Overview of Medical Care of the HIV-infected Patient

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Role of Primary Care

- Approximately 50,000 patients are diagnosed with HIV infection annually in the United States, and the number of people living with HIV infection continues to increase.
- Recent guidelines advocate earlier initiation of ART.
- HIV-infected patients are living longer, and some will develop complications of therapy and other comorbid conditions.
- Along with these patients, the first generation of HIV practitioners is maturing, and many will retire over the next 10 years.
- Future primary care practitioners will have substantial responsibility for the care of this patient population.
Increased HIV Screening of Population

Increased Survival of HIV-Infected Patients

Increased Number of Patients, Many on Antiretroviral Therapy, Requiring HIV Care

Aging of Patient Population and Development of Long-Term Treatment Complications and Comorbid Medical Conditions

Need for Increased Primary Care Involvement in HIV Care

Decreased Capacity for Provision of Primary Care to HIV-infected Patients

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
Primary Care Practitioner Responsibilities in HIV Care

- 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 US

[Bar chart showing percentages of diagnosed HIV patients linked to care, remained in care, prescribed antiretroviral therapy, and viral load suppressed.]

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Outline

- Initial Evaluation of New Patient
- General Approach to Care
- Long-Term Complications and Comorbidities
- Immunization Guidelines
- HIV Infection in the Older Patient
History

- Risk behaviors
- Knowledge of HIV infection
- Emotional response
- Family/social situation
- Employment/insurance status
- General health issues
- Syphilis, other STDs, TB, hepatitis
Physical Examination

- Integument: seborrhea, psoriasis, EF, onychomycosis, HSV, VZV, KS, generalized adenopathy
- HEENT: CMV retinitis, CWS, thrush, OHL, ANUG
- Pulmonary: PCP
- Gastrointestinal: organomegaly
- Genitourinary: vaginitis, PID, HPV, cervical and anal dysplasia/carcinoma
- Neurological: mental status, focal central/peripheral findings
Baseline Laboratory Evaluation

- CBC, differential count
- BUN/creatinine, LFTs
- glucose, lipid profile
- CD4 cell count
- HIV viral load
- HIV genotype test
- RPR or VDRL
- hepatitis A, B, and C serologies
- toxoplasmosis serology
- PPD or interferon-gamma test
- Pap smear in women
- Chlamydia and GC tests in persons at risk
- Consider anal Pap smear in persons at risk
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• Initial Evaluation of New Patient
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Stratified Management: CD4 Count > 200

- Initiate ART in all patients after addressing factors that could negatively affect adherence
- Strength of recommendation and evidence supporting it are higher for CD4 count 500-200 than for CD4 count > 500
- Discuss individual and public health benefits
- Address immunizations, health care maintenance, and patient education issues
Stratified Management: CD4 Count < 200

- Initiate ART in all patients after addressing factors that could negatively affect adherence
- Strength of recommendation and evidence supporting it are highest
- Initiate antimicrobial prophylaxis for PCP (<200), toxo (<100 w/ +IgG toxo titer), and MAC (<50) as warranted
- Consider periodic dilated funduscopic exams to screen for CMV infection (<50-100)
- Address immunizations, health care maintenance, and patient education issues
CD4 Cell Count Monitoring

• CD4 count response to antiretroviral therapy varies widely, but a poor response is rarely an indication for modifying regimen

• In patients with suppressed viral loads who are immune reconstituted, the CD4 count provides limited information

• CD4 count testing is recommended at baseline and every 3 to 6 months thereafter

• It may be extended to every 12 months in patients who are clinically stable with a suppressed viral load for \( \geq 2 \) years and is optional for those with CD4 count \( > 500/\text{mm}^3 \) in this setting

DHHS guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents
Viral Load Monitoring

- For most individuals who are adherent to their antiretroviral regimens and who do not harbor resistance mutations to the prescribed drugs, viral suppression is generally achieved in 12 to 24 weeks.
- Viral load testing is recommended at baseline, 2 to 4 weeks after ART initiation, every 4 to 8 weeks until the viral load is suppressed, and every 3 to 4 months thereafter.
- It may be extended to every 6 months in patients with a suppressed viral load for ≥2 years.

DHHS guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents.
Factors Having Negative Impact on Adherence

- Lack of education about HIV infection
- Denial, anxiety, or depression
- Alcohol or drug use
- Poor social situation
- Inadequate health insurance
- Number of medications or pills
- Frequency of dosing
- Stringent dosing requirements
- Presence of adverse effects or long-term complications
- Poor clinician-patient relationship
Priorities at Office Visits

- Acute and recurrent chronic problems
  Diagnosis and treatment
- Opportunistic infection prophylaxis
  Initiation, maintenance, or discontinuation
- Antiretroviral therapy
  Initiation or maintenance
- Health care maintenance issues
  HIV-related immunizations and screening
  Other age- and sex-appropriate screening
- Patient education issues
  HIV infection
  Risk behavior reduction
  Food, pets, travel, other concerns
Evaluation of New Symptoms

- Fever, cough/dyspnea, diarrhea, neurologic complaints, and skin lesions are most common.
- Differential diagnosis broadens in patients with low CD4 count to include opportunistic diseases.
- Likelihood of opportunistic disease increases as CD4 count drops below threshold for condition.
- Algorithmic approaches to diagnosis are available.
- Clinical judgment should be determining factor; it is not necessary to perform diagnostic testing in all patients.
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Long-Term Complications and Comorbidities

- Lipodystrophy syndrome
- Coronary artery disease
- Premature bone loss
- Avascular necrosis of the hips
- Lactic acidemia/acidosis
- Peripheral neuropathy
LDS Clinical Manifestations

- **Lipid metabolism**
  - Increased triglycerides
  - Increased cholesterol, LDL, cholesterol/HDL ratio
  - Decreased HDL

- **Glucose metabolism**
  - Insulin resistance
  - Glucose intolerance
  - Diabetes mellitus

- **Fat accumulation**
  - Increase visceral fat
  - Buffalo hump
  - Lipomatisos
  - Gynecomastia

- **Fat atrophy**
  - Face, extremities, buttocks
Management of Lipodystrophy Syndrome

**Hyperlipidemia, insulin resistance**
- Diet and exercise
- Switch therapy
  - Older PI → ATV or NNRTI
- Statins/fibrates
- Insulin-sensitizing drugs

**Visceral fat accumulation**
- Diet and exercise
- Switch therapy
  - Older PI → NNRTI
  - Growth hormone or GHRF
- Cosmetic surgery

**Subcutaneous fat wasting**
- Switch therapy
  - Older PI → NNRTI
  - Insulin-sensitizing drugs
- Statins/fibrates
- Insulin-sensitizing drugs
- Growth hormone or GHRF
- Local Rx
  - (polylactic acid, calcium hydroxylapatite)
Major Risk Factors for Coronary Artery Disease (CAD)

- Age (men ≥45 years, women ≥55 years)
- High LDL cholesterol (>160 mg/dL) *
- Low HDL cholesterol (<40 mg/dL)
- Hypertension
- Family history of premature CAD
- Diabetes mellitus
- Cigarette smoking

* With CAD, DM, or multiple risk factors, the desirable level for LDL cholesterol decreases; <100 mg/dL is ideal.

The Risk of Coronary Artery Disease in HIV-infected Patients
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.
• 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
We do not know how to incorporate HIV infection and its treatment into cardiac risk calculators.
• Dyslipidemia is common in HIV-infected patients on ART; it may be isolated or seen in combination with other features of lipodystrophy syndrome
• HIV-infected patients should be evaluated and treated for dyslipidemia in a similar fashion to seronegative patients
• 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 CAD risks
• Protease inhibitors, particularly ritonavir, increase most statin levels
• Simvastatin and lovastatin are contraindicated with PIs and cobicistat
• Pravastatin, atorvastatin, and rosuvastatin are generally acceptable alternatives
• It is prudent to start with low dose and to monitor LFTs and CPK on treatment
Hypertriglyceridemia

- It may be beneficial to treat significant hypertriglyceridemia
- Possible indications for treatment of isolated hypertriglyceridemia include overt coronary artery disease, a strong family history of coronary disease, and multiple coexisting cardiac risk factors
- Diet and exercise may be useful for initial management
- Consider fish oil, fenofibrate, or gemfibrozil for treatment of isolated hypertriglyceridemia >500-1000 mg/dl to prevent pancreatitis
- No important ART interactions for commonly used drugs
Premature Bone Loss

- Osteopenia, osteoporosis, and pathological fractures have been described
- Tenofovir, alterations in vitamin D metabolism, and lactic acidemia from NRTI therapy may be responsible for bone loss
- HIV infection itself may also be a contributing factor
- Immobility, cigarette smoking, excessive alcohol use, chronic renal disease, hypogonadism, hyperparathyroidism, hyperthyroidism, and steroid use accentuate bone loss
- Utility of bone densitometry in patients on ART without other risk factors for premature bone loss is uncertain
- 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

Lactic Acidemia/Acidosis

- Symptoms of mild to moderate lactic acidemia include fatigue, anorexia, weight loss, gastrointestinal complaints, and increased liver function tests.

- Although lactic acidemia is common, it has poor predictive value for decompensated lactic acidosis.

- Routine lactate monitoring in the absence of symptoms is unlikely to be helpful.

- However, if symptoms are present and an increased lactate is confirmed, modification of antiretroviral therapy is warranted.
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Immunization Principles in HIV Infection

• Avoid live vaccine preparations, especially in patients with a low CD4 count, unless the benefits clearly outweigh risks

• Vaccines are generally more immunogenic in patients with higher CD4 counts and lower VLs and should be delayed pending immune reconstitution when appropriate

• Immunologic response to vaccine preparations should be assessed when possible in HIV-infected patients

• Limited data on the clinical effectiveness of vaccine preparations in this population
Pneumococcal Vaccine (1)

• Rationale: HIV-infected patients are at increased risk for serious pneumococcal infections, including pneumonia and bacteremia

• May result from altered antibody production leading to decreased opsonization

• There are two types: 1) 23-valent polysaccharide vaccine; 2) 13-valent conjugate vaccine

• Recent revision of the recommendations for immunocompromised persons
Pneumococcal Vaccine (2)

- Pneumococcal vaccine-naïve persons:
  PCV13 first followed by PPSV23 at least 8 weeks later and second PPSV23 dose 5 years later

- Previous vaccination with PPSV23:
  PCV13 at least one year after the last PPSV23 dose; for those who require additional doses of PPSV23, the first should be given no sooner than 8 weeks after PCV13 and at least 5 years after most recent PPSV23 dose
Hepatitis B Vaccine

• Rationale: HIV-infected patients are at increased risk for hepatitis B infection, which is spread in identical fashion but 100-fold easier to transmit; approximately 10% will develop chronic infection

• Recommendation: Administer to patients without evidence of past or present hepatitis B infection; vaccine dose varies with preparation but is given at 0, 1, and 6 months

• Check HBsAb after completing immunization series

• Giving higher dose booster or repeating series should be considered for nonresponders
Hepatitis A Vaccine

- **Rationale:** Many HIV-infected patients (MSMs and IDUs) are at increased risk for hepatitis A because of their behaviors; others (e.g., those with chronic liver disease) are at increased risk of morbidity from the infection.

- **Recommendation:** Administer to patients with above risk behaviors and patients with chronic liver disease; debate as to whether candidates should be screened with anti-HAV; vaccine dose varies with preparation but is given at 0 and 6 months.
Influenza Vaccine

- Rationale: HIV-infected patients appear to be at increased risk for complications of influenza.
- However, there is limited literature on subject.
- Recommendation: Administer inactivated seasonal flu vaccine to all patients; especially important for those at risk for influenza exposure or complications from other underlying conditions.
- Do not use live (intranasal) vaccine preparation.
Human Papillomavirus Vaccine

- Rationale: Many HIV-infected patients are at increased for HPV infection, which is the most common STD in the world; HPV infection confers an increased risk for cervical dysplasia in women and anal dysplasia in MSM.

- Recommendation: Administer to females and males aged 9-26 years at 0, 2, and 6 months; consider in other patients as well.

- Studies in this patient population are ongoing.
Other Vaccine Preparations

- Hemophilus influenza vaccine: Administer to asplenic (anatomically or functionally) patients and those with recurrent hemophilus infection
- Varicella and MMR vaccines: Consider in HIV-infected patients with CD4 count $\geq 200$ who do not have evidence of immunity
- Tetanus toxoid: Every ten years; one-time substitution of Tdap for Td booster is advised
- Zoster vaccine: Contraindicated in patients with CD4 count $< 200$
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HIV Infection in the Older Patient (1)

- Approximately 30% of HIV-infected persons are ≥50 years of age
- Limited data on effects of ART in older persons
- Older persons may be diagnosed later and have more advanced HIV at presentation
- Medication adherence is generally good
HIV Infection in the Older Patient (2)

- HIV-infected patients accumulate “age-related” diseases at younger age
- Neurocognitive disorders and non–AIDS-defining cancers are also more prevalent
- Hypothesis that increased immune activation and long-term chronic inflammation contribute to premature aging in this population
- Independent risk factors include age, male sex, nadir CD4 count below 200/mm3, and ART
Chronic Complications by Age and HIV Status

Summary

• Primary care practitioners have a significant role in the care of HIV-infected patients

• HIV infection lends itself to a standardized approach to initial evaluation, and patient management should be individualized based upon clinical status and CD4 cell count

• Long-term comorbidities associated with HIV infection and its treatment will become increasingly common over time

• Appropriate immunizations and age- and sex-related health care maintenance issues should be incorporated into care

• Understanding the effect of HIV infection on the aging process is important in managing older patients with this disease