50+ SHADES OF GREY, AGING WITH HIV

REBECCA GLASSMAN, MD
INSTRUCTOR OF MEDICINE, HARVARD MEDICAL SCHOOL
MR. C

- 71 years old
- Diagnosed with HIV in 1998 at the age of 54 when he developed PCP pneumonia
  - Other AIDS defining illnesses: Kaposi sarcoma
  - He has been on multiple anti-retroviral regimens
  - Well-controlled with viral suppression since 2014
- Medications include:
  - Lisinopril 2.5
  - Metoprolol 25
  - Pravastatin 80
  - ASA 81
  - Ranitidine 150
  - Abacavir-lamivudine 600-300
  - Raltegravir 400 BID

He presents for regular primary care follow-up
AS A MEMBER OF HIS CARE TEAM, YOU MAY MAY WONDER...

- How does he compare with other HIV+ patients his age?
- How does HIV effect his aging process?
- What specific co-morbidities should you consider in relation to his HIV?
- Will his medications cause any issues given his age, co-morbidities and other medications?
As of 2015, >50% of Americans infected with HIV are over the age of 50
EPIDEMIOLOGY

• In 2013, 21% of new HIV diagnoses were age > 50
PATIENTS OVER 50 ARE...

• Less likely to be tested by physicians
• Acquiring the disease via:
  • For men, male-to-male contact
  • For women, heterosexual contact

• More likely to have acquired disease later in life
• More likely to present at a later stage of disease
  • In 2013, 27% of AIDS diagnoses were in patients age >50
• More likely to develop opportunistic infections
% Survival 12 months after diagnosis by age

Adapted from Centers for Disease Control and Prevention
PATHOPHYSIOLOGY

Chronic immune activation

Accelerated aging of lymphocytes

IL-2 and thymic dysregulation

UpToDate. Wolters Kluwer Health, 2014
RESPONSE TO TREATMENT

- Higher rates of adherence
- No difference in virologic response
- Decreased immunologic response with increasing age

Table 2. Adjusted hazard odds ratios (aHOR) and 95% confidence intervals (95% CI) of virologic and immunologic response to HAART within 24 months following HAART initiation, NA-ACCORD, 1998–2008.

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>HIV-1 RNA suppression (&lt;500 copies/ml)</th>
<th>CD4 cell count increase of 100 cells/µl</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>aHOR(^a)</td>
<td>95% CI</td>
</tr>
<tr>
<td>18–&lt;30</td>
<td>REF</td>
<td>–</td>
</tr>
<tr>
<td>30–&lt;40</td>
<td>0.71</td>
<td>0.89–1.05</td>
</tr>
<tr>
<td>40–&lt;50</td>
<td>0.66</td>
<td>0.89–1.04</td>
</tr>
<tr>
<td>50–&lt;60</td>
<td>1.00</td>
<td>0.91–1.10</td>
</tr>
<tr>
<td>≥60</td>
<td>1.05</td>
<td>0.92–1.20</td>
</tr>
</tbody>
</table>
COMORBIDITIES

- Cases:
  - ≤ 40 yrs: N = 542, 16% 3% 80% 15%
  - 41 to 50 yrs: N = 1724, 31% 17% 35% 6%
  - 51 to 60 yrs: N = 452, 42% 17% 29% 4%
  - > 60 yrs: N = 136, 21% 15% 31% 6%

- Controls:
  - ≤ 40 yrs: N = 1626, 90% 9% 0.5%
  - 41 to 50 yrs: N = 5172, 80% 23% 1.9%
  - 51 to 60 yrs: N = 1356, 65% 15% 6.6%
  - > 60 yrs: N = 408, 42% 15% 18.7%

Pp prevalence:
- Cases: 3.9% 9.0% 20.0% 46.9%
- Controls: 0.5% 1.9% 6.6% 18.7%

Legend:
- No age-related diseases
- 1 comorbidity
- 2 comorbidities
- 3 comorbidities
- 4 comorbidities
MR. C

- 71 years old
- Diagnosed with HIV in 1998 at the age of 54 when he developed PCP pneumonia
  - Other AIDS defining illnesses: Kaposi sarcoma
  - He has been on multiple anti-retroviral regimens
  - Well-controlled with viral suppression since 2014
- Medications include:
  - Lisinopril 2.5
  - Metoprolol 25
  - Pravastatin 80
  - ASA 81
  - Ranitidine 150
  - Abacavir-lamivudine 600-300
  - Raltegravir 400 BID
# CARDIOVASCULAR DISEASE

## 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><strong>Uninfected</strong></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><strong>HIV Infected</strong></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>
</tbody>
</table>

- **Uninfected**
- **HIV Infected**

Abbreviations: AMI, acute myocardial infarction; HIV, human immunodeficiency virus.

*An ellipsis indicates that a rate was not calculated because there were 0 events.*
CARDIOVASCULAR DISEASE

• CVD mortality rates have decreased approximately 50% over the last decade
• Despite this, in patients with virologic suppression, there continues to be a 53% higher rate of CVD mortality in HIV infected patients
CARDIOVASCULAR DISEASE

- Subclinical atherosclerosis
- LV dysfunction
- Chronic inflammation
- Sepsis
- Cocaine

CVD

- HIV Medications
  - Abacavir
  - Zidovudine/stavudine
  - Older PIs
  - Tenofovir

- Other diseases
- Traditional CVD Risk Factors

TRADITIONAL CVD RISK FACTORS

Traditional risk factors for coronary artery disease:

- Age (men ≥ 45 years, women ≥ 55 years)
- High LDL cholesterol (> 160 mg/dL)
- Low HDL cholesterol (< 40 mg/dL)
- Hypertension
- Family history of premature coronary artery disease (CAD)
- Diabetes mellitus (DM)
- Cigarette smoking
MANAGEMENT OF CVD RISK FACTORS

**Diabetes Mellitus**
- Goal A1c < 6.5
- Nonpharmacologic management:
  - Weight reduction
  - Increase physical activity
- Initial pharmacologic management:
  - Metformin
  - Sulfonylureas

**Cigarette Smoking**
- Encourage smoking cessation at every visit
- Offer combination approach including behavioral therapy and pharmacologic options
  - Nicotine replacement
  - Bupropion
  - Varenicline
MANAGEMENT OF CVD RISK FACTORS

Hypertension

- Goal <140/90
- Nonpharmacologic management:
  - Weight reduction
  - Increase physical activity
  - Sodium restriction
- Initial pharmacologic management:
  - Thiazide diuretic
  - ACE inhibitor
  - Calcium channel blocker

Hyperlipidemia

- Goal Total chol < 200
- Goal LDL < 130
- Goal HDL > 50
- Perform cardiovascular risk assessment to determine which patients would benefit from lipid lowering therapy**
CARDIOVASCULAR RISK ASSESSMENT

Risk Assessment Tool for Estimating Your 10-year Risk of Having a Heart Attack

The risk assessment tool below uses information from the Framingham Heart Study to predict the patient’s chance of having a heart attack in the next 10 years. This tool is designed for adults aged 20 and older who do not have heart disease or diabetes. To find your risk score, enter your information in the calculator below.

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Male</th>
<th>Female</th>
<th>Total Cholesterol (mg/dL)</th>
<th>HDL Cholesterol (mg/dL)</th>
<th>Systolic Blood Pressure (mmHg)</th>
<th>Current on any medication to treat high blood pressure</th>
</tr>
</thead>
</table>

[Calculate Your 10-Year Risk]

The American Heart Association and the American College of Cardiology are excited to provide a series of new cardiovascular prevention guidelines for the assessment of cardiovascular risk. Lifestyle modifications that reduce risk, management of elevated blood cholesterol, and management of increased body weight in adults. To support the implementation of these guidelines, the new Pooled Cohort Equations CV Risk Calculator and additional Prevention Guideline Tools are available below. Others may be developed and available in the near future.
MANAGEMENT OF CVD RISK FACTORS

• **Routine screening:**
  • Blood pressure check, annually and more frequently as indicated
  • Lipids, creatinine, A1c/glucose every 6-12 months

• **Medication considerations:**
  • Minimize abacavir use in patients with known cardiovascular disease or risk factors for CVD
  • Discontinue older PIs and NRTIs which may increase risk of lipodystrophy, insulin resistance and hyperlipidemia
PREMATURE BONE LOSS

38 % higher risk of fragility fractures in HIV infected patients
PREMATURE BONE LOSS

Bone loss

- HIV infection
- Medications
- Tobacco use
- Immobility
- Organ dysfunction
- Chronic renal disease
- Hypogonadism
- Hyperparathyroidism
- Hyperthyroidism
- Tenofovir
- Protease inhibitors
- Older NRTIs
Recommendations for bone densitometry screening by IDSA/HIVMA:
• Perform in postmenopausal women and in men over the age of 50

FRAX: WHO Fracture Risk Assessment Tool
• Evaluates 10 year probability of hip fracture and major osteoporotic fracture for untreated patients aged 40-90
• Uses clinical risk factors and femoral neck BMD
SCREENING FOR PREMATURE BONE LOSS

Calculation Tool

Please answer the questions below to calculate the ten year probability of fracture with BMD.

Country: US (Caucasian)  Name/ID:  About the risk factors

Questionnaire:
1. Age (between 40 and 90 years) or Date of Birth
   Age:  Date of Birth:  
   Y:  M:  D:  
2. Sex  Male  Female
3. Weight (kg)  
4. Height (cm)  
5. Previous Fracture  No  Yes
6. Parent Fractured Hip  No  Yes
7. Current Smoking  No  Yes
8. Glucocorticoids  No  Yes
10. Secondary osteoporosis  No  Yes
11. Alcohol 3 or more units/day  No  Yes
12. Femoral neck BMD (g/cm²)  
   Select BMD:  

Weight Conversion
Pounds  kg  

Height Conversion
Inches  cm  

http://www.shef.ac.uk/FRAX/
SCREENING FOR PREMATURE BONE LOSS

HIV-uninfected
(N=17,387)

HIV-infected
(N=7064)

HIV-infected
with HIV as cause of secondary osteoporosis

O/E=1.29
(95% CI: 1.19, 1.40)

O/E=1.62
(95% CI: 1.45, 1.81)

O/E=1.20
(95% CI: 1.08, 1.34)

J Acquir Immune Defic Syndr 2016 [Epub ahead of print]
SCREENING FOR PREMATURE BONE LOSS

• Perform DEXA scan in all post menopausal women and men >50
• When performing FRAX assessment, consider including HIV as secondary cause of osteoporosis
• Encourage regular exercise and smoking cessation
• Calcium and vitamin D for high-risk patients
NON-AIDS DEFINING MALIGNANCY

• Decreased rate of AIDS defining cancers
  • Kaposi sarcoma
  • Non-Hodgkins lymphoma

• Increasing rate of non-AIDS defining cancers
  • Anal
  • Prostate
  • Cervical
  • Liver
  • Colorectal
  • Hogkin lymphoma
  • Lung

Top Antivir Med 2014;22(3):660-665
NON-AIDS DEFINING MALIGNANCY

Figure 2. Observed and expected cases of cancer, by age, in the HIV-infected and general populations in the United States, 1996-2007. Expected cases in the general population are modeled to match the age distribution of the HIV-infected population. Adapted from [source].
NON-AIDS DEFINING MALIGNANCY

- Improved survival
- HIV infection
- Viruses (EBV, HPV, HBV)
- NADC
- Increased immune activation
- High smoking rates
- Immunosenescence
- Activation of oncogenes
CANCER SCREENING

- **Biannual mammography** in women aged 50 to 74 years; individualize for younger ages
- **Colonoscopy every 10 years** starting at age 50; earlier and more often if history of polyps or inflammatory bowel disease
- Prostate Cancer: Consider **annual digital exam** in males aged 50 to 74 years; prostate-specific antigen (PSA) testing is no longer recommended in most patients
- **Pap smear annually**: may consider less frequent pap smears if HPV co-testing is negative
- **Annual anal pap smear** in men who have sex with men; every 6 months if abnormalities have been identified previously
- **Lung cancer screening** recommended in smokers over the age of 55 with a 30+ pack-year smoking history, or who have quit within 15 years. However, high rate of false positives and incidental findings in HIV population
IMMUNIZATIONS

- Avoid live vaccine preparations
  - Pneumococcal
    - PCV13 followed by PPSV23 at least 8 weeks later with second PPSV23 5 years later
    - If previous PPSV23, wait to give PCV13 for at least one year
  - Influenza
    - Not live intranasal
  - Varicella
    - If CD4 >200
  - Zoster ?
<table>
<thead>
<tr>
<th>Intervention</th>
<th>Recommendation</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood pressure check</td>
<td>Perform annually in all patients</td>
<td>Inspect for anal warts, malignancy, prostate abnormalities in men</td>
</tr>
<tr>
<td>Digital rectal exam</td>
<td>Consider annually in all patients</td>
<td>Exam with tonometry is advised every 2-3 y in all patients ≥50 y</td>
</tr>
<tr>
<td>Ophthalmologic exam</td>
<td>Perform dilated exam every 6–12 mo in patients with a CD4 count &lt;50 cells/µL</td>
<td>Use conventional mental health interview or standardized test</td>
</tr>
<tr>
<td>Depression screening</td>
<td>Perform annually in all patients</td>
<td>Consider testing 1–3 mo after starting or modifying antiretroviral therapy. HbA1c may be used for screening. Consider threshold cutoff of 5.8%. HbA1c level should be performed every 6 mo in patients with diabetes mellitus</td>
</tr>
<tr>
<td>Fasting glucose and/or HbA1c</td>
<td>Perform every 6–12 mo in all patients</td>
<td>Consider testing 1–3 mo after starting or modifying antiretroviral therapy. More frequent testing may be indicated in patients at high risk for STDs</td>
</tr>
<tr>
<td>Fasting lipid profile</td>
<td>Perform every 6–12 mo in all patients</td>
<td>More frequent testing may be indicated in patients at high risk for STDs. Repeat testing 3 mo later if positive</td>
</tr>
<tr>
<td>Syphilis serology</td>
<td>Perform annually in patients at risk for STDs</td>
<td>More frequent testing may be indicated in patients at high risk, especially if increase in serum transaminases</td>
</tr>
<tr>
<td>Gonorrhea and chlamydia testing</td>
<td>Perform annually in patients at risk for STDs (see text for details)</td>
<td>Repeat testing 3 mo later if positive</td>
</tr>
<tr>
<td>Hepatitis C testing</td>
<td>Perform annually in patients at risk, eg, injection drug users and MSM</td>
<td>No need to repeat in patients with prior positive TST; additional tuberculosis testing may be indicated depending on potential exposure</td>
</tr>
<tr>
<td>Trichomoniasis</td>
<td>Perform annually in all women</td>
<td>More frequent testing is indicated in patients with a history of adenomatous polyps; testing at an earlier age may be advised in patients with a strong family history of colon cancer</td>
</tr>
<tr>
<td>TST or IGRA</td>
<td>Perform at baseline and annually in patients at risk for tuberculosis</td>
<td>Some authorities advise initiation of screening starting at age 40 y based on an individual risk/benefit assessment</td>
</tr>
<tr>
<td>Colorectal cancer screening</td>
<td>Perform at age 50 y in asymptomatic patients at average risk</td>
<td>Detection of premature bone loss requires periodic monitoring thereafter; risk factors for premature bone loss include white race, small body habitus, sedentary lifestyle, cigarette smoking, alcoholism, phenytoin therapy, corticosteroid therapy, hyperparathyroidism, vitamin D deficiency, thyroid disease, and hypogonadism</td>
</tr>
<tr>
<td>Mammography</td>
<td>Perform annually in all women age ≥50 y</td>
<td>Screening test for abdominal aortic aneurysm</td>
</tr>
<tr>
<td>Cervical Pap smear</td>
<td>Perform annually in all women after 2 normal Pap tests documented during the first year following HIV diagnosis</td>
<td>Issues may include sexual behavior, alcohol and drug counseling, diet, exercise, tobacco use, medication, smoking cessation, and seat belt use.</td>
</tr>
<tr>
<td>Bone densitometry</td>
<td>Perform baseline exam in postmenopausal women and men age ≥50 y</td>
<td></td>
</tr>
<tr>
<td>Abdominal ultrasonography</td>
<td>Perform once in men aged 65–75 y who have ever smoked</td>
<td></td>
</tr>
<tr>
<td>Patient education</td>
<td>Address regularly in all patients</td>
<td></td>
</tr>
</tbody>
</table>
CARING FOR OLDER PATIENTS INFECTED WITH HIV

- >50% of HIV infected patients are over the age 50
- HIV causes chronic immune activation, IL-2 and thymic dysfunction, as well as accelerated aging of T cells
- There is a less robust immunologic response to HIV medications in older patients
- HIV-infected patients accumulate “age-related” diseases at a younger chronological age
- Cardiovascular disease is prevalent in HIV infected patients
  - CAD risk calculators do not account for potential increased risk in this population
- Routine cancer screening is essential in this population
- Premature bone loss can occur as a result of HIV infection and its treatment
  - FRAX scores should include HIV as a secondary osteoporosis risk factor
REFERENCES