

HIV and Aging

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Disclosures

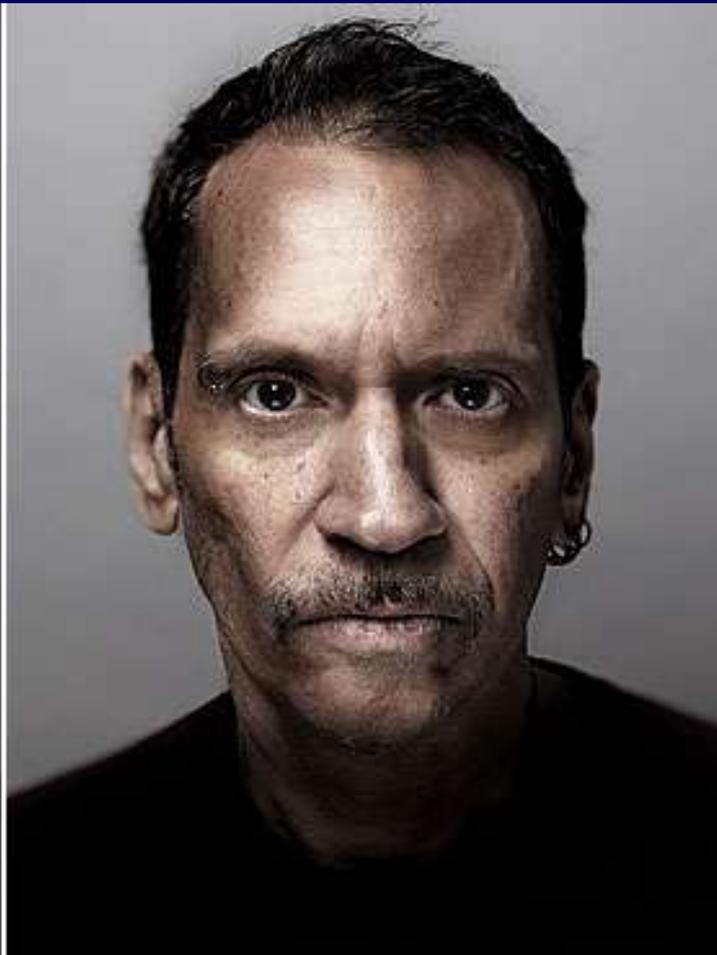
Outline

- **Scope of the Problem**
- **Immune System Effects and Inflammation**
- **Frailty**
- **Cardiovascular Disease**
- **Bone Disease**
- **Neurologic Conditions**
- **Cancer**
- **Recommendations**

Another Type of AIDS Crisis



Russell Steinke. Age: 56 / HIV: 23 years
Has suffered from: memory loss, nerve damage in feet, lipodystrophy, fatigue

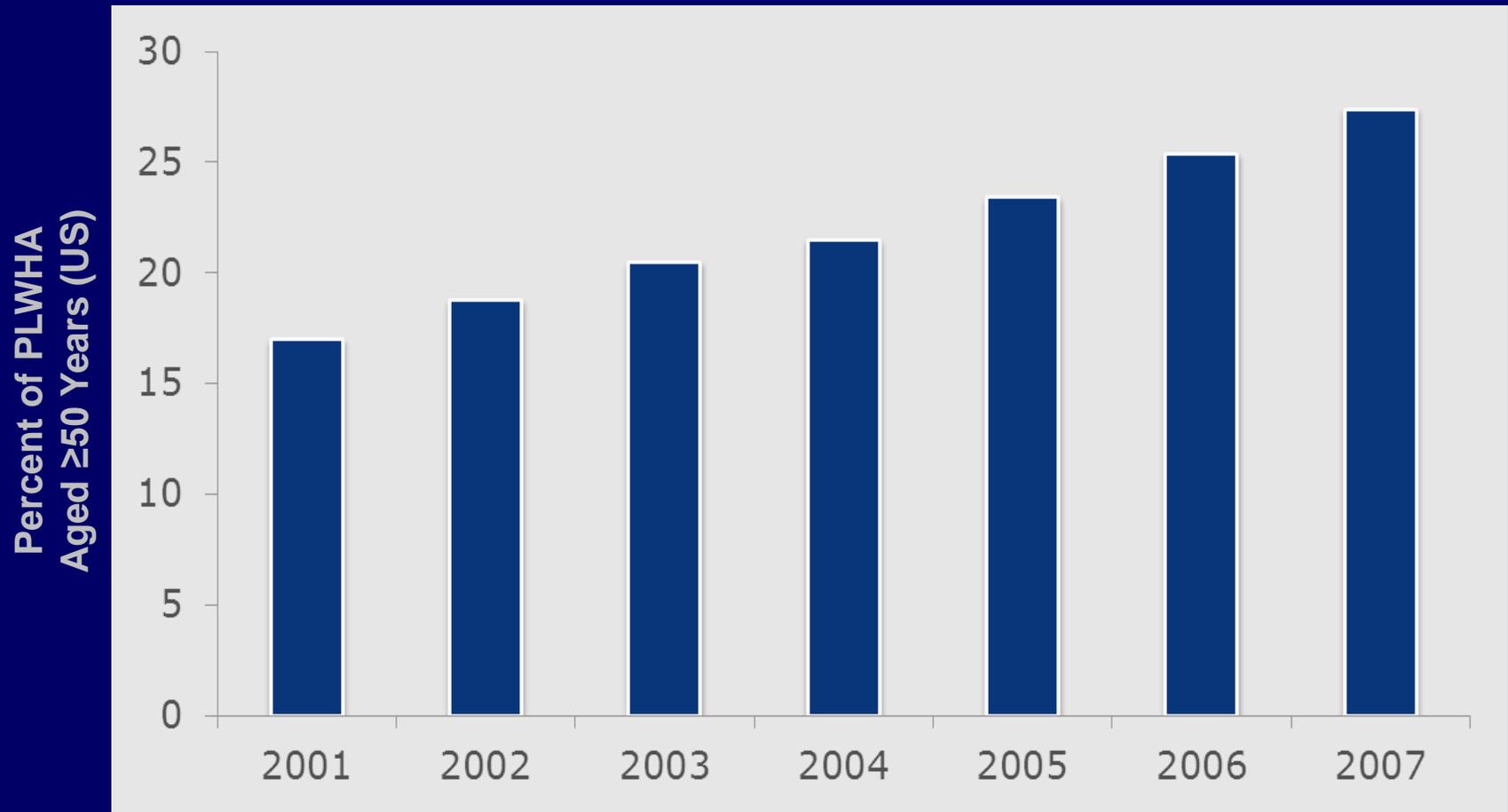


Enrico McLane. Age: 52 / HIV: 17 years
Has suffered from: short-term memory loss, two hip replacements

Scope of the Problem

- **HAART has transformed HIV infection from a certain death sentence to a chronic illness**
- **At the end of 2008 an estimated 1.2 million adults and adolescents in the US had HIV infection**

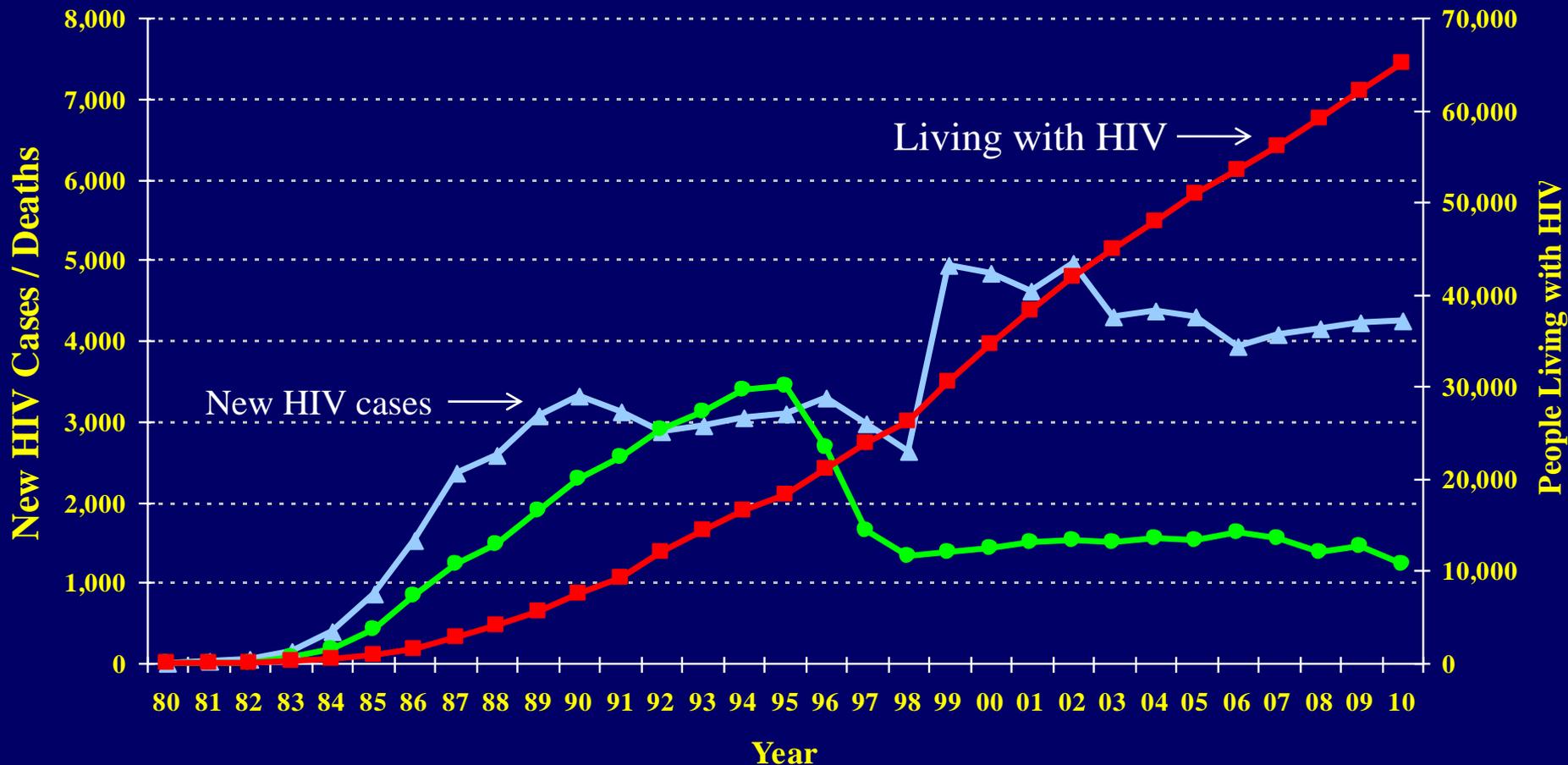
Increasing Age Among HIV+ Persons: US



Scope of the Problem: HIV Over 50

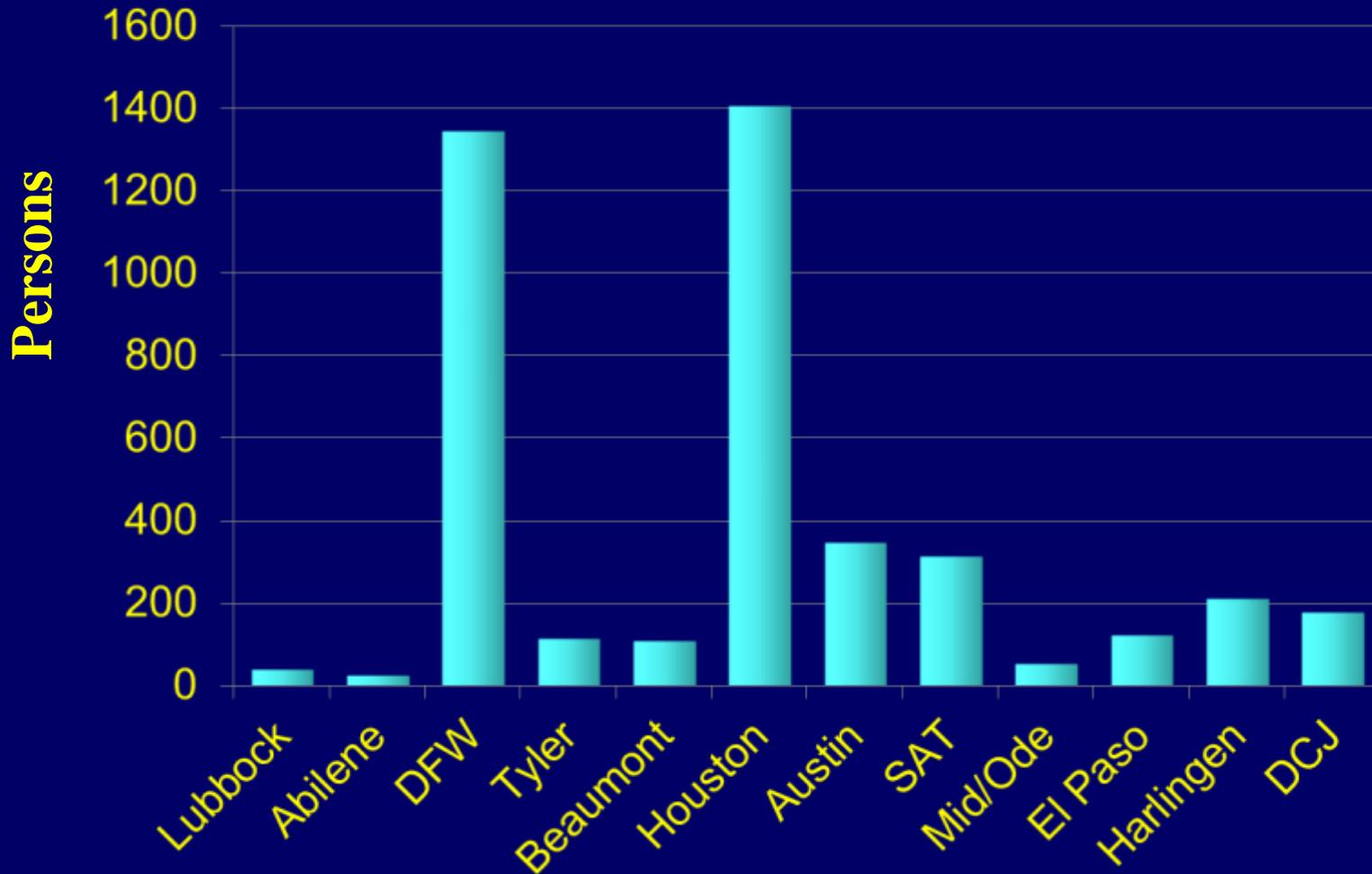
- **2007: 25% of people living with HIV in the US were ≥ 50 years old**
- **2012: approximately 30% of the people living with HIV in the US are ≥ 50 years old**
- **2015: one half of all persons living with HIV in the US will be ≥ 50 years old**

Newly Diagnosed HIV Cases, Deaths, and People Living with HIV: Texas, 1980-2010

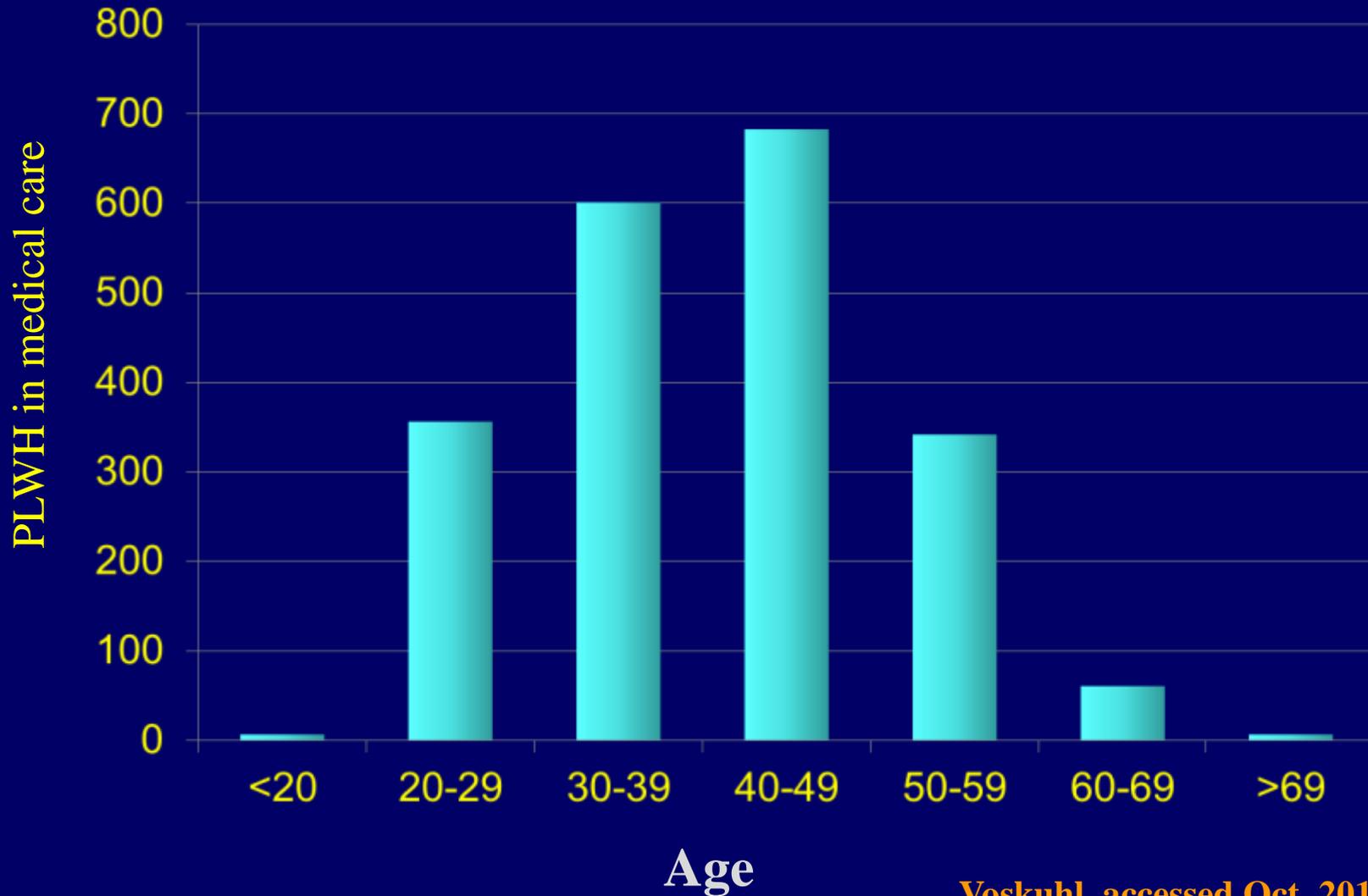


*2009-2010 death data are provisional.

New HIV Diagnoses, TX



Age at AIDS Arms



Scope of the Problem

Contracting HIV

- **There may be an increased risk for acquisition and transmission of HIV in older individuals**
 - **Belief that HIV only affects younger people**
 - **Training in safer sexual activities**
 - **Sexual negotiation skills**
 - **HIV prevention education is mostly targeted at younger people**

Identified Risks of Contracting or Transmitting HIV In Older Individuals

- **Newly widowed or divorced**
- **Postmenopausal women may be less concerned about pregnancy prevention (decreased condom use)**
- **Low estrogen causes vaginal dryness and thinning**
- **Men with erectile dysfunction may spurn condom use**

HIV Prevention

- **Sexual mores**
 - Sex doesn't stop at 50
- **Age is not a condom**
- **Older people inject drugs**
 - Other illicit drugs
 - Alcohol use

HIV Testing Recommendations

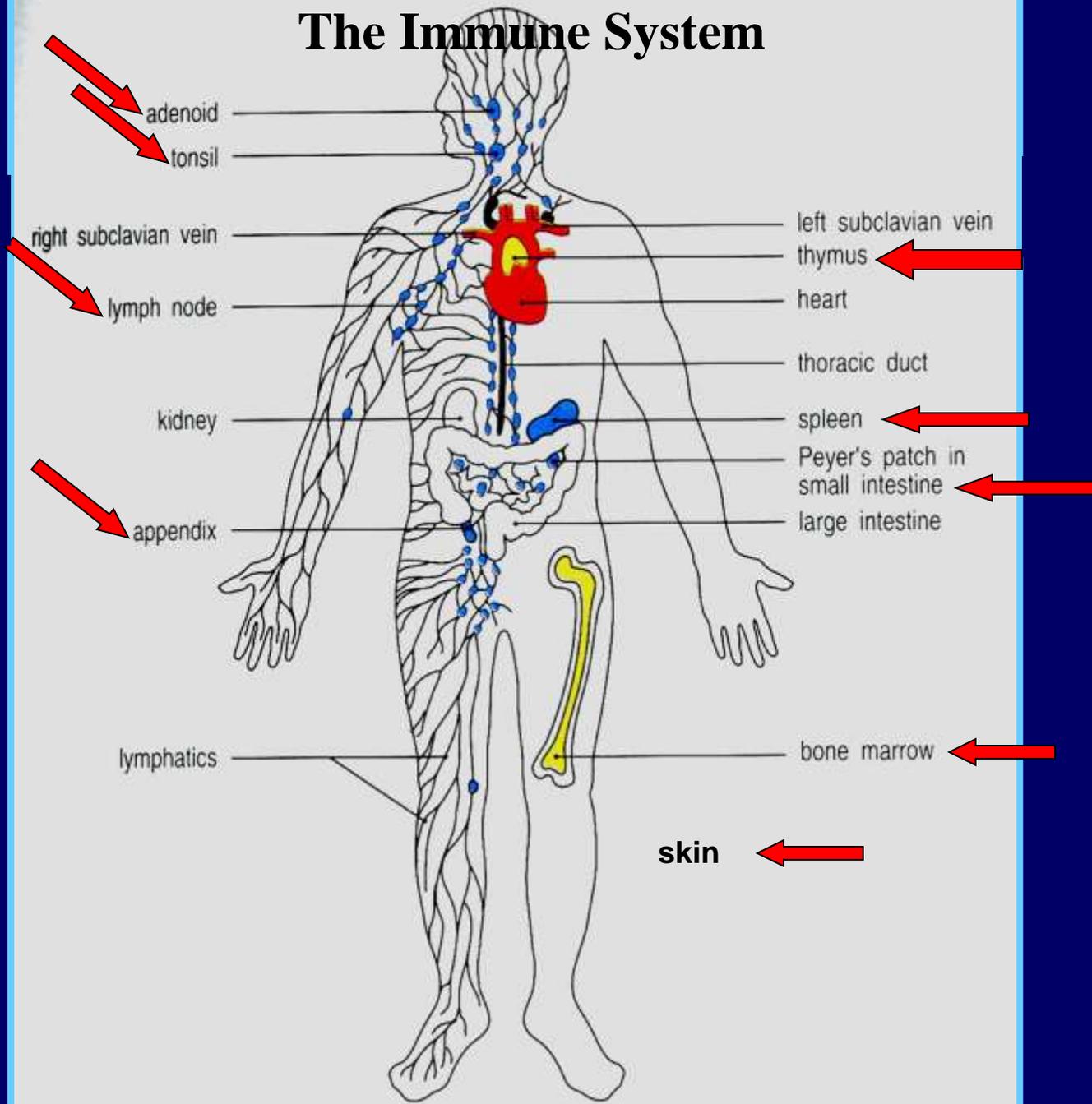
- **Since 2006 the CDC has recommended routine screening of all individuals up to age 64**
- **In 2008 only 35% of adults aged 45-64 had ever been tested for HIV**
- **Consider screening adults aged 65 and older**

Life Expectancy is not Normal with HIV

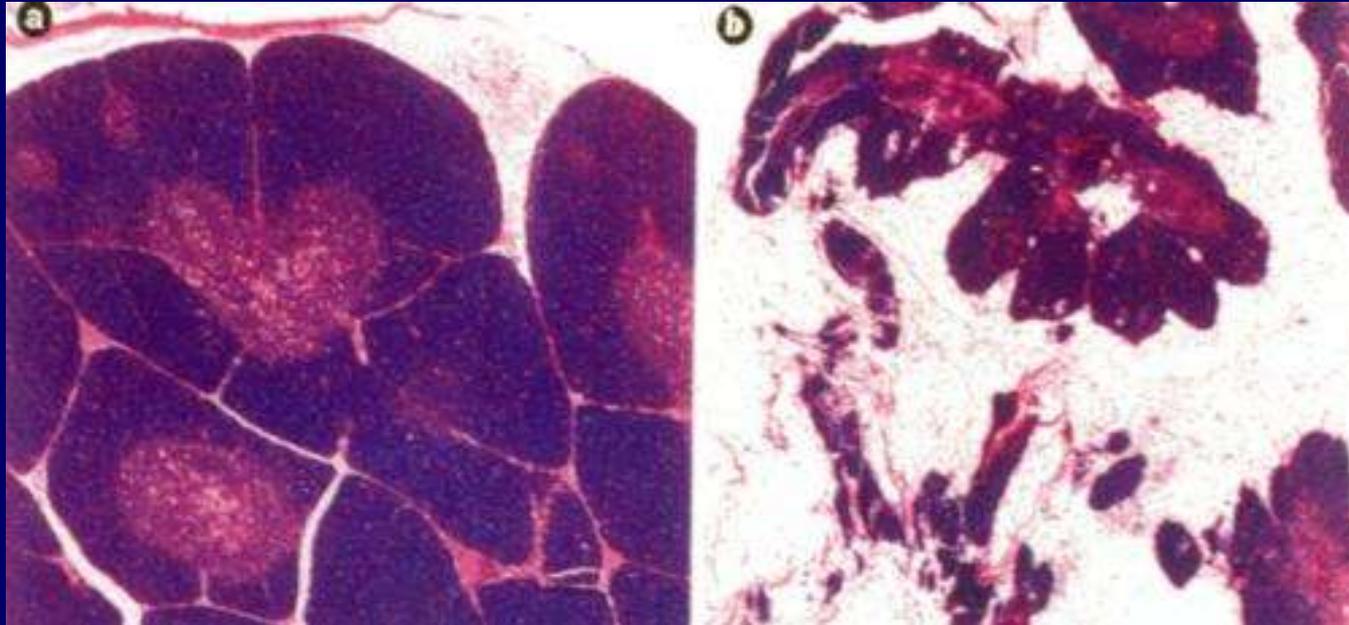
Baseline CD4 cell count

At HAART Initiation:	<100	100-199	≥200
A 20 yr old will live to (years)	52	62	70
A 35 yr old will live to (years)	62	65	72
Remaining Life Lost (%)	46%	27%	14%

The Immune System



Chronological aging is associated with multiple changes in the immune system

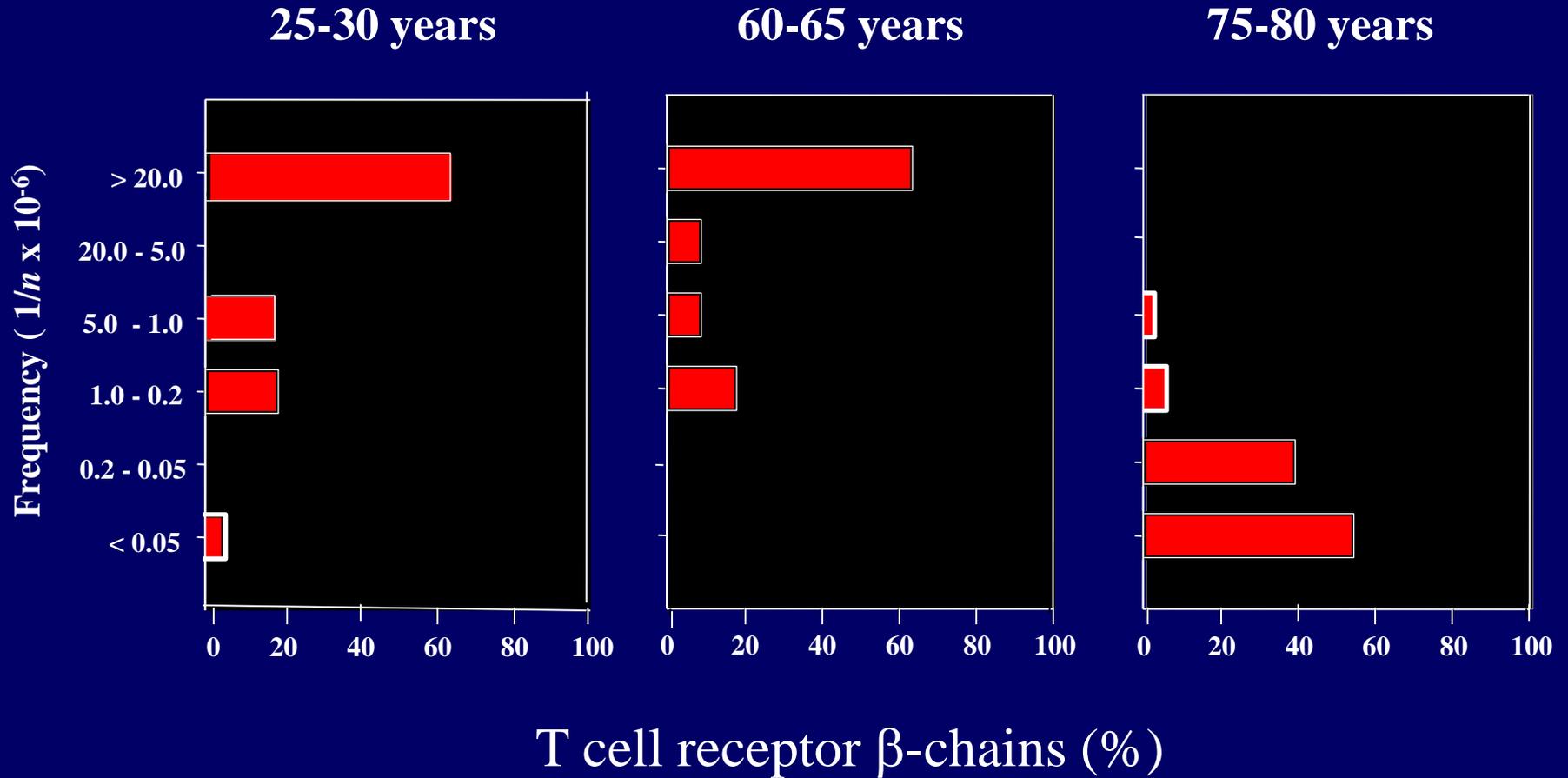


Normal thymus

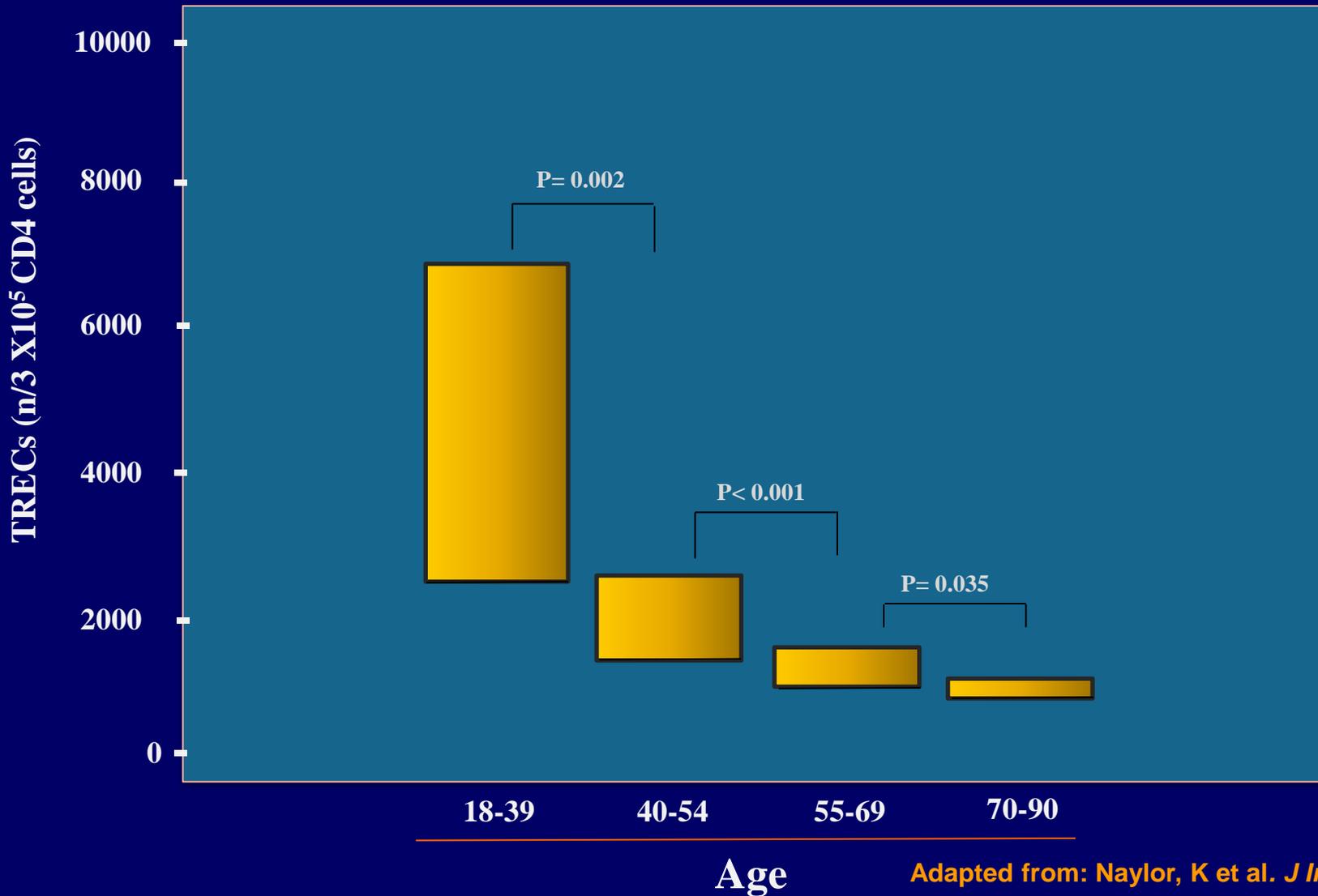
Aged thymus

**Thymus tissue
microscopically**

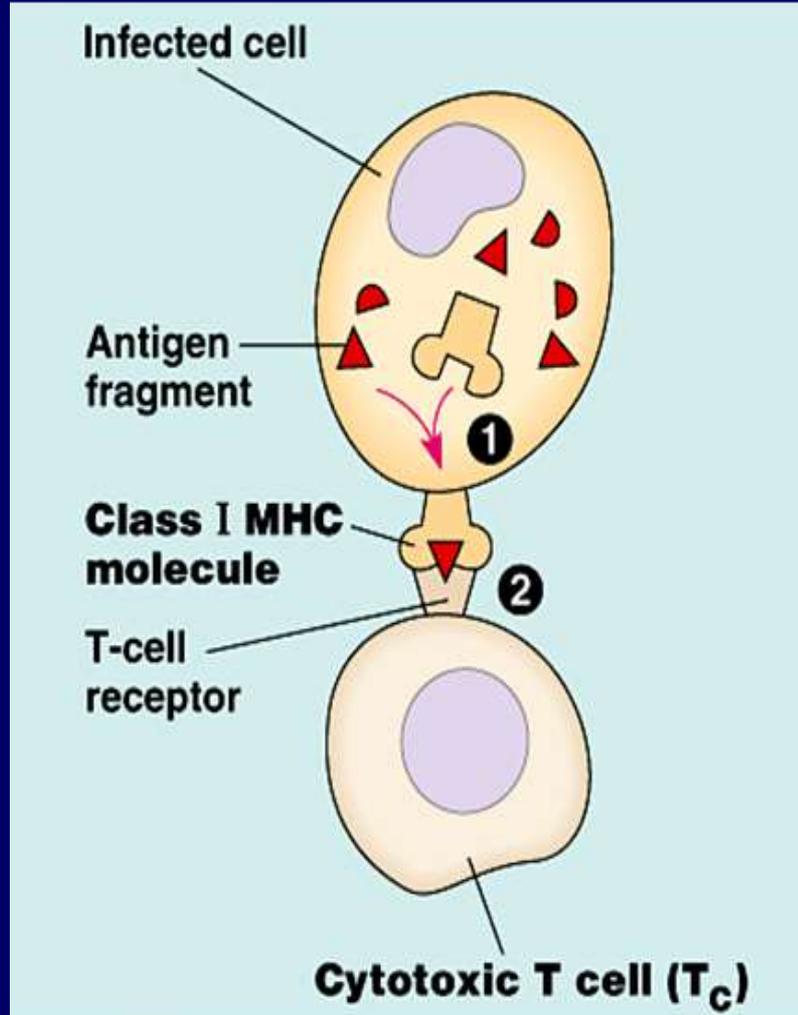
Reduced T cell diversity with aging: Naive CD4 T cells



Age-dependent decline in T cells from thymus



Cytotoxic T cells kill infected CD4 cells

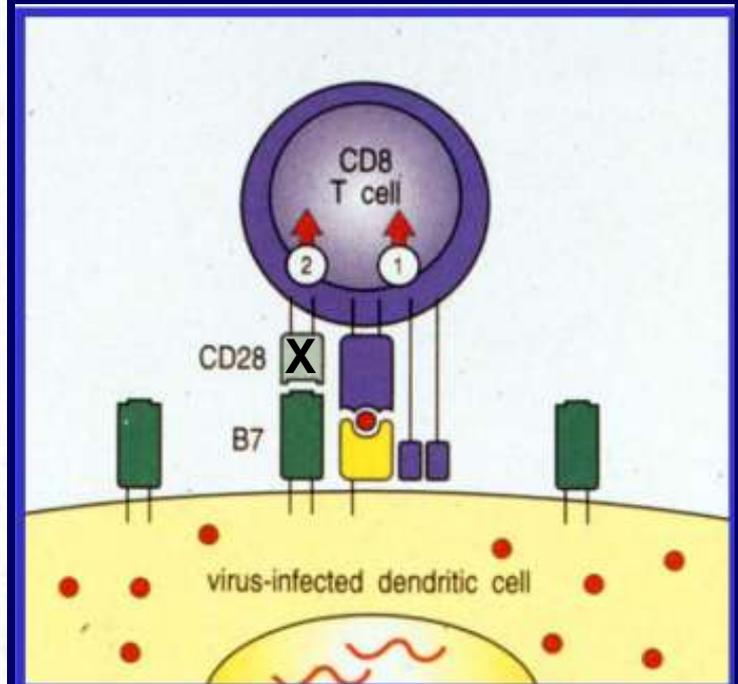
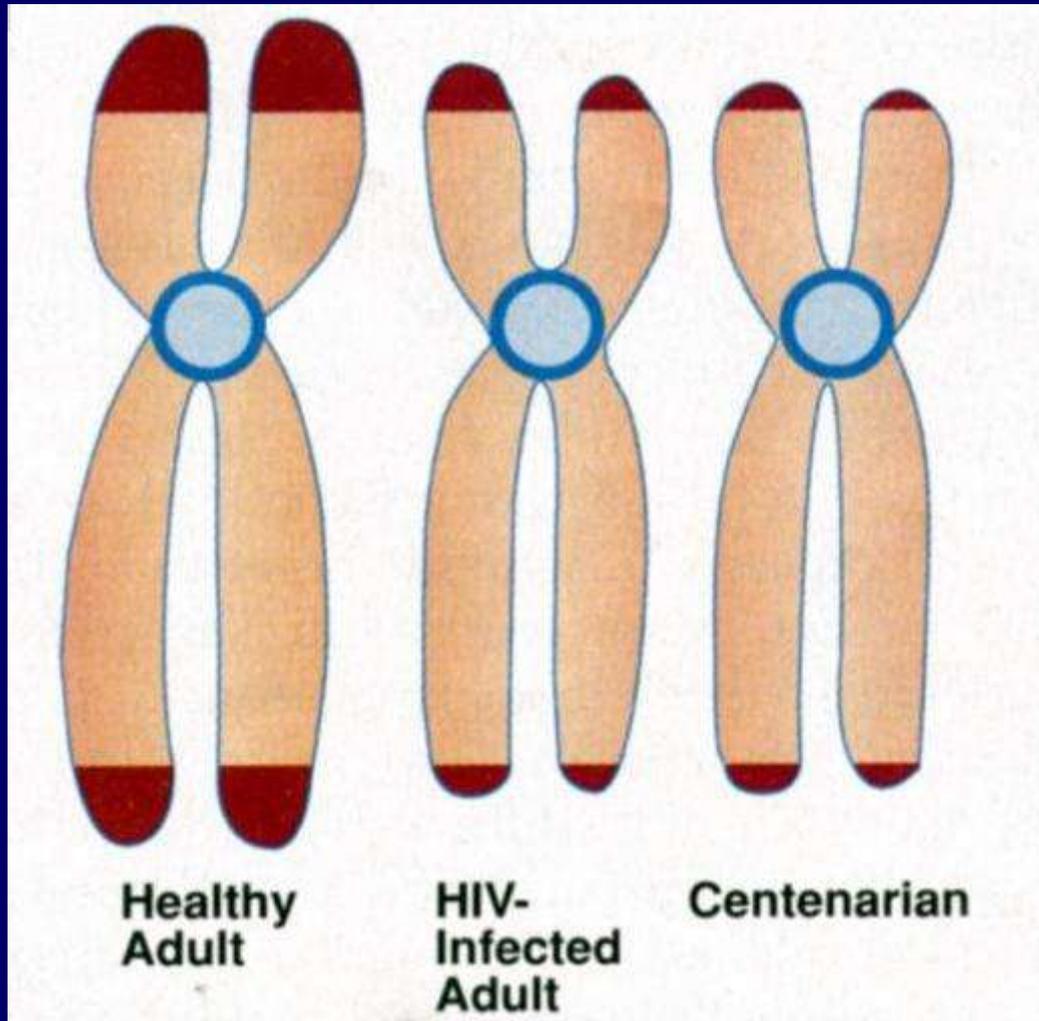


- Kills infected cells
- Kills cancer cells
- Induces inflammation
- Chronic infections keep cascade activated

Senescent CD8 cells

- Irreversible state of growth arrest
- Consequence of extensive cell division
- Altered function and gene expression
- ↑ Proinflammatory cytokines (TNF α , IL-6)
- Shortened telomeres
- CytotoxicT cells with these same features are increased in younger persons with HIV

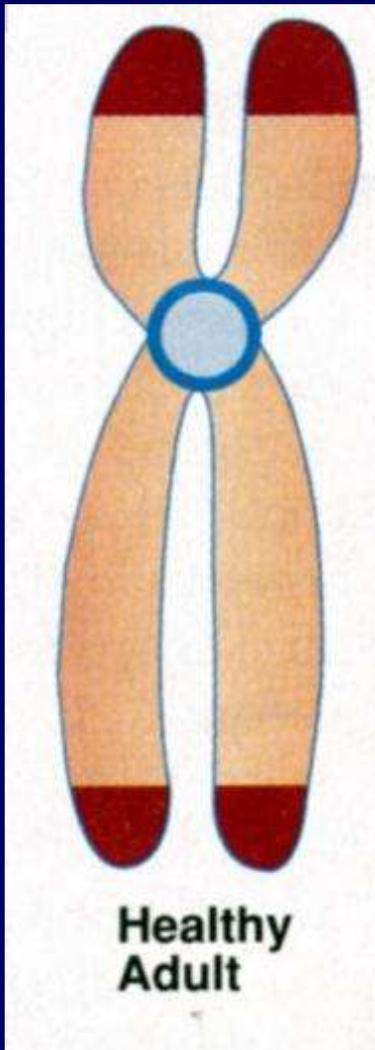
HIV: Premature telomere shortening in chronically activated, senescent T cells



Senescent T cells and Telomeres

- **Telomere length correlates with mortality**
 - **Multiple disease states**
 - **CVD, DM, Alzheimer's, AMI, stress**
 - **HIV**
 - **CD28 part of immune profile that is predictive**

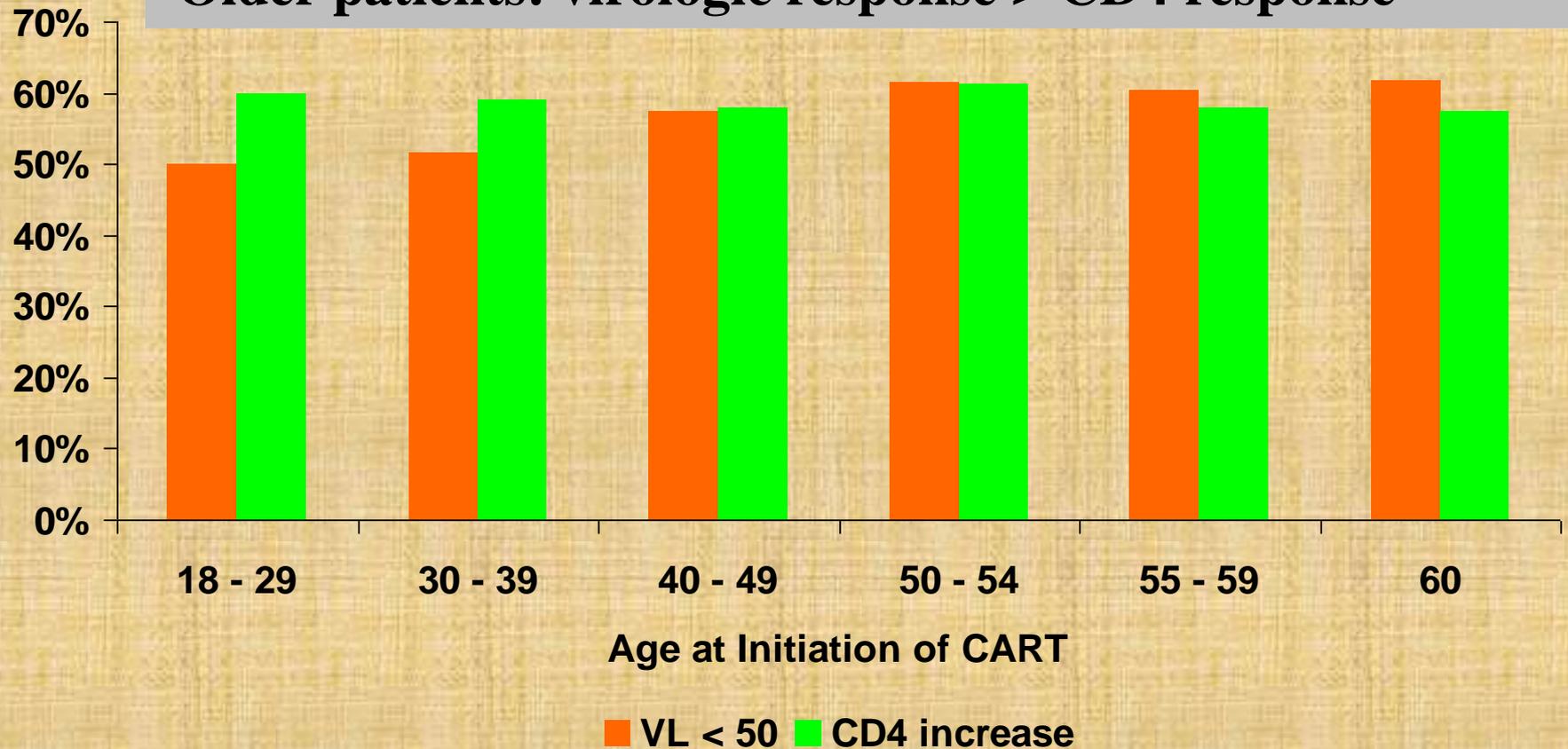
Telomerase: enzyme that re-elongates telomeres



- Present in germ cells, stem cells, and activated immune cells
- Killer T cells with highest telomerase activity in HIV-1 controllers

Twelve Month Virologic & Immunologic Response to HAART by Age

Younger patients: CD4 response > virologic response
Older patients: virologic response > CD4 response



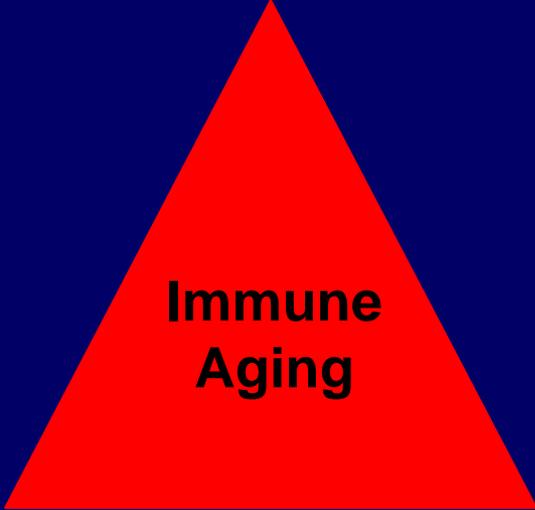
Aging and Immune Function

Summary

- **HIV infection may accelerate aging of the immune system via chronic inflammation**
- **Reduced number, diversity, and proliferation of T-cells**
- **Decreased size and function of the thymus**
- **Reduced telomere (chromosome) length**
- **Less immune response to HAART**

Immune deficiency

- Poor vaccine response
 - Infections
 - Cancer



**Immune
Aging**

Chronic inflammation

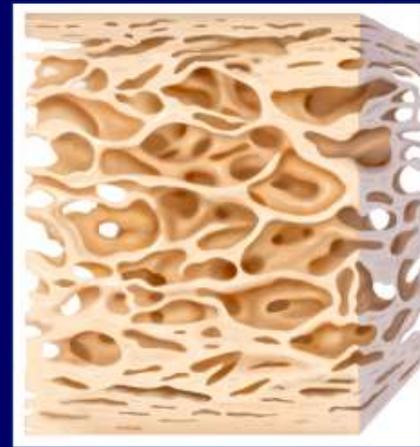
- Coronary artery disease
- Alzheimer's disease
- Osteoporosis
- Frailty

Autoimmunity

- Autoantibody production
- Polymyalgia rheumatica
- Giant cell arteritis
- Rheumatoid arthritis

Osteoporosis

- HIV infection has been associated with reduced bone mineral density and an increased risk of fragility fractures
- Vit D
- Screen by DEXA Scan

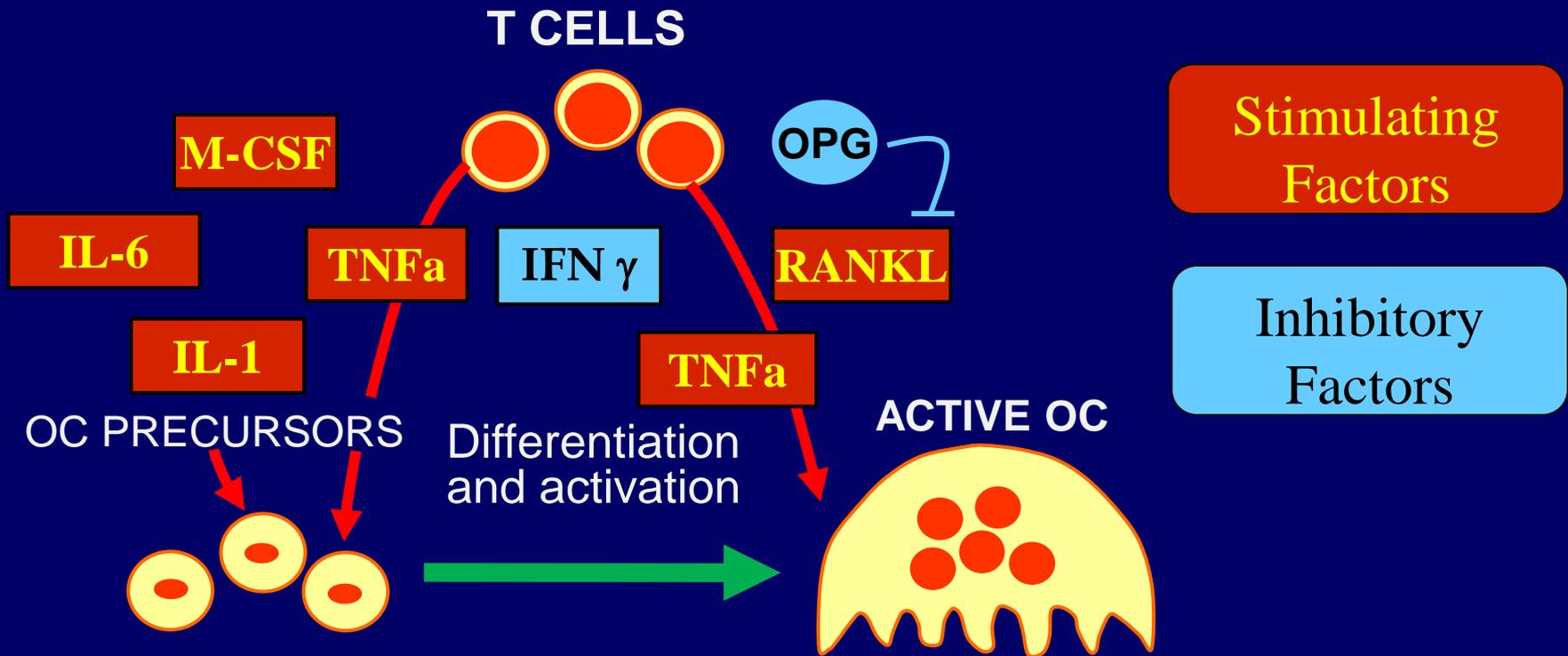


Normal bone



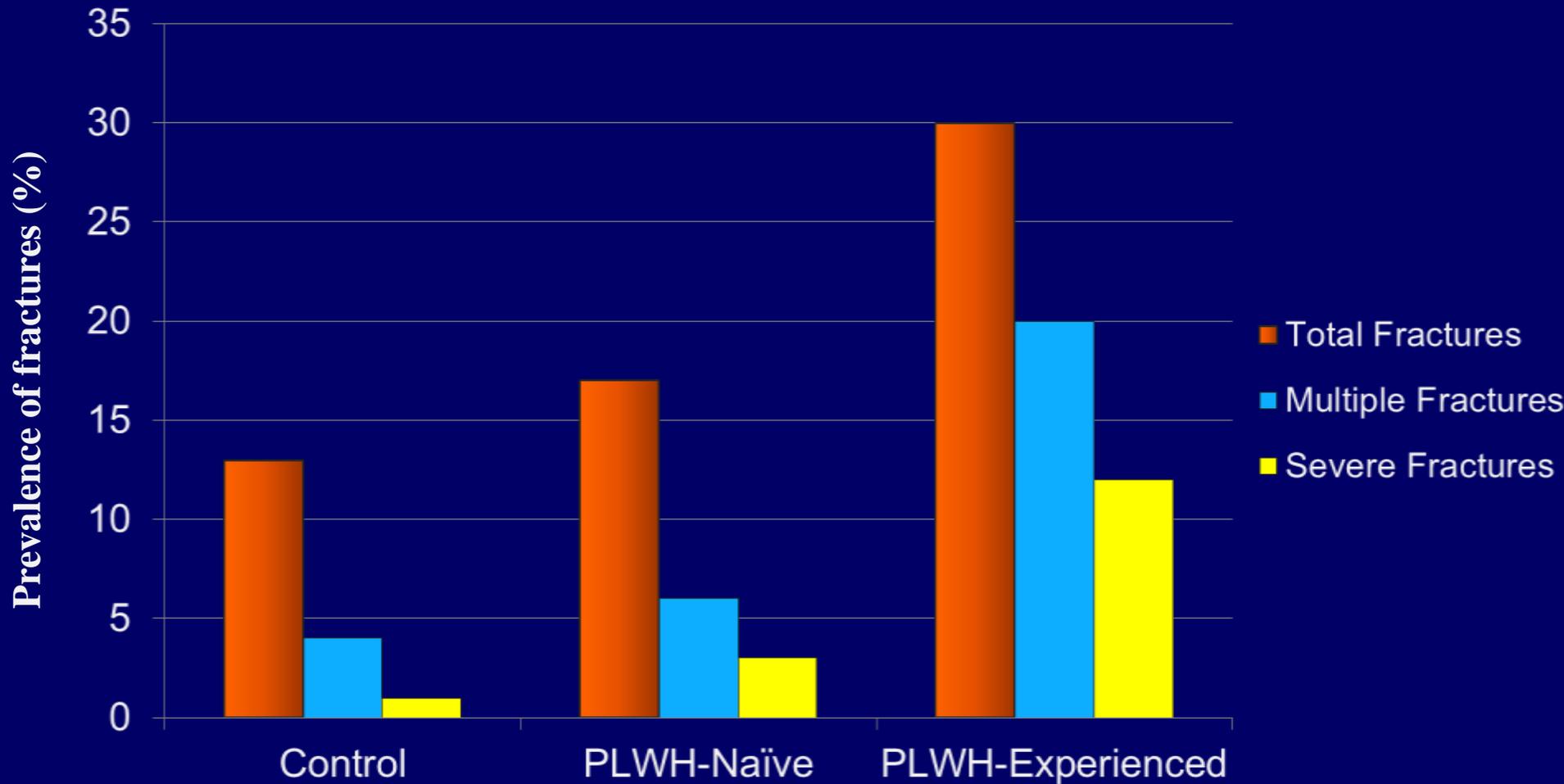
Osteoporosis

T lymphocytes secrete factors that regulate bone-destroying osteoclasts



Senescent CD8+ T cells: \uparrow TNF α , IL-6, RANKL; \downarrow IFN γ

Increased Fractures in PLWH



Risk Factors for Bone Loss

- **Being female**
- **Family history of bone loss or fracture**
- **Race (White or Asian)**
- **Diet low in calcium or vitamin D**
- **Being thin or having a small frame**
- **Smoking and/or excessive alcohol use**
- **Use of certain medicines**
- **Low Estrogen / Testosterone**

Reducing Risk of Osteoporosis

- **Weight-bearing exercise**
- **Stop Smoking**
- **Minimize Alcohol**
- **Sufficient Calcium Intake**
- **Sufficient Vitamin D**
- **Proton Pump Inhibitors**

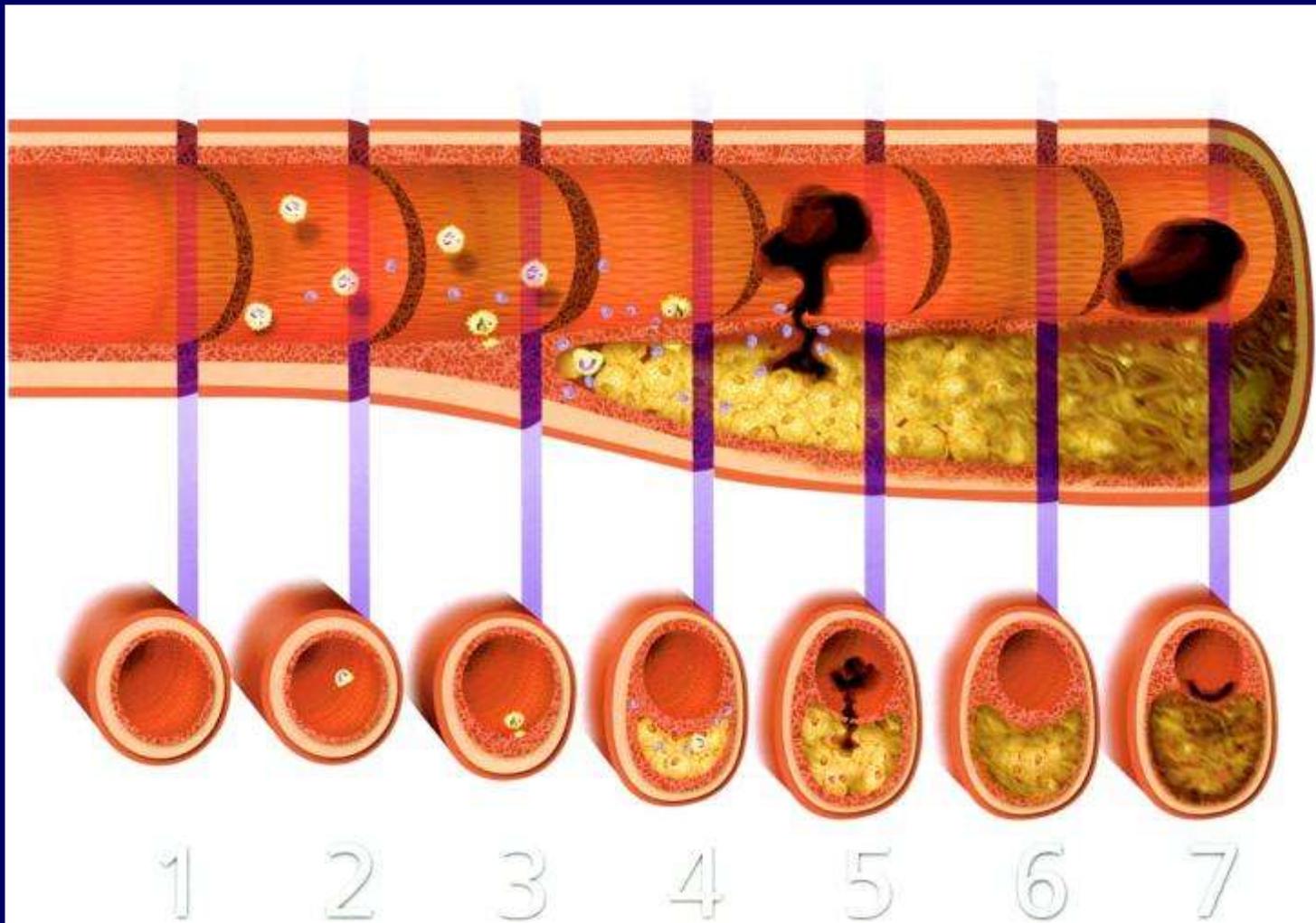


Coronary artery disease

- **Much learned about chronic inflammation**
 - Endothelial cells and cytokines
 - T cells involved in this cascade
 - Inflammation cascade leads to thrombus/occlusion
 - Chronic CMV implicated as driving CVD in immunocompromised (transplant patients)*

Coronary artery disease

Initiation, progression, and complication of human coronary atherosclerotic plaque



Myocardial Infarction

- **HIV-infected individuals had approximately a 2-fold increase in the risk of MI**
- **The risk of HIV was similar to that of having diabetes or smoking**

Modifiable Risk Factors: Smoking

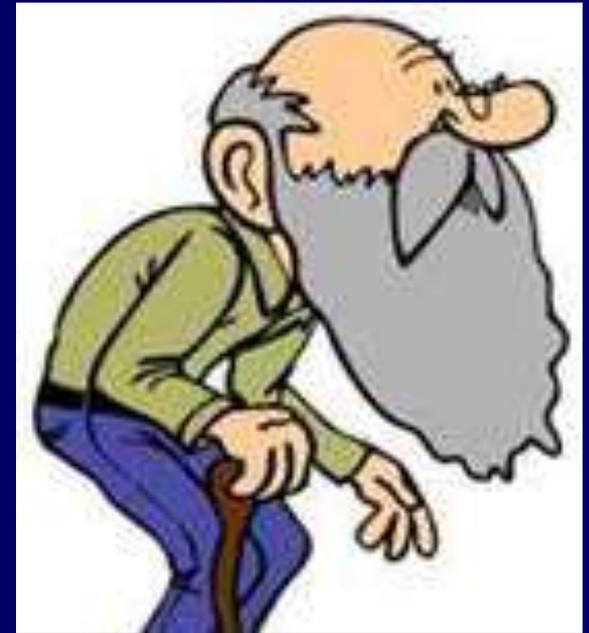
**SMOKING IS THE STRONGEST MODIFIABLE RISK
FACTOR FOR CARDIOVASCULAR DISEASE**

CV Modifiable risk factors

- **Smoking**
- **Weight**
- **Exercise**
- **Lipid control**
- **Diabetes control**
- **Blood pressure control**

Frailty

- **Frailty is defined as having 3 of the following**
 - Unintentional weight loss (≥ 10 pound/last yr)
 - Exhaustion
 - Slowness
 - Low level of physical activity



Frailty in HIV

- **HIV associated with a >10-year earlier occurrence of a pattern similar to frailty**
 - Risk of frailty is increased with decreasing CD4 cell count
 - Older age, lower educational level, and clinical AIDS associated with frailty
- **Frailty associated with risk of AIDS or death, even if HIV is controlled**
- **Associated with central obesity and fat redistribution**

Neurologic Conditions

- **40-70% of patients with HIV have nervous system impairment**
- **Screening is important**
 - Depression common in HIV clinics
 - Self-administered testing
 - Substance abuse occurs in elderly
- **Treatment of anxiety with SSRI's with fewer adverse events than benzodiazepenes**

Neurologic Conditions

Primary vs. Secondary

Primary

- Neurocognitive disorders
- Peripheral Neuropathy
- HIV-associated myelopathy

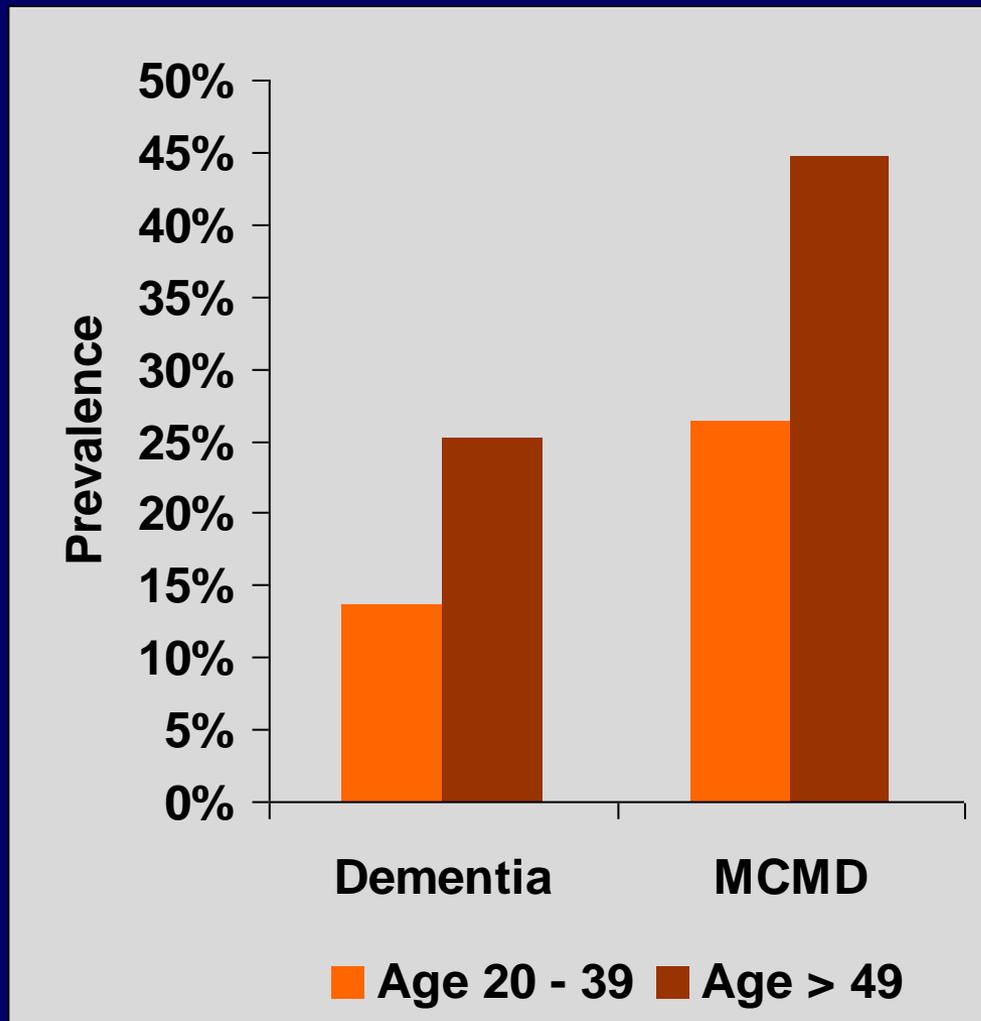
Secondary

- Cryptococcal Meningitis <5%
- Toxoplasmosis <5%
- CMV <5%
- Neurosyphilis <5%
- PML <5%

Prevalence of Primary Neurologic Conditions

- **Mild Cognitive Impairment >50%**
- **Dementia <10%**
- **Neuropathy 40%**
- **Myelopathy 5-10%**

HIV-Associated Dementia by Age



- Older patients 3 times more likely to have HIV-associated dementia, mild cognitive motor disorder (MCMD)
- Associated with lower CD4 count in older patients

HIV-Associated Neurocognitive Impairment

- **Cognition**
 - memory loss, concentration, mental slowing, comprehension
- **Motor**
 - Unsteady gait, poor coordination, tremor
- **Behavior**
 - Apathy, depression, agitation, mania

Neuropathy Types

Distal Polyneuropathy



Mononeuropathy Multiplex



Inflammatory Demyelinating Polyneuropathy



Mononeuropathy



Brachial Plexopathy



Prevention of Neuropathy

- **Manage underlying medical conditions (HIV, diabetes)**
- **Consume a diet rich in fruits, vegetables, and whole grains**
- **Assure adequate intake of vitamins**
- **Exercise**
- **Minimize alcohol consumption**
- **Avoid certain older HIV drugs**
- **Avoid toxic chemicals**

Prevention of Dementia

- **Decrease modifiable cardiovascular risk factors**
- **Stay mentally alert by learning new hobbies**
 - reading, solving crossword puzzles, playing board games
- **Have leisure activities**
 - playing a musical instrument, dancing
- **Stay involved socially**
 - Attend group functions, community activities

Cancer

- HIV infection is associated with an increased risk of many cancers
- Some are attributable to HIV-related immune suppression
- Telomeres and chronic inflammation possible culprits



Cancer Prevention

- **Avoid tobacco (including secondhand smoke)**
- **Eat a healthy diet**
 - **Limit processed meat and red meat**
 - **Eat at least 2 ½ cups of vegetables and fruits a day**
 - **Choose whole grains instead of refined grains**
- **Stay lean and get regular exercise**
- **Sun exposure**
 - **10 AM – 4 PM is the most intense**
 - **Sunscreen SPF ≥ 15**
 - **Wear a hat**
- **Limit alcohol: 1 drink a day for women/2 drink for men**

Medications

- **Polypharmacy**
- **Drug Interactions**
- **Older individuals tend to be more adherent with antiretroviral medications**
- **Older individuals have slower CD4 recovery after starting antiretroviral therapy**
- **Older individuals are more susceptible to side effects from antiretroviral medication**

Other Issues

- Planning for health care costs
- Long-term care planning
- Living Wills and Advance Directives
- Navigating the Health Care System



Modifiable Risk Factors

- **Smoking**
- **Lipids (cholesterol and triglycerides)**
- **Blood pressure**
- **Physical inactivity**
- **Obesity**
- **Diabetes**
- **Vitamins**
 - including VitD
- **DEXA**
- **Alcohol use**
- **Illegal drug use**
- **Diet**
- **Immunizations**

DHHS Guidelines 2012

- **Antiretroviral therapy (HAART) is recommended in patients >50 years of age, regardless of CD4 count**
 - risk of non-AIDS related complications may increase
 - immunologic response to ART may be reduced

Summary

- **Ever changing HIV landscape**
- **Chronic inflammation and senescent T cells leads to immune aging**
- **Multiple organs involved**
- **Focus on modifiable risk factors**

Resources

- ❑ www.aahivm.org/hivandagingforum
- ❑ www.aidsinfo.nih.gov
- ❑ http://www.aidsmeds.com/articles/2614_20293.shtml
 - **For patients and community**



2012 HIV/STD Conference