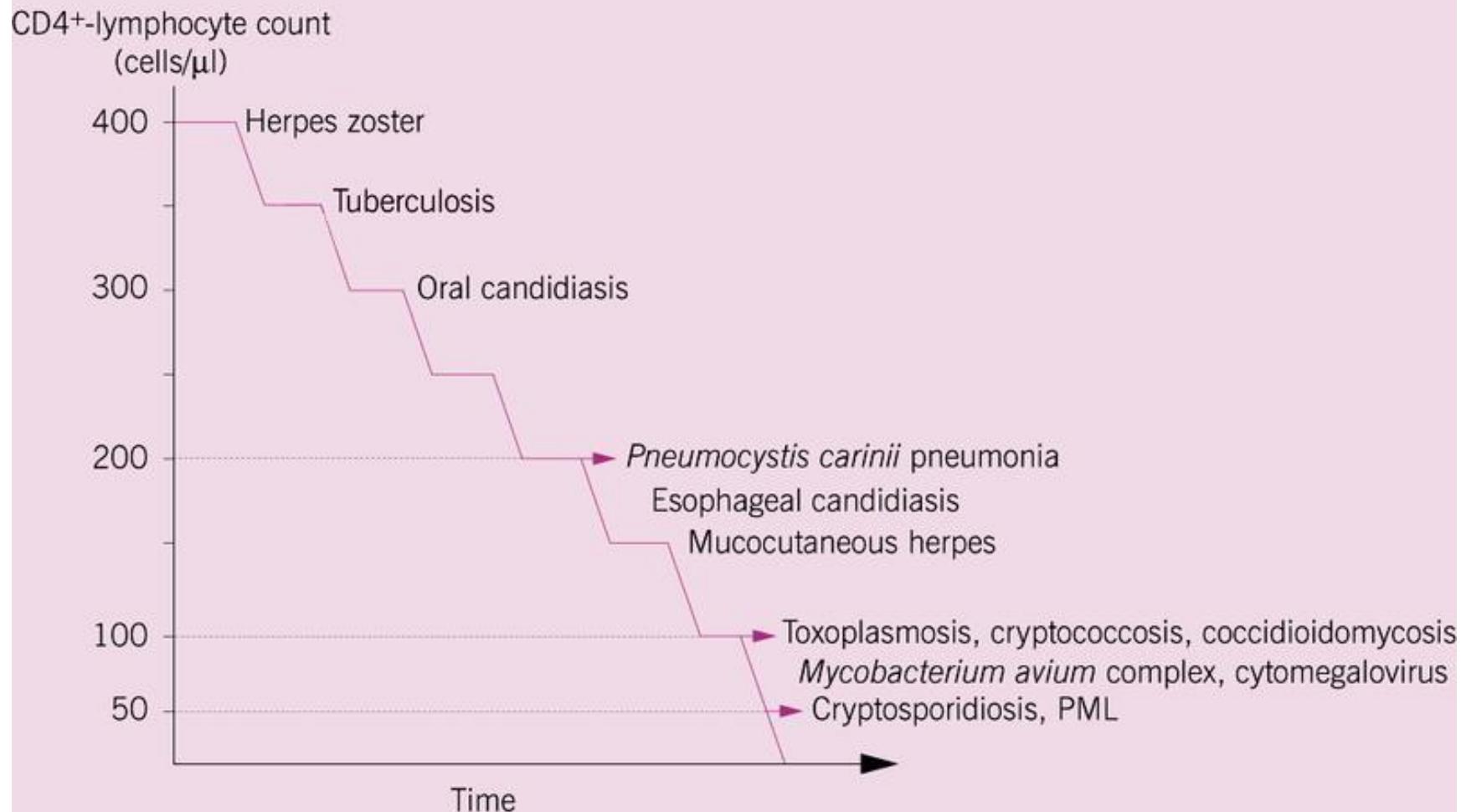
- End stage of the HIV infection
- In the absence of Rx death in 2-3 yrs
- Risk of death & opportunistic infections increase when

CD4 <50 000/ml

Viral load & immune response



ASSOCIATION BETWEEN OPPORTUNISTIC INFECTIONS AND CD4⁺-LYMPHOCYTE COUNT



Malignancies associated with AIDS

- Kaposi's sarcoma
- Non-Hodgkin's lymphoma
- Primary cerebral lymphoma

Diagnosis

- Serology
 - Screening; ELISA
 - Confirmatory: western blot
- Virus detection: PCR
- Antigen detection: GP 24

Treatment of HIV infection

- Aims
 - To delay progression to AIDS
 - To prevent opportunistic infections
 - To reduce viral load
 - To keep the CD4 count as high as possible

Treatment

- Nucleoside analogue reverse transcriptase inhibitors
 - Zidivudine, didanosine
- Non-nucleoside analogue reverse transcriptase inhibitors
 - Nevirapine
- Protease inhibitors
 - Indinavir, nelfinavir

Treatment

- Present approach:
 - Combined treatment
 - HAART

HIV 2012 Update

HHS ANTIRETROVIRAL THERAPY RECOMMENDATIONS

US Health and Human Services (HHS)

March 27, 2012 Antiretroviral Therapy Guidelines



Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents



Developed by the HHS Panel on Antiretroviral Guidelines for
Adults and Adolescents – A Working Group of the
Office of AIDS Research Advisory Council (OARAC)

How to Cite the Adult and Adolescent Guidelines:

Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services. 1-239. Available at <http://www.aidsinfo.nih.gov/ContentFiles/AdultAndAdolescentGL.pdf>. Section accessed [insert date] [insert page number, table number, etc. if applicable]

It is emphasized that concepts relevant to HIV management evolve rapidly. The Panel has a mechanism to update recommendations on a regular basis, and the most recent information is available on the AIDSinfo website (<http://aidsinfo.nih.gov>).

Downloaded from <http://aidsinfo.nih.gov/guidelines> on 3/27/2012



access AIDSinfo
mobile site

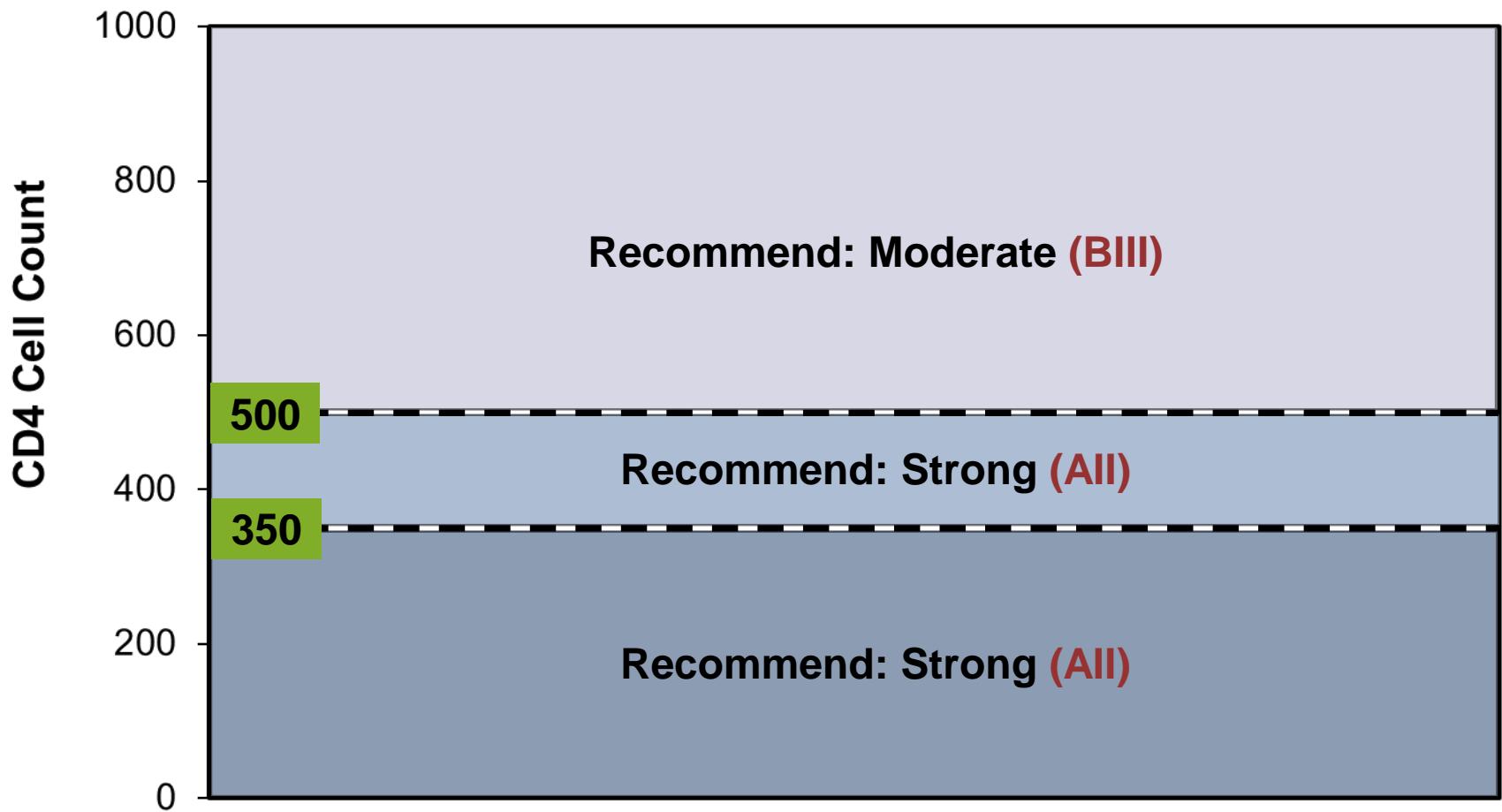


Case History

- A 28-year-old man was diagnosed with HIV about 18 months ago.
- He is seen in the clinic for follow up.
- CD4 counts have been 770, 710, 640, and 610 cells/mm³.
- He has no active medical, mental health, or substance abuse issues. He is sexually active with other men and uses condoms most of the time.
- **Would you recommend starting antiretroviral therapy?**

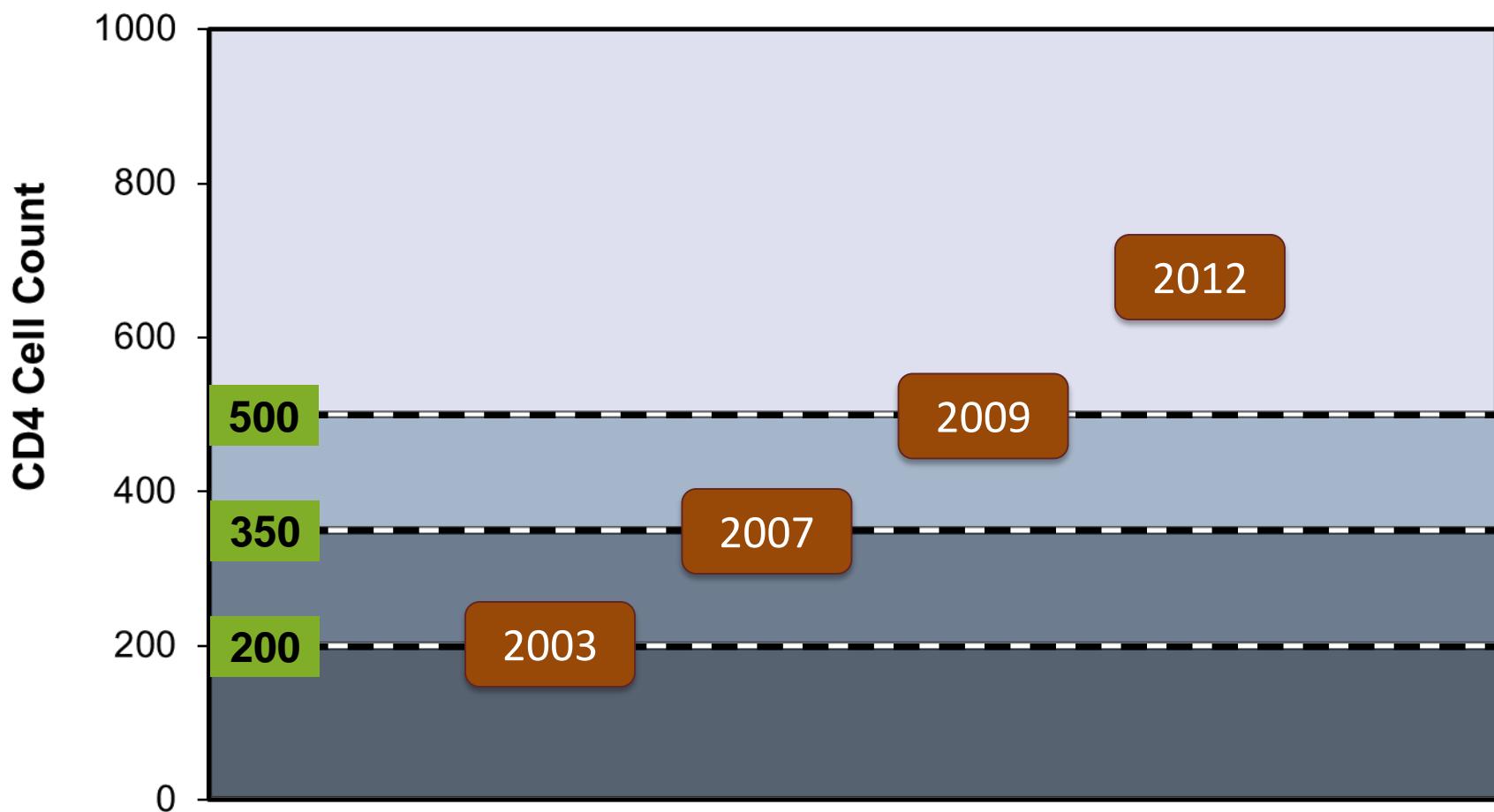
HHS Antiretroviral Therapy Guidelines: March 2012

Initiating Therapy in Treatment-Naïve Patients

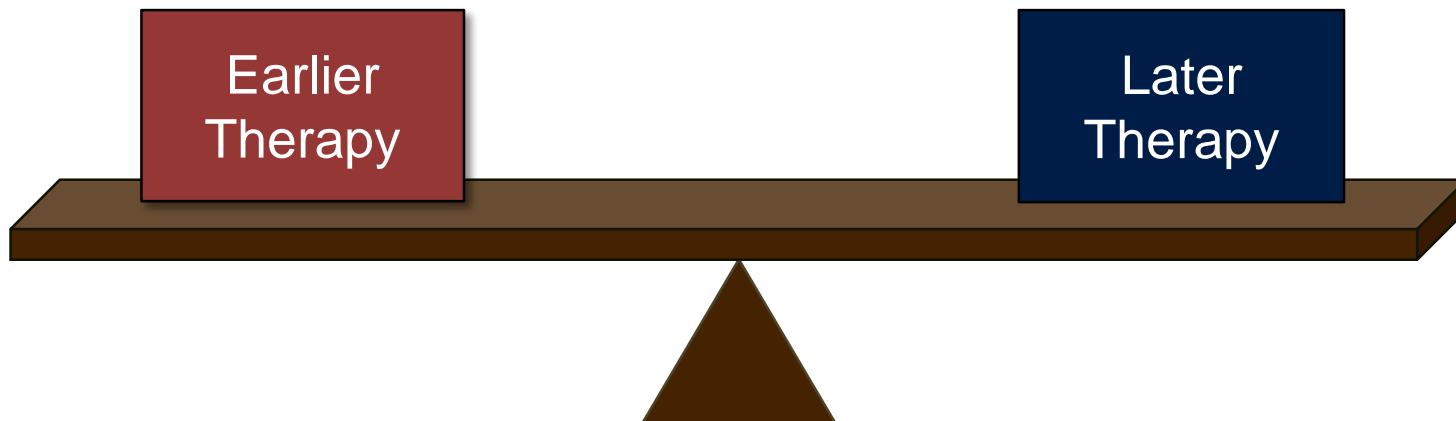


Initiating Antiretroviral Therapy in Treatment-Naïve Patients

Change in CD4 Threshold in HHS Guidelines



HHS Antiretroviral Therapy Guidelines: March 2012 Initiating Therapy in Treatment-Naïve Patients



Initiating Antiretroviral Therapy

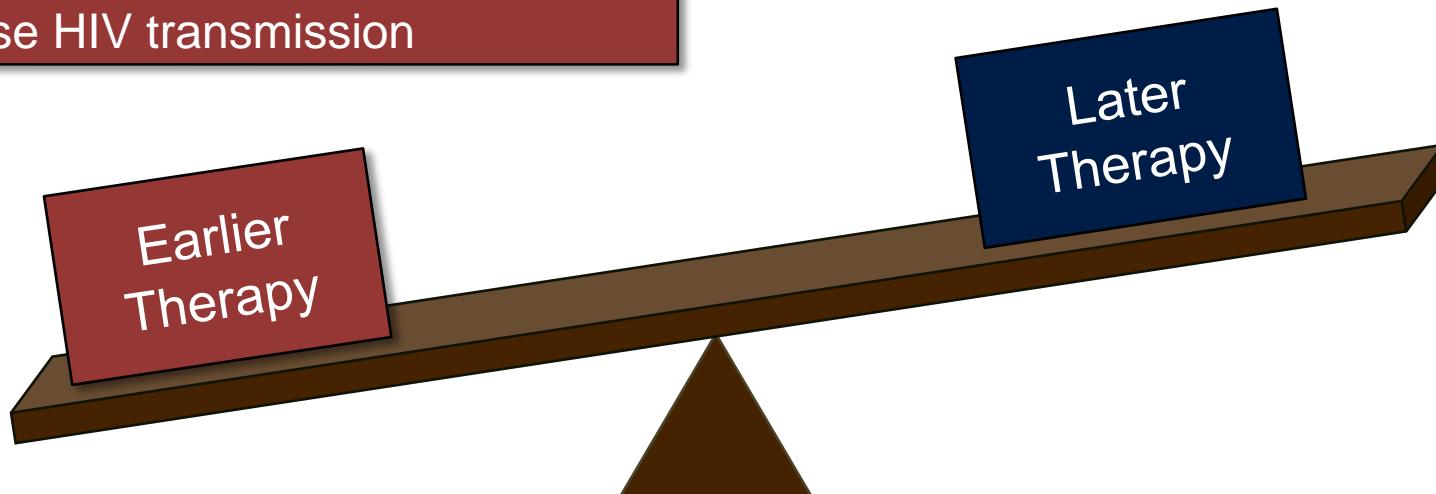
Why are we treating earlier with antiretroviral therapy?

HHS Antiretroviral Therapy Guidelines: March 2012

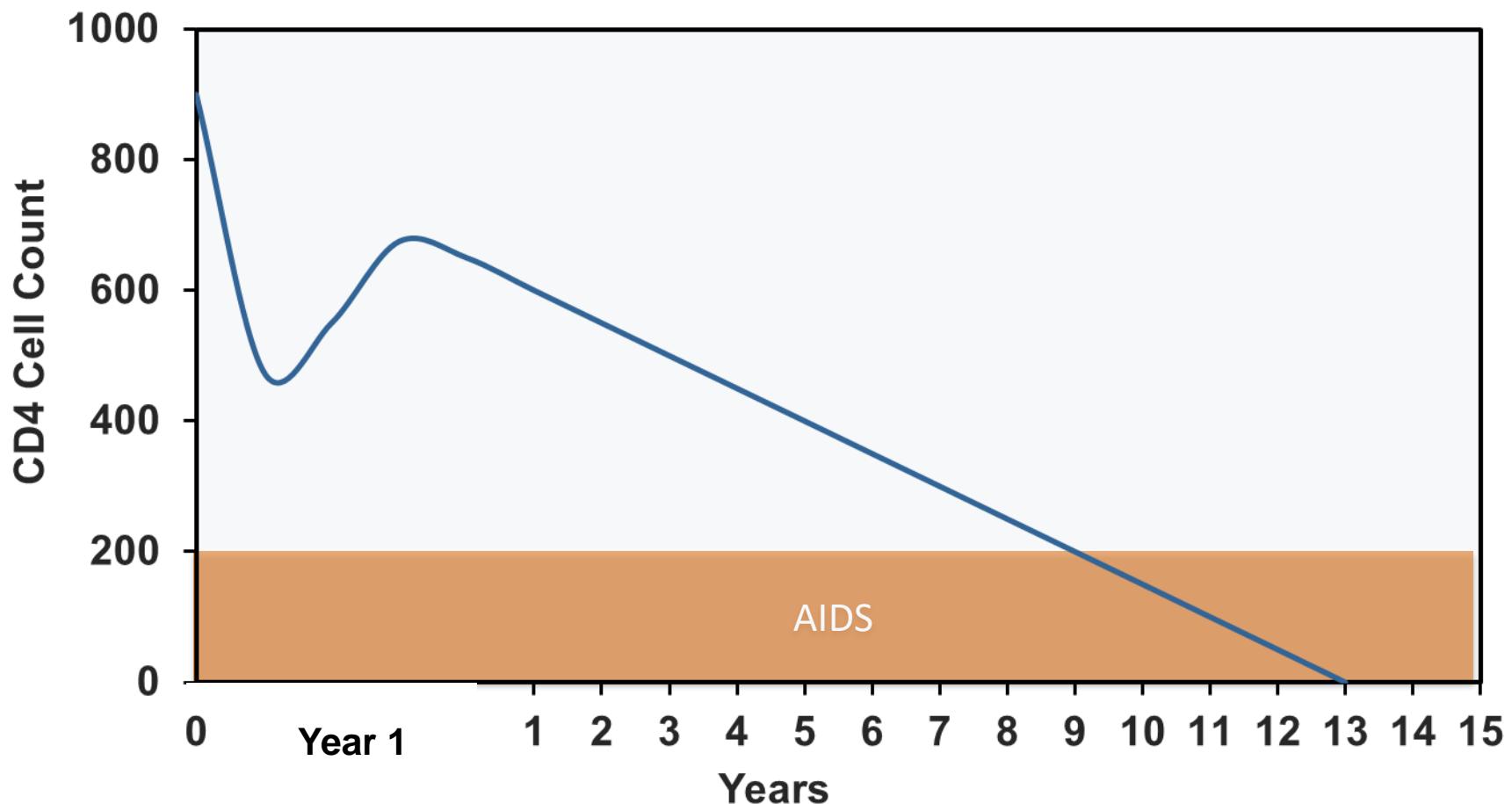
Factors Affecting Decision on When to Initiate Therapy

- More effective regimens
- More convenient regimens
- Better tolerated therapy
- Less long-term toxicity
- Better immune recovery
- Lower rates of resistance
- More treatment options
- Concerns for uncontrolled viremia
- Decrease HIV transmission

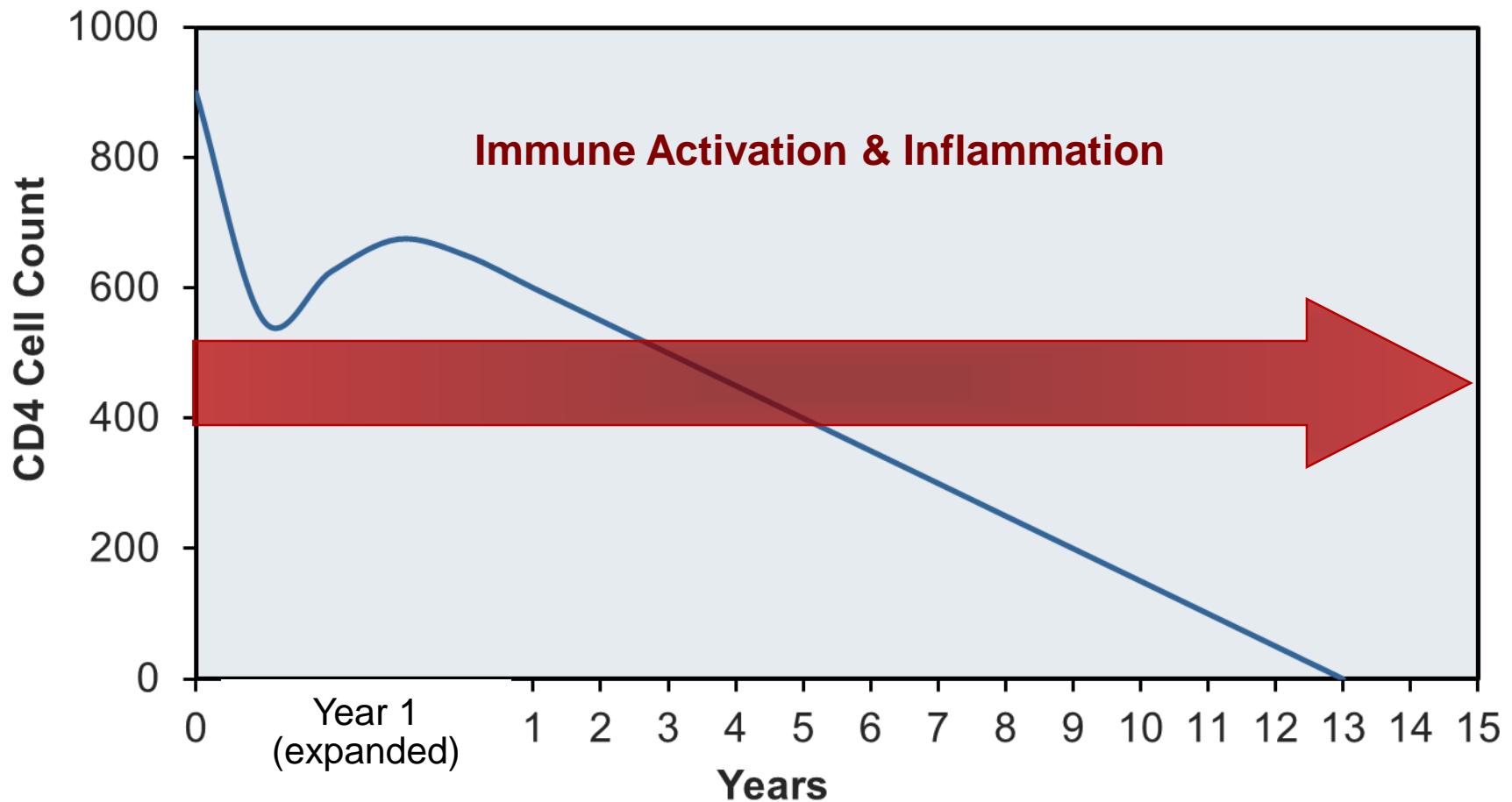
- Lack of RCT data supporting early Rx
- Potential drug toxicity
- Drug and monitoring cost
- Potential negative impact on QOL



CD4 Cell Progression (without Antiretroviral Therapy)



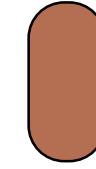
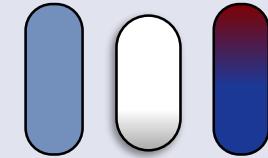
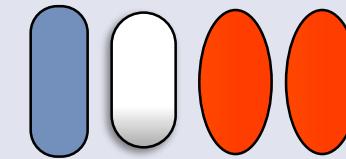
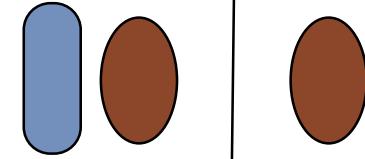
Chronic Immune Activation and Inflammation



Chronic Inflammation Impact on HIV-Infected Persons

- Increased risk of heart disease
- Increased risk of stroke
- Increased risk of cancer

DHHS Antiretroviral Therapy Guidelines: October 2011 Preferred Regimens for ARV-Naïve Patients: Pill Burden

Class	Therapy	Pill Burden
NNRTI-Based	Efavirenz-Tenofovir-Emtricitabine	
PI-Based	Ritonavir + Atazanavir + Tenofovir-Emtricitabine	
	Darunavir + Ritonavir + Tenofovir-Emtricitabine	
INSTI-Based	Raltegravir + Tenofovir-Emtricitabine	

HHS Antiretroviral Therapy Guidelines: March 2012

Preferred Regimens for ARV-Naïve Patients: Pill Burden

Class	Therapy	*AWP (Monthly)
NNRTI-Based	Efavirenz-Tenofovir-Emtricitabine	\$2081
PI-Based	Ritonavir + Atazanavir + Tenofovir-Emtricitabine	\$2860
	Darunavir + Ritonavir + Tenofovir-Emtricitabine	\$2925
INSTI-Based	Raltegravir + Tenofovir-Emtricitabine	\$2562

*AWP = average wholesale price

2011: New FDA-Approved HIV Medications (or New Preparations of Older Medications)

- Nevirapine XR (*Viramune XR*): 400 mg tablet



- Etravirine (*Intelence*): 200 mg tablet



- Rilpivirine (*Edurant*): 25 mg tablet



- Tenofovir-Emtricitabine-Rilpivirine (*Complera*): 1 pill qd



Just **25%** of people with HIV
are successfully keeping
their virus under control
through treatment; **75%** are not



AIDS related illnesses

- Seborrheic dermatitis

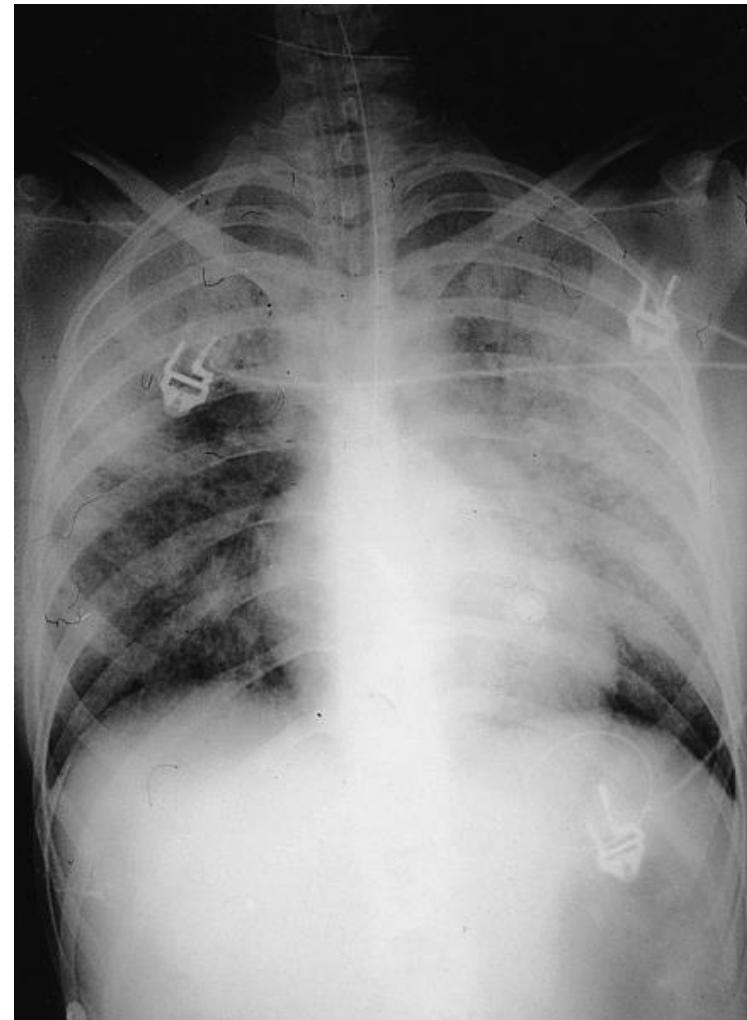


Case History



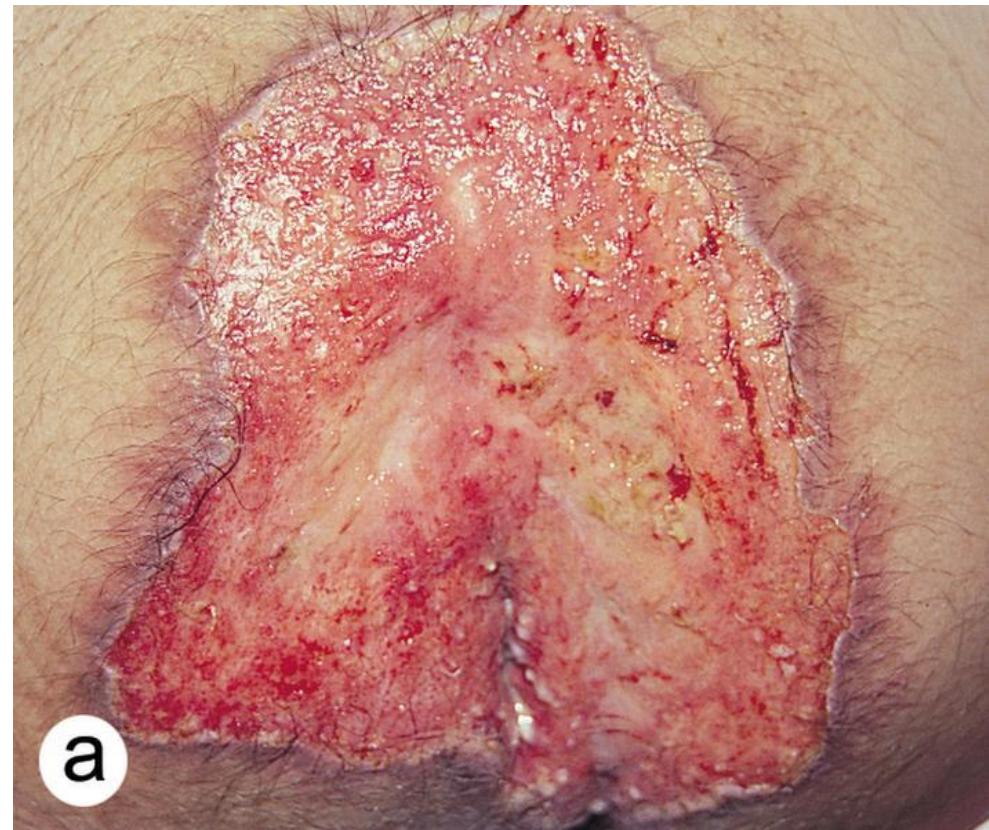
AIDS related illnesses

- Pneumocystis pneumonia



AIDS related illnesses

- Severe herpes infections



AIDS related illnesses

Cytomegalovirus retinitis



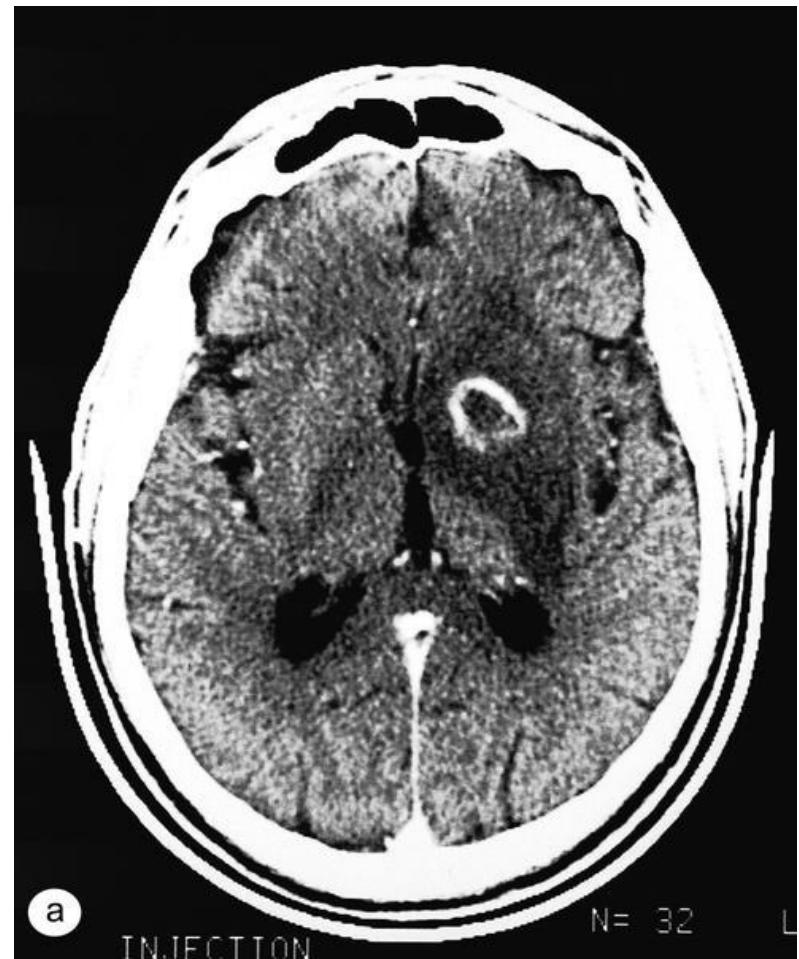
AIDS related illnesses

- Multi-dermatomal herpes zoster



AIDS related illnesses

- Cerebral toxoplasmosis



AIDS related illnesses

- Kaposi's sarcoma



HIV 2012 Update

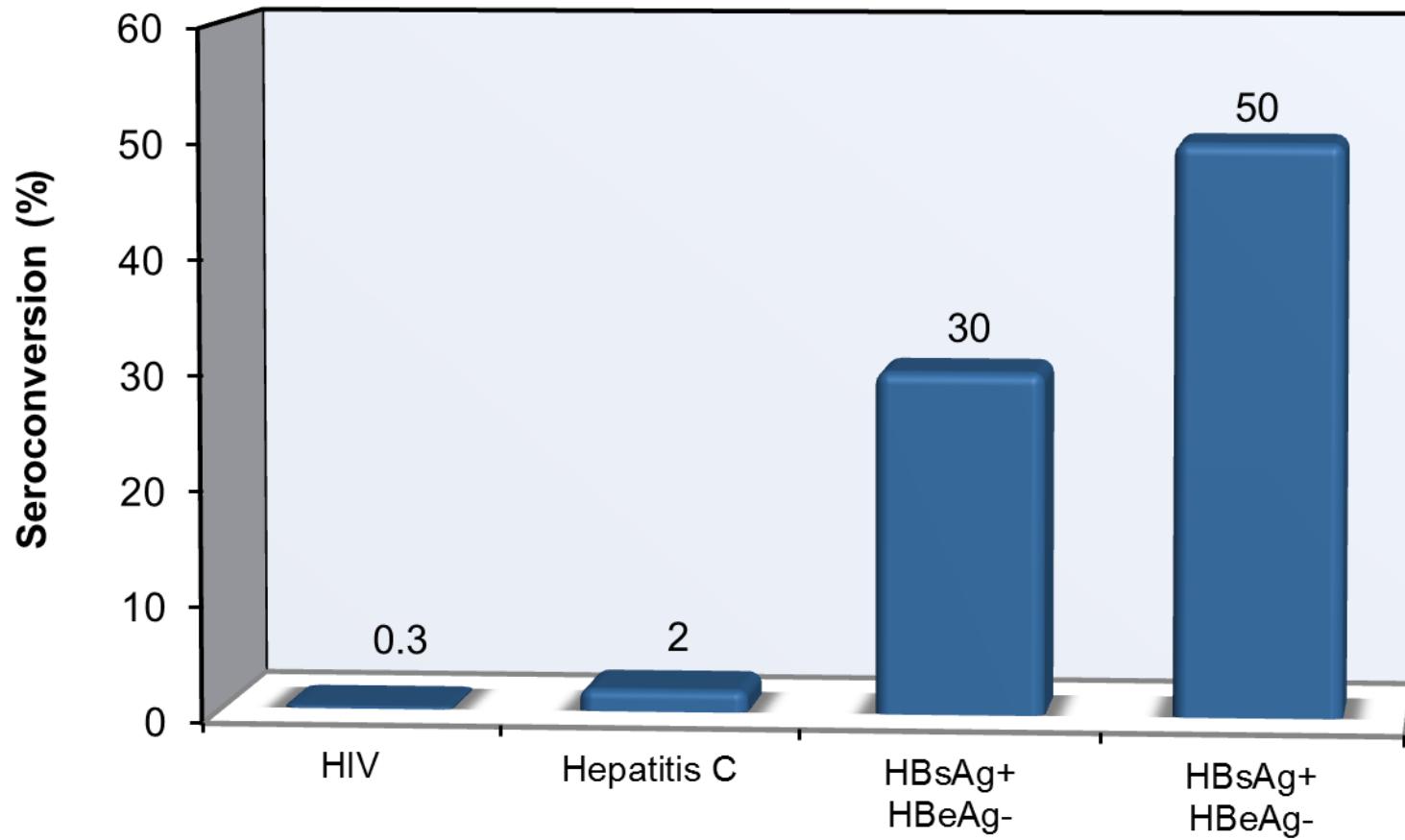
POSTEXPOSURE PROPHYLAXIS



Question

- **What is the risk of acquiring HIV from a needlestick injury when all following are present:**
 - HIV-infected source patient not on antiretroviral therapy
 - Needlestick involved venipuncture needle
 - Skin on hand punctured
 - No antiretroviral postexposure prophylaxis given

Estimated Risk of Seroconversion with Percutaneous Injury





Case History

HIV Exposure in a Health Care Worker

- A 29-year-old nurse sticks herself in the finger with a needle when drawing blood from a patient
- The source patient is HIV-positive and HCV-negative
- The nurse is immune to hepatitis B
- The source patient has never been on antiretroviral therapy
- HIV RNA level of 96,000 copies/ml

In addition to washing the wound, what PEP would you recommend for this nurse?

Logistic-Regression Analysis of Risk Factors for HIV Transmission after Percutaneous Exposure to HIV-Infected Blood

Risk Factors for HIV Seroconversion in Health Care Workers	
Risk Factor	Adjusted Odds Ratio
Deep Injury	15.0
Visible Blood on Device	6.2
Terminal Illness in Source Patient	5.6
Needle in Source Vein/Artery	4.3
PEP with Zidovudine (AZT)	0.19

Recommended HIV PEP after Percutaneous Exposure

Known Source HIV Status

Percutaneous Exposure Type	Source Infection Status	
	HIV+ Class 1*	HIV+ Class 2^
Less Severe [¶]	Recommend Basic 2-drug PEP	Recommend Expanded \geq 3-drug PEP
More Severe [#]	Recommend Expanded 3-drug PEP	Recommend Expanded \geq 3-drug PEP

[¶] **Less Severe:** e.g., solid needle or superficial injury

[#] **More Severe:** e.g., large-bore hollow needle, deep puncture, visible blood on device, or needle used in patient's artery or vein

***HIV+ Class 1:** Asymptomatic HIV infection or low viral load (e.g., <1,500 copies/mL)

[^]**HIV+ Class 2:** Symptomatic HIV, AIDS, acute seroconversion, or known high viral load

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2005 Recommended PEP Antiretroviral Therapy

Preferred Basic and Expanded Regimens

Drugs for Basic Regimens (28 days)	Drugs for Expanded Regimen (28 days) Basic Regimen Plus:
Preferred Regimens	
Zidovudine-Lamivudine (<i>Combivir</i>)	Lopinavir-Ritonavir (<i>Kaletra</i>)
Tenofovir + Emtricitabine (<i>Truvada</i>)	
Alternative Regimens	
Stavudine (<i>Zerit</i>) + Lamivudine (<i>Epivir</i>)	Atazanavir (<i>Reyataz</i>) + Ritonavir (<i>Norvir</i>)
Stavudine (<i>Zerit</i>) + Emtricitabine (<i>Emtriva</i>)	Fosamprenavir (<i>Lexiva</i>) + Ritonavir (<i>Norvir</i>)
Didanosine (<i>Videx</i>) + Lamivudine (<i>Epivir</i>)	Saquinavir (<i>Invirase</i>) + Ritonavir (<i>Norvir</i>)
Didanosine (<i>Videx</i>) + Emtricitabine (<i>Emtriva</i>)	Nelfinavir (<i>Viracept</i>) Efavirenz (<i>Viracept</i>)

Prevention

Potential of HIV prevention: National Success Stories

- Thailand's 100% condom program
- Uganda's remarkable decrease in HIV prevalence and incidence
- Senegal's sustained success in minimizing HIV incidence
- Zimbabwe's declining prevalence due to behavior change
- Declining risk and prevalence in Caribbean countries

Interventions differ across epidemic profiles: Condom promotion

	<u>Condom Promotion</u>
<u>Low-level Epidemic</u>	Address market inefficiencies in condom procurement and focus distribution on key populations
<u>Concentrated Epidemic</u>	Intensify distribution and promotion to key populations and link to VCT and STI care
<u>Generalized Low-Level Epidemic</u>	Subsidize social marketing of condoms: strengthen distribution to ensure universal access
<u>Generalized High-Level Epidemic</u>	Promote condom use and distribute condoms free in all possible venues

What Works? Evidence for Effectiveness and Cost-Effectiveness

	Effectiveness	Cost-Effectiveness
Circumcision	+	++
Surveillance	None	None
IEC	None	None
School-based education	-	-
Abstinence education	-	-
VCT	++	++
Peer-based programs	++	++
Condom promotion, distribution & IEC	++	+
Condom social marketing	?	?
STI Treatment	++	++

What Works? Evidence for Effectiveness and Cost-Effectiveness (cont)

	Effectiveness	Cost-Effectiveness
ART to reduce MTCT	++	++
MTCT, feeding substitution	+	None
Harm reduction, IDUs	++	++
IDU Drug substitution	?	None
Blood Safety	++	++
Universal Precautions	++	None
ART for PEP	+	-
ART for PREP	+	None
Vaccines	?	None
Behavior Δ for HIV+'s	+	None

I am a sister, a writer, and a best friend.
And I am living with HIV.

Let's stop HIV together
—Regan



Regan (left) has lived with HIV since 1998.

Get the facts. Get tested. Get involved.

www.ActAgainstAIDS.org



CDC

ACT
against
AIDS

I am a boyfriend, a volunteer, and an artist.
And I am living with HIV.

Let's stop HIV together.TM
-Christopher



Christopher (left) has lived with HIV since 2011.

Get the facts. Get tested. Get involved.

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- Thank you Mom.....

