Learning Objectives

After attending this presentation, learners will be able to:

- Explain the role of primary care in HIV management
- Describe the general effects of aging on HIV infection
- Manage specific comorbidities in the HIV-infected patient
- Implement relevant healthcare maintenance issues
Increased HIV Screening of Population
Increased Survival of HIV-infected Patients
Increased Number of Patients, Many on Antiretroviral Therapy, Pending HIV Care
Stable or Increased Primary Care Demand
Decreased Number of Medical Residents Pursuing Primary Care
Inadequate Training of Medical Residents in HIV Outpatient Medicine
First Generation of HIV Practitioners Nearing Retirement in Next 10 Years

New HIV Diagnoses by Age
United States, 2015

People Living with HIV by Age
United States, 2014
Primary Care Responsibilities

- Universal HIV screening and prevention
- Antiretroviral therapy* and medication adherence
- Prophylaxis of opportunistic infections
- Management of comorbid conditions
- Immunizations
- Other HIV-related health care maintenance issues
- Age- and sex-related health care maintenance issues

* Involvement may vary depending upon interest and experience of primary care practitioners and availability of HIV specialists

Overview of HIV Care and Treatment in the US


Effects of Aging
Chronic Complications by Age and HIV Status

- Retrospective analysis of HIV-infected outpatients compared to seronegative persons (case-control study) from 2002 through 2009
- Examined cardiovascular disease, hypertension, diabetes mellitus, bone fractures, and renal failure
- Independent predictors of polyopathy (p < 0.001) included older age (OR 1.11), male gender (OR 1.77), CD4 nadir below 200 (OR 4.46), and duration of antiretroviral therapy (OR 1.01)

Distribution of Age-related Comorbidities Stratified by Age

Prevalence of Different Age-related Comorbidities

Comorbidity Trends in HIV-infected Patients
Specific Comorbidities

HIV Infection and Coronary Artery Disease (1)

- Incidence of CAD is relatively low but higher than that in HIV-negative patients matched for age and gender
- Studies have demonstrated an increase in subclinical atherosclerosis (e.g., carotid intima media thickness) and clinical endpoints (e.g., acute myocardial infarction)
- HIV infection is associated with increased soluble and cellular markers of inflammation, endothelial dysfunction, and altered coagulation, all of which have been shown to contribute to cardiovascular disease

HIV Infection and Coronary Artery Disease (2)

- Degree to which HIV infection itself, antiretroviral therapy, and traditional risk factors contribute to increased risk in this population is unknown
- Protease inhibitor class appears to be associated with higher risk of CAD; data regarding abacavir are inconsistent
- Discontinuation of ART is associated with a higher risk of CAD
- High prevalence of traditional risk factors in this population
The Risk of Coronary Artery Disease in HIV-infected Patients

<table>
<thead>
<tr>
<th>Table 1. Rates of AMI by HIV Status and Type Group</th>
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<tbody>
<tr>
<td>Status</td>
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<tr>
<td>----------------------------------------------</td>
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<tr>
<td>HIV-infected</td>
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<tr>
<td>HIV-negative</td>
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<td>HIV-negative, non-CD4 count ≥ 200</td>
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<td>HIV-negative, non-CD4 count &lt; 200</td>
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<tr>
<td>HIV-negative, non-CD4 count 300 - 500</td>
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<tr>
<td>HIV-negative, non-CD4 count 500 - 700</td>
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<tr>
<td>HIV-negative, non-CD4 count ≥ 700</td>
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Hypertension
- Similar approach to that in patients without HIV infection
- Newly redefined:
  - Stage 1 – Systolic 130-139 mmHg or diastolic 80-89 mmHg
  - Stage 2 – Systolic ≥140 mmHg or diastolic ≥ 90 mmHg
- In the absence of history or physical exam pointing to secondary hypertension, baseline evaluation should include renal function, potassium, urinalysis, and electrocardiogram
- Nonpharmacologic management consists of modest salt restriction, increased physical activity, and weight reduction
- Initial drug therapy should consist of thiazide diuretic, ACE inhibitor or receptor blocker, or calcium channel blocker in most patients
- For those who are more than 20/10 mmHg above goal, ACE inhibitor or receptor blocker plus calcium channel blocker is recommended
- No important ART interactions for commonly used drugs

Diabetes Mellitus
- HIV infection probably increases risk of DM (BMJ Open Diabetes Res Care http://dx.doi.org/10.1136/bmjdrc-2016-000304)
- Similar approach to that in patients without HIV infection
- Diagnosis is often based upon fasting glucose ≥ 126 mg/dl or HgbA1c ≥ 6.5%
- Treatment goals include prevention of symptomatic hyperglycemia and vascular complications; HgbA1c target ≤ 7.0%
- Nonpharmacologic management consists of weight reduction through dietary modification and increased physical activity
- Initial drug therapy generally consists of metformin with sulfonylurea (e.g., glibizide) added as the second agent
- Metformin may cause lactic acidemia as do older NRTI drugs
- No other important ART interactions for commonly used drugs
- DM and HIV have particularly detrimental effect on renal function (J Acquir Immune Defic Syndr 2012;60:390)
Cigarette Smoking
- HIV-infected patients are more likely to smoke and less likely to quit compared to general population (Ann Intern Med 2015;162:335-44)
- No evidence that specific smoking cessation approaches are more or less effective
- Management includes behavioral intervention and/or pharmacologic therapy; evidence suggests that combination approach works better than either alone
- Drug options include nicotine replacement (e.g., patch, gum, lozenge), bupropion, and varenicline, which can be used alone or in combination
- No important ART interactions for commonly used drugs

Hyperlipidemia
- Dyslipidemia is common in HIV-infected patients on ART; it may be isolated or seen in combination with other features of LDS
- HIV-infected patients should be evaluated and treated for dyslipidemia in a similar fashion to seronegative persons
- Cardiac risk factor assessment should be considered when designing an initial ART regimen; avoid protease inhibitors (except possibly atazanavir) and abacavir if there are other risks
- Protease inhibitors, particularly ritonavir, increase most statin levels
- Simvastatin and lovastatin are contraindicated with protease inhibitors and cobicistat; pravastatin, atorvastatin, and rosuvastatin can be used as alternatives
- Prudent to start with low dose and to monitor LFTs and CPK on treatment

Premature Bone Loss (1)
- Osteopenia, osteoporosis, and pathological fractures have been described
- Osteopenia is asymptomatic condition
- Osteoporosis may present with fractures of vertebrae, forearms, or hips
- HIV infection itself, TDF, protease inhibitors, alterations in vitamin D metabolism, and lactic acidemia related to older NRTI drugs may be contributing factors to premature bone loss
Premature Bone Loss (2)

- Immobility, cigarette smoking, excessive alcohol use, chronic renal disease, hypogonadism, hyperparathyroidism, hyperthyroidism, and steroid use accentuate bone loss
- Optimal use of bone densitometry as a screening test in this population is uncertain; HIVMA advises baseline in postmenopausal women and men ≥ 50 years of age
- Calcium and vitamin D should be given in high-risk patients; regular exercise and smoking cessation should be advised

Antiretroviral Exposure and Risk of Osteoporotic Fractures

Malignancies

- Observational studies suggest that lung, hepatic, and anal cancers occur at younger age in HIV-infected adults compared to seronegative persons
- Using 15 HIV and cancer registry databases in the US, including 212,055 persons with AIDS, the age of diagnosis of non-AIDS-defining cancers was examined
- Only lung and anal cancers were seen in AIDS patients at younger age (median 50 years old vs. 54; p < 0.001) than expected
**Pulmonary Diseases**

- Veterans Aging Cohort Study consisting of 33,420 HIV-infected patients and 66,840 seronegative controls
- Subjects were matched by age, sex, race, and ethnicity
- Incidence of chronic obstructive pulmonary disease, lung cancer, pulmonary hypertension, and pulmonary fibrosis was significantly higher in the HIV-infected group

Crothers K et al. Am J Respir Crit Care Med 2011;183:388.

**Cognitive Dysfunction**

- Epidemiologic findings suggest that increasing age is risk factor for HIV-associated dementia, although the studies are small
- Longitudinal study comparing 106 HIV-infected patients over 50 years of age to 96 patients between 20-39 years of age showed a three-fold higher risk of dementia on multivariate analysis
- Study adjusted for race, education, depression, substance abuse, ART, CD4 count, and viral load


**Healthcare Maintenance**
Cancer Screening (1)

- Breast Cancer: Biannual mammography in women aged 50 to 74 years; individualize for younger ages
- Cervical Cancer: Annual Pap test in women after 2 normal Pap tests documented; role of HPV testing in HIV-infected patients is unclear
- Colon Cancer: Colonoscopy every 10 years starting at age 50; earlier and more often screening if history of polyps or inflammatory bowel disease
- Prostate Cancer: Discuss the benefits and risks of prostate-specific antigen (PSA) testing in males aged 55 to 69 years and in patients with family history

Adapted from content in "Guidelines for the Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents."
Cancer Screening (2)

- Lung Cancer: Annual screening for lung cancer with low-dose computed tomography in adults aged 55 to 80 years who have a 30 pack-year smoking history and currently smoke or have quit within the past 15 years. Screening should be discontinued once a person has not smoked for 15 years or develops a health problem that substantially limits life expectancy or the ability or willingness to have curative lung surgery.

Infectious Diseases Screening

- Sexually Transmitted Diseases: Annual chlamydia, gonorrhea, and syphilis testing in adults at ongoing risk for STDs
- Tuberculosis: Annual PPD or interferon-gamma testing in adults at ongoing risk for tuberculosis

Cardiovascular Disease

- Hypertension: Regular blood pressure checks
- Abdominal Aortic Aneurysm: One-time ultrasound in men ages 65-75 who ever smoked
- Aspirin Prophylaxis (CVD and colon cancer): Adults aged 50 to 69 years who have a 10% or greater 10-year CVD risk, are not at increased risk for bleeding, and have a life expectancy of at least 10 years
Summary

- There is an increased need for primary care services for HIV-infected patients at the same time that there is potentially decreased capacity to provide them.
- Both generalist and infectious disease practitioners have important contributions to make in providing high quality primary care to this patient population.
- HIV-infected patients may develop "age-related" diseases at a younger chronological age.
- Incidence of coronary artery disease (CAD) is higher than that in HIV-negative patients matched for age and gender.
- CAD risk calculator results need to be interpreted in context of increased risk in the HIV-infected population.
- HIV infection and its treatment and comorbidities are associated with premature bone loss.
- Lung, hepatic, and anal cancers may occur at a younger age in HIV-infected patients.
- Appropriate immunizations and age- and sex-related health care maintenance issues should be routinely addressed as part of comprehensive care.