Learning Objectives

Upon completion of this presentation, learners should be better able to:

• Recognize specific clinical care challenges of older HIV-infected patients
• Adapt geriatric guiding principles into your HIV Clinic
Faculty and Planning Committee Disclosures
Please consult your program book.

Off-Label Disclosure
There will be no off-label/investigational uses discussed in this presentation.
• Recent trends in epidemiology and cause of death
• Pathogenesis: aging and chronic HIV
• Comorbid conditions: aging and chronic HIV
• Clinical care: special considerations
• Lifestyle modifications: exercise is the best medicine
“By 2015, half of the U.S. population living with the human immunodeficiency virus (HIV) infection will be older than 50 years of age.”
Why the increase in older (50+ years) HIV-infected adults?

New cases of HIV infection in older adults

A public health challenge... and whole separate talk
More people living with HIV infection every year in the U.S.

CDC surveillance data

Each year: 56K new infections-18K deaths=38K*
Projected Proportion of those Living With HIV in United States 50+ Years 2001-2017


Slide courtesy of Amy Justice
Figure 5. HIV Infected Veterans in VHA Care 2008 - Age by Decade of Life

Age by Decade of Life

Percent of all Veterans with HIV/AIDS

Decade of Life

Under 30 Years Old
30 to 39
40 to 49
50 to 59
60 to 69
70 and Above
Figure 4. Cause of death in the Data Collection on Adverse Events in Anti-HIV Drugs study (based on data from Hooshyar et al. [137])

R. Effros et al., CID 2008;47:542
II. Pathogenesis: Aging and Chronic HIV

THE 3 STAGES OF MAN
Primary Aging

Genetic
Molecular
Cellular

Secondary Aging
Diet
Physical Activity
Smoking

Tertiary Aging
Cardiovascular Disease
Metabolic Disease
Pulmonary disease
Cancer

birth
AGING
deadth

Oursler 2012
Primary Aging and HIV

- Apoptosis
- DNA mutations
- Telomere shortening ↑
- Endocrine dysregulation ↑
- Mitochondrial dysfunction ↑
- Accumulation free radicals ↑
- Inflammation ↑
Biomarkers of inflammation predict all-cause mortality in HIV negative and infected adults

<table>
<thead>
<tr>
<th>CRP</th>
<th>HIV Neg.(^1)</th>
<th>HIV Pos.(^2)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>HR (95%CI)</td>
</tr>
<tr>
<td>&lt; 1mg/L</td>
<td>3,587</td>
<td>ref.</td>
</tr>
<tr>
<td>1-3 mg/L</td>
<td>317</td>
<td>2.3 (1.3-4.1)</td>
</tr>
<tr>
<td>&gt;3 mg/L</td>
<td>1,433</td>
<td>1.4 (1.2-1.5)</td>
</tr>
</tbody>
</table>

1. JJ Cao, Circulation, 2007; CHS, 65+ yo adults, 12 year fu
2. P Tien, JAIDS, 2010; FRAM, 5-year fu
Role of inflammation and thrombosis in atherosclerosis and HIV

J Baker and D Duprez, Current Opinion in HIV and AIDS, 2010
HIV smokers with emphysema have higher alveolar macrophage matrix metalloproteinases

Kaner RJ, Crystal RG. J Leukoc Biol 2009
Primary Aging

- Genetic
- Molecular
- Cellular

Secondary Aging
- Diet
- Physical Activity
- Smoking
- Illicit drugs & alcohol

Tertiary Aging
- Cardiovascular Disease
- Metabolic Disease
- Pulmonary disease
- Cancer

HIV
- HAART toxicity

Oursler 2012
III. Comorbid Conditions: Aging and Chronic HIV
Prevalence of COPD increased in HIV across age groups
Risk of MI increases with age and HIV

Table 2. Rates of AMI by HIV Status and Age Group

<table>
<thead>
<tr>
<th>Status</th>
<th>&lt;30</th>
<th>30-39</th>
<th>40-49</th>
<th>50-59</th>
<th>60-69</th>
<th>70-79</th>
<th>80-89</th>
<th>&gt;89</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uninfected</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of participants</td>
<td>1175</td>
<td>6783</td>
<td>21866</td>
<td>19805</td>
<td>4209</td>
<td>1120</td>
<td>148</td>
<td>3</td>
</tr>
<tr>
<td>No. of AMI events</td>
<td>0</td>
<td>10</td>
<td>164</td>
<td>218</td>
<td>66</td>
<td>36</td>
<td>14</td>
<td>0</td>
</tr>
<tr>
<td>AMI rates per 1000</td>
<td>0.3</td>
<td>1.5</td>
<td>2.2</td>
<td>3.3</td>
<td>6.7</td>
<td>21.5</td>
<td>...</td>
<td></td>
</tr>
<tr>
<td>person-years (95% CI)</td>
<td>(0.2-0.6)</td>
<td>(1.3-1.7)</td>
<td>(1.9-2.5)</td>
<td>(2.6-4.2)</td>
<td>(4.8-9.2)</td>
<td>(12.7-36.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV Infected</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of participants</td>
<td>725</td>
<td>3848</td>
<td>10575</td>
<td>9342</td>
<td>2065</td>
<td>557</td>
<td>56</td>
<td>0</td>
</tr>
<tr>
<td>No. of AMI events</td>
<td>0</td>
<td>13</td>
<td>105</td>
<td>171</td>
<td>46</td>
<td>25</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>AMI rates per 1000</td>
<td>0.7</td>
<td>2.0</td>
<td>3.9</td>
<td>5.0</td>
<td>10.0</td>
<td>13.5</td>
<td>...</td>
<td></td>
</tr>
<tr>
<td>person-years (95% CI)</td>
<td>(0.4-1.2)</td>
<td>(1.6-2.4)</td>
<td>(3.3-4.5)</td>
<td>(3.8-6.7)</td>
<td>(6.7-14.7)</td>
<td>(4.3-42.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incidence rate ratio (95% CI)</td>
<td>2.19</td>
<td>1.34</td>
<td>1.80</td>
<td>1.53</td>
<td>1.50</td>
<td>0.63</td>
<td>...</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(0.89-5.58)</td>
<td>(1.04-1.72)</td>
<td>(1.47-1.21)</td>
<td>(1.03-2.26)</td>
<td>(0.86-2.57)</td>
<td>(0.12-2.25)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: AMI, acute myocardial infarction; HIV, human immunodeficiency virus.
a An ellipsis indicates that a rate was not calculated because there were 0 events.

Freiberg MS, JAMA Intern Med. 2013
Lipodystrophy Syndrome

Overlap with Components of the Metabolic Syndrome

<table>
<thead>
<tr>
<th>Morphologic Changes</th>
<th>Metabolic Disturbances</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central obesity</td>
<td>Insulin resistance</td>
</tr>
<tr>
<td>Dorsocervical fat enlargement</td>
<td>Impaired glucose tolerance</td>
</tr>
<tr>
<td>Breast enlargement</td>
<td>Increased triglycerides</td>
</tr>
<tr>
<td>Lipoatrophy Extremities</td>
<td>Decreased HDL cholesterol</td>
</tr>
<tr>
<td>Lipoatrophy Face</td>
<td>Increased LDL cholesterol</td>
</tr>
</tbody>
</table>
Increased risk of bone fractures in HIV

V Triant et al, J Clin Endocrin Metab, 2008
HIV Associated Neurocognitive Disorders (HAND)

• The 3 components of HAND are common and frequently undiagnosed\(^1\)
  – 2% HIV-associated dementia
  – 12% HIV-associated mild neurocognitive disorder
  – 33% Asymptomatic neurocognitive impairment

• Older age complicates diagnosis: cognitive decline seen as aging

• There are No clear treatments beyond achieving non-detectable HIV viral load

Heaton et al, Neurology 2010
IV. Clinical care: special considerations
46 year old man diagnosed HIV +
54 years old, after 2 years HAART

<table>
<thead>
<tr>
<th>Year</th>
<th>CD4 Cell Count (mm³)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1995</td>
<td>95</td>
</tr>
<tr>
<td>2001</td>
<td>20</td>
</tr>
<tr>
<td>2003</td>
<td>161</td>
</tr>
<tr>
<td>2005</td>
<td>233</td>
</tr>
</tbody>
</table>

HIV +

HAART
Weight and CD4 continue to rise

HIV +

HAART

Central Obesity

LDL: 86
HDL: 34
TG: 146
FG: 84
Insulin: 22
CD4 Cell Count (mm3)
0
50
100
150
200
250
56 years old: healthy, fit, 10yrs HIV+

Post 16 wk exercise & diet in PAN

HIV +
HAART

LDL: 87
↑ HDL: 52
↓ TG: 110
↓ FG: 74
↓ Insulin: 7
ART in the older HIV-infected patient

- No age-specific ART recommendations
- Viral response not affected by age
- CD4 response may be delayed
- Consider age-related comorbid conditions
- Consider drug interactions
  - Don’t forget the OTC (antacids, NSAIDS, tylenol)
  - Impaired creatinine clearance
  - Reduced hepatic function

http://aidsinfo.nih.gov/guidelines
Multimorbidity and multiple pills

B Hasse, CID, 2011
Summary Report from the Human Immunodeficiency Virus and Aging Consensus Project: Treatment Strategies for Clinicians Managing Older Individuals with the Human Immunodeficiency Virus

Work Group for the HIV and Aging Consensus Project

- Cardiovascular Risk Reduction, Diabetes Mellitus
- Monitoring Renal Function and Hypertension
- Drug-Drug Interactions and Polypharmacy
- Viral Hepatitis Screening
- Cancer Screening
- COPD
- Immunizations
- Sexual Health
- Osteoporosis
- Advanced Directives
- Neurocognitive Changes, Psychiatric Illness, Substance Use

JAGS, 60:974-979, 2012
“We recommend screening all post-menopausal women and men and men aged ≥ 50 years… with a DXA scan.”
Strategies Are Needed:

- Screening for cognitive loss, including asymptomatic patients
- Testing for reversible causes of dementia
- Early access to HAART
- Community-based resources
## Preventive care: should it be different in older HIV adults?

<table>
<thead>
<tr>
<th>Conditions with Increased Risk in HIV</th>
<th>Observational Studies</th>
<th>Modifications</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Obstructive Lung Disease</strong></td>
<td>Additive negative effect of smoking and HIV(^1)</td>
<td>Increase emphasis on smoking cessation?</td>
</tr>
<tr>
<td><strong>Myocardial Infarction</strong></td>
<td>HIV is an independent risk factor(^3)</td>
<td>HIV in Framingham Score?</td>
</tr>
<tr>
<td></td>
<td>Aspirin attenuates platelet activation in HIV(^2)</td>
<td>Lower age threshold for daily aspirin?</td>
</tr>
<tr>
<td><strong>Fragility Fractures</strong></td>
<td>Increased risk in HIV(^4)</td>
<td>Early DEXA screening</td>
</tr>
<tr>
<td><strong>Neurocognitive Decline</strong></td>
<td>High prevalence in HIV(^5)</td>
<td>Screen asymptomatic patients?</td>
</tr>
<tr>
<td><strong>Anal Cancer</strong></td>
<td>Increased risk in HIV + groups(^6)</td>
<td>Annual digital rectal exam Anal Pap smear? HPV vaccination?</td>
</tr>
</tbody>
</table>

\(^1\)Kaner, 2009; \(^2\)O’Brien, 2013; \(^3\)Freiberg, 2013; \(^4\)Triant, 2008; \(^5\)Heaton, 2010; \(^6\)D’Souza, 2008
V. Exercise as the best medicine

“What fits your busy schedule better, exercising one hour a day or being dead 24 hours a day?”
HIV infection, antiretroviral treatment, ageing, and non-AIDS related morbidity

Steven G Deeks, Andrew N Phillips

Box 2 Non-AIDS related complications that may be more common in patients with HIV

- Hypertension
- Diabetes mellitus and insulin resistance
- Cardiovascular disease
- Pulmonary hypertension
- Cancer
- Osteopenia and osteoporosis
- Liver failure
- Kidney failure
- Peripheral neuropathy
- Frailty
- Cognitive decline and dementia

EXERCISE Is Effective Prevention & Treatment
Exercise interventions that improve components of lipodystrophy syndrome

<table>
<thead>
<tr>
<th>Exercise Intervention *</th>
<th>total N</th>
<th>mean age</th>
<th>Effect</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pioglitazone vs. Pioglitazone + AEX + RT</td>
<td>39</td>
<td>45 y</td>
<td>Both ↓ insulin resistance, No ∆ lipids</td>
<td>Yarasheski, 2011</td>
</tr>
<tr>
<td>AEX vs. RT</td>
<td>18</td>
<td>50 y</td>
<td>Both ↓ insulin resistance, ↑ Lean mass in RT</td>
<td>Lindegaard, 2008</td>
</tr>
<tr>
<td>Metformin vs. metformin + exercise</td>
<td>37</td>
<td>43 y</td>
<td>↓% body fat, ↓ insulin resistance</td>
<td>Grinspoon, 2004</td>
</tr>
<tr>
<td>10 wks AEX + RT</td>
<td>6</td>
<td>41 y</td>
<td>↓ Cholesterol 17%</td>
<td>Jones, 2001</td>
</tr>
<tr>
<td>8 wks RT</td>
<td>18</td>
<td>42 y</td>
<td>↓ Triglycerides, ↑ lean mass</td>
<td>Yarashesheski, 2001</td>
</tr>
</tbody>
</table>

* Exercise modality: Aerobic exercise (AEX), resistance training (RT)
Muscle mass is lower in HIV+ men compared to healthy controls.
Implications of low muscle mass in chronic HIV

- R. Scherzer et al., *AIDS*, 2011
  - 5-year, all-cause mortality in 922 HIV-infected subjects in FRAM
  - Low appendicular muscle mass with 2 fold increased risk death, adjusted for age, race, CVD, and HIV factors, CRP, fibrinogen

- K. Erlandson et al., *JAIDS* 2013
  - 78 HIV-infected adults on ART, ND viral load, age 45-65 years
  - 1/3 patients met ASMI cut-offs for low muscle mass
  - 1/2 patients with poor physical function met criteria for sarcopenia

- B. Buehring et al., *Journal of Clinical Densitometry*, 2012
  - 66 HIV-infected men, median age 42 years
  - Associated with low bone mineral density
Effects of resistance training in HIV

  - RCT of metformin + (RT + low intensity AEX) vs. metformin alone
  - Increased CSA and improved muscle quality, which was independently associated with improved fasting insulin
  - Thigh CSA decreased 7 cm^2 (4%) in metformin alone group

  - Increased strength 44% and lean body mass 2.3%
  - Both independently associated with function

- de Souza et al, *Clinics*, 2008
  - Only study with older (62+ yr) HIV-infected adults
  - Strength increased 74-122% (p < 0.02)
  - Improved chair stand and short distance walk
Exercise decreases biomarkers of inflammation in older adults without HIV

RA Martins, Eur J Appl Physiol 2010
Role of Exercise in Prevention and Treatment

"Yes, yes, yes—now seriously what can we do to improve our health?"

1. Exercise
2. Exercise
3. Exercise
4. Exercise
5. Exercise
6. Exercise
7. Exercise
8. etc.

ED FISCHER '08
CDC recommendation for weekly physical activity in adults 65+ yo

1. 150 minutes of moderate aerobic activity/week and 2 strength training sessions/week
2. Stretching and calisthenics 3x/week
3. 150 minutes of walking/week
4. Get out of chair and go to kitchen each commercial break
CDC recommendation for weekly physical activity in adults 65+ yo

1. 150 minutes of moderate aerobic activity/week and 2 strength training sessions/week
Aerobic Activities

For **substantial health benefits**, adults need to do at least

- **2 hours and 30 minutes** (150 minutes) each week of relatively **moderate-intensity** aerobic activity,

  OR

- **1 hour and 15 minutes** (75 minutes) each week of relatively **vigorous-intensity** aerobic activity,

  OR

- A mix of **moderate- and vigorous-intensity** aerobic activity.

Aerobic activity should be performed for **at least 10 minutes at a time**, preferably, **spread throughout the week**.

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Muscle Strengthening Activities

Muscle strengthening should be done **2 or more days a week**.

- All major muscle groups should be worked. These are the legs, hips, back, abdomen, chest, shoulders, and arms.

- Exercises for each muscle group should be repeated 8 to 12 times per set. As exercises become easier, increase the weight or do another set.
Recommendations for exercise in older HIV adults

- Exercise strategies are needed that target the pathogenesis of HIV in aging
- Further exercise research in older HIV-infected adults is needed to determine the optimal exercise mode and intensity
- Comprehensive lifestyle recommendations need to consider additive negative effects of medication and lifestyle factors
• Clinical care of older HIV-infected patients offers specific and unique challenges

• There is overlap in the pathogeneses of aging and HIV with similar comorbid conditions

• Prevention and treatment guidelines
  – Should be based on recommendations in Geriatrics
  – Need to be adapted for older HIV adults
  – May need to vary by age at infection or length of infection
  – Further research is urgently needed