Primary Care Guidelines for the Management of Persons Infected With HIV: 2013 Update by the HIV Medicine Association of the Infectious Diseases Society of America

Judith A. Aberg, Joel E. Gallant, Khalil G. Ghanem, Patricia Emmanuel, Barry S. Zingman, and Michael A. Horberg

Evidence-based guidelines for the management of persons infected with human immunodeficiency virus (HIV) were prepared by an expert panel of the HIV Medicine Association of the Infectious Diseases Society of America. These updated guidelines replace those published in 2009. The guidelines are intended for use by healthcare providers who care for HIV-infected patients. Since 2009, new antiretroviral drugs and classes have become available, and the prognosis of persons with HIV infection continues to improve. However, with fewer complications and increased survival, HIV-infected persons are increasingly developing common health problems that also affect the general population. Some of these conditions may be related to HIV infection itself or its treatment. HIV-infected persons should be managed and monitored for all relevant age- and sex-specific health problems. New information based on publications from the period 2009–2013 has been incorporated into this document.

Keywords. HIV; primary care; guidelines; HIV monitoring; HIV metabolic; HIV vaccines; sexually transmitted diseases.

EXECUTIVE SUMMARY

Summary of Changes
These updated guidelines replace those published in 2009 [1]. The following general changes have been made to the document since the previous publication:

- The Grading of Recommendations Assessment, Development and Evaluation (GRADE) system was used in the updating of this guideline. Recommendations are graded as either being strong or weak and the quality of the evidence is graded as high, moderate, low, or very low.
- Recommendations on the optimal way to diagnose HIV have given way to expanded recommendations on the initial evaluation and immediate follow-up for HIV-infected patients. Easy-to-use tables have also been added.
- Recommendations for long-term complications have been removed.
- A new section was added on metabolic comorbidities, replacing the need for separate guidelines on dyslipidemia, which had been previously published [2].
- A more robust section and table on sexually transmitted diseases has been added.

Formatting changes have also been incorporated to help readers easily identify the recommendations.

Summarized below are the recommendations made in the updated guidelines for the management of persons infected with HIV. Each section of the guideline begins with a specific clinical question and is followed by numbered recommendations and a summary
of the most relevant evidence in support of the recommenda-
tions. The Panel followed a process used in the develop-
ment of other IDSA guidelines, which included a systematic
weighting of the strength of recommendation and quality of
evidence using the GRADE system [3–8] (Table 1). A detailed
description of the methods, background, and evidence summaries
that support each of the recommendations can be found in the full
text of the guidelines.

RECOMMENDATIONS FOR THE MANAGEMENT
OF PERSONS INFECTED WITH HIV

I. What initial evaluation and immediate follow-up should be
performed for HIV-infected patients?
Recommendations
1. A comprehensive present and past medical history, physi-
cal examination, medication/social/family history, and
review of systems, including HIV-related information,
should be obtained for all patients upon initiation of care
(strong recommendation, moderate quality evidence).

HIV Disease Tests
Serological Assays for HIV
Recommendation
2. Patients who have no documentation of their HIV seros-
tatus or who were tested anonymously should have an HIV
serologic test performed upon initiation of care (strong rec-
ommendation, low quality evidence).

CD4 Cell Counts and Percentages
Recommendations
3. A CD4 cell count with percentage should be obtained
upon initiation of care (strong recommendation, high quality
evidence).
4. Measurement of the CD8 cell count and the ratio of CD4
cells to CD8 cells is unnecessary as the results are not used in
clinical decision making (strong recommendation, high
quality evidence).

Plasma HIV RNA Levels
Recommendation
5. A quantitative HIV RNA (viral load) level should be ob-
tained upon initiation of care (strong recommendation, high
quality evidence).

HIV Resistance Testing
Recommendations
6. Because drug-resistant virus can be transmitted from one
person to another, all patients should be assessed for trans-
mitted drug resistance with an HIV genotype test upon
initiation of care (strong recommendation, high quality evi-
dence). If therapy is deferred, repeat testing at the time of an-
tiretroviral therapy (ART) initiation should be considered
because of the potential for superinfection (weak recommenda-
tion, low quality evidence).
7. Resistance testing is also indicated for patients who are
experiencing virologic failure to guide modification of ART
(strong recommendation, high quality evidence).
8. In persons failing integrase strand transfer inhibitor
(INSTI)–based regimens, genotypic testing for INSTI resis-
tance should be ordered (strong recommendation, high
quality evidence).

Coreceptor Tropism Assay
Recommendation
9. Tropism testing should be performed if the use of a CCR5
antagonist is being considered (strong recommendation, high
quality evidence).

Laboratory Tests
Complete Blood Count and Chemistry Panel
Recommendation
10. A complete blood count with differential white blood
cell count and chemistry panel should be obtained upon ini-
tiation of care (strong recommendation, high quality evi-
dence).

Glucose-6-Phosphate Dehydrogenase
Recommendation
11. Screening for glucose-6-phosphate dehydrogenase
(G6PD) deficiency is recommended upon entry into care or
before starting therapy with an oxidant drug in patients with
a predisposing racial or ethnic background (strong recom-
mendation, moderate quality evidence).

Fasting Lipid Profile
Recommendation
12. Because many antiretroviral drugs, HIV infection itself,
and host factors are associated with increased cholesterol
and triglyceride levels, a fasting lipid profile should be ob-
tained upon initiation of care (strong recommendation, high
quality evidence).

HLA B*5701 Screening
Recommendations
13. HLA-B*5701 testing should be performed before initiat-
ing abacavir therapy (strong recommendation, high quality
evidence).
14. Patients who are positive for the HLA B*5701 haplotype
are at high risk for hypersensitivity reaction and should not
<table>
<thead>
<tr>
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<th>Title</th>
<th>URL</th>
<th>Issuing Agency</th>
<th>Reference</th>
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<td>Transitioning HIV-Infected Adolescents Into Adult Care, 2011</td>
<td><a href="http://www.hivguidelines.org/clinical-guidelines/adolescents/transitioning-hiv-infected-adolescents-into-adult-care/">http://www.hivguidelines.org/clinical-guidelines/adolescents/transitioning-hiv-infected-adolescents-into-adult-care/</a></td>
<td>New York State Department of Health AIDS Institute</td>
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<td>ART and management guidelines for adults, adolescents, infants, and children</td>
<td>There are &gt;30 guidelines covering a broad range of topics in the prevention, diagnosis, and management of HIV and its associated comorbidities</td>
<td><a href="http://www.hivguidelines.org/clinical-guidelines/">http://www.hivguidelines.org/clinical-guidelines/</a></td>
<td>New York State Department of Health AIDS Institute</td>
<td>[105]</td>
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<td>ART for pediatric patients</td>
<td>Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection</td>
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<td>Diabetes</td>
<td>Standards of Medical Care in Diabetes–2013</td>
<td><a href="http://care.diabetesjournals.org/content/36/Supplement_1/Supplement_1.pdf">http://care.diabetesjournals.org/content/36/Supplement_1/Supplement_1.pdf</a></td>
<td>American Diabetes Association</td>
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<td><a href="http://www.cdc.gov/mmwr/preview/mmwrhtml/mm514a1.htm">http://www.cdc.gov/mmwr/preview/mmwrhtml/mm514a1.htm</a></td>
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<td>Mental health</td>
<td>Mental Health Care for People With HIV Infection: Clinical Guidelines for the Primary Care Practitioner</td>
<td><a href="http://www.hivguidelines.org/clinical-guidelines/">http://www.hivguidelines.org/clinical-guidelines/</a></td>
<td>New York State Department of Health AIDS Institute</td>
<td>[14]</td>
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</tbody>
</table>
be treated with abacavir (strong recommendation, high quality evidence).

**Urinalysis and Calculated Creatinine Clearance Recommendations**

15. A baseline urinalysis and calculated creatinine clearance or estimated glomerular filtration rate should be obtained, especially in black HIV-infected patients and those with advanced disease or comorbid conditions, because of an increased risk of nephropathy (strong recommendation, high quality evidence).

16. Urinalysis and calculated creatinine clearance assay should also be performed prior to initiating drugs such as tenofovir or indinavir that have the potential for nephrotoxicity (strong recommendation, moderate quality evidence).

**Coinfection and Comorbidity Laboratory Tests Tuberculosis Screening Recommendations**

17. Upon initiation of care, HIV-infected patients without a history of tuberculosis or a prior positive tuberculosis screening test should be tested for *Mycobacterium tuberculosis* infection by either a tuberculin skin test (TST) or by an interferon-γ release assay (IGRA) (strong recommendation, high quality evidence). Those with positive test results should be treated for latent *M. tuberculosis* infection after active tuberculosis has been excluded [9, 10] (strong recommendation, high quality evidence).

18. Repeat testing is recommended in patients with advanced HIV disease who initially had negative TST or IGRA results but subsequently experienced an increase in the CD4
Recommendations
Viral Hepatitis Screening and Vaccination Recommendations

22. HIV-infected patients should be screened for evidence of hepatitis B virus (HBV) infection upon initiation of care by detection of hepatitis B surface antigen (HBsAg), hepatitis B surface antibody (HBsAb), and antibody to hepatitis B total core antigen (anti-HBc or HbcAb) (strong recommendation, high quality evidence), and those who are susceptible to infection should be vaccinated against HBV (strong recommendation, high quality evidence). HBsAb should be repeated 1–2 months or at the next scheduled visit after the third vaccine was given to assess for immunogenicity. A second series of vaccine is recommended for those whose HBsAb levels are negative or <10 IU/mL after primary vaccine series (strong recommendation, high quality evidence).

23. Vaccination should be recommended for nonimmune sexual partners of patients who are positive for HBsAg (strong recommendation, high quality evidence).

24. Patients who are negative for HBsAg and HBsAb but positive for anti-HBc should be screened for chronic HBV infection by determination of HBV DNA; those without evidence of chronic infection should consider vaccination (strong recommendation, low quality evidence).

25. HIV-infected patients should be screened for hepatitis C virus (HCV) infection upon initiation of care by a test for HCV antibody and annually thereafter for those at risk (strong recommendation, high quality evidence).

26. HCV RNA should be ordered on all those with a positive HCV antibody test to assess for active HCV disease (strong recommendation, high quality evidence).

27. Infants born to HBV- and /or HCV-infected women should be tested for HBV and HCV transmission, respectively (strong recommendation, high quality evidence).

28. Hepatitis A vaccination is recommended for all susceptible men who have sex with men (MSM), as well as other susceptible individuals with indications for hepatitis A vaccine (eg, injection drug users, persons with chronic liver disease, travelers to countries with high endemicity, or patients who are infected with hepatitis B and/or C) (strong recommendation, high quality evidence). Hepatitis A total or IgG antibody should be repeated 1–2 months or at the next scheduled visit after the second vaccine to assess for immunogenicity. A repeat vaccine series is recommended in those who remain seronegative (strong recommendation, high quality evidence).

29. Hepatitis A vaccine may be considered for all other nonimmune patients (negative anti-HAV total or IgG antibody) (weak recommendation, low quality evidence).

Serologic Testing for Toxoplasma gondii
Recommendations

20. All HIV-infected patients should be tested for prior exposure to T. gondii by measuring anti-Toxoplasma IgG upon initiation of care (strong recommendation, moderate quality evidence).

21. Toxoplasma-seronegative adults, representing 70%–90% of the US population, should be counseled on how to avoid new infection (weak recommendation, moderate quality evidence).

Screening and Vaccination Recommendations for Herpes Viruses
Recommendations

30. Patients at lower risk of cytomegalovirus (CMV) infection (eg, populations other than MSM or injection drug users, both of which may be assumed to be seropositive) should be tested for latent CMV infection with an anti-CMV IgG upon initiation of care (strong recommendation, moderate quality evidence).

31. Patients who are susceptible to varicella zoster virus (VZV) (those who have not been vaccinated, have no history of varicella or herpes zoster, or are seronegative for VZV) should receive postexposure prophylaxis with varicella zoster immune globulin (VariZIG) as soon as possible (but within 10 days) after exposure to a person with varicella or shingles (strong recommendation, moderate quality evidence).

32. Varicella primary vaccination may be considered in HIV-infected, VZV-seronegative persons aged >8 years with CD4 cell counts >200 cells/µL (moderate recommendation, low quality evidence) and in HIV-infected children aged 1–8 years with CD4 cell percentages >15% (strong recommendation, moderate quality evidence).

Screening for Syphilis
Recommendations

33. All patients should be screened for syphilis upon initiation of care and periodically thereafter, depending on risk (strong recommendation, high quality evidence).

34. A lumbar puncture should always be performed for patients with a reactive syphilis serology who have neurologic or ocular symptoms or signs, irrespective of past syphilis treatment history (strong recommendation, high quality evidence).
35. A lumbar puncture should be performed in patients who experience serologic treatment failure (ie, whose nontreponemal titers fail to decline 4-fold after stage-appropriate therapy, or whose titers increase 4-fold if reinfection is ruled out) (weak recommendation, low quality evidence).

Screening for Other Sexually Transmitted Diseases (Refer to Section II for Information on Routine Sexually Transmitted Disease Screening)

Recommendation
36. All women should be screened for trichomoniiasis, and all women aged ≤25 years should be screened for Chlamydia trachomatis infection (strong recommendation, high quality evidence).
37. Men and women should be screened for gonorrhea and chlamydia infection at initial presentation and then annually if at risk for infection (strong recommendation, high quality evidence).
38. Retesting in 3 months is indicated in men and women found to be positive for gonorrhea and chlamydial infections and women found to be positive for trichomoniiasis on initial screening, because of high reinfection rates (strong recommendation, moderate quality evidence).
39. All of these conditions should be screened for periodically thereafter, depending on the population, reported behaviors, the presence of other sexually transmitted diseases (STDs) in the patient or his/her partner(s), and the prevalence of STDs in the community (strong recommendation, low quality evidence).

Cervical Cancer Screening and Prevention

Recommendations
40. HIV-infected women should have a cervical Pap test performed upon initiation of care, and this test should be repeated at 6 months and annually thereafter if results are normal (strong recommendation, moderate quality evidence).
41. Women with atypical squamous cells (both ASC-US [atypical squamous cells of unknown significance] and ASC-H [ASC, cannot rule out high-grade squamous intraepithelial lesion]), atypical glandular cells, low-grade or high-grade squamous intraepithelial lesion, or squamous carcinoma noted by Pap testing should undergo colposcopy and directed biopsy, with further treatment as indicated by results of evaluation (strong recommendation, high quality evidence).

Screening for Anal Human Papillomavirus

Recommendation
42. HIV-infected men and women with human papillomavirus (HPV) infection are at increased risk for anal dysplasia and cancer. MSM, women with a history of receptive anal intercourse or abnormal cervical Pap test results, and all HIV-infected persons with genital warts should have anal Pap tests (weak recommendation, moderate quality evidence).
43. HPV vaccination is recommended for all females aged 9–26 years and all males aged 9–21 years. Males aged 22–26 years should also be vaccinated if not vaccinated at younger ages (strong recommendation, high quality evidence).

Serum Testosterone Level

Recommendation
44. Morning serum testosterone levels are recommended in adult men with decreased libido, erectile dysfunction, reduced bone mass or low trauma fractures, hot flashes, or sweats, and should be considered in the setting of less specific symptoms such as fatigue and depression (strong recommendation, moderate quality evidence).
45. Obtaining testosterone levels in women in nonresearch settings is not recommended (strong recommendation, low quality evidence).

Chest Radiography

Recommendation
46. A baseline chest radiograph should be obtained in all HIV-infected patients with a positive tuberculosis screening test result to rule out active tuberculosis; it may also be useful in other patients who are likely to have preexisting lung abnormalities (strong recommendation, moderate quality evidence).

Other Laboratory Tests

Recommendation
47. Routine testing for cryptococcal infection with serum cryptococcal antigen or for disseminated Mycobacterium avium complex infection by culture of blood for acid-fast bacilli are not recommended, but may be considered in selected patients with CD4 cell counts <50 cells/µL (strong recommendation, moderate quality evidence).

Behavioral Intervention

Recommendations
48. General messages regarding risk reduction should be provided at all healthcare encounters, regardless of risk behaviors reported by the patient or perceived risk on the part of the healthcare provider. Such messages can be delivered by the provider, by others in the healthcare setting, or by educational materials (eg, pamphlets, posters, and videos) in the healthcare setting (strong recommendation, low quality evidence).
49. Tailored messages are critical for patients who report persistent high-risk behavior or who have symptoms or signs of STDs. In nearly all situations, the provider should
offer brief counseling; in general, persons exhibiting risk behavior should also be referred to programs capable of offering more extensive intervention programs (strong recommendation, moderate quality evidence).

Schedule-of-Care Evaluation for HIV-Infected Patients

Adults

Recommendations

50. Viral load is generally monitored every 3–4 months in untreated patients and patients on stable ART. This interval may be prolonged to 6 months for adherent patients whose viral load has been suppressed for more than 2–3 years and whose clinical and immunologic status is stable. Viral load should be monitored more frequently after initiation or change in ART: preferably within 2–4 weeks, and not more than 8 weeks, after initiation or modification, with repeat testing every 4–8 weeks until viral load becomes undetectable (strong recommendation, moderate quality evidence).

51. CD4 cell counts should be monitored both to assess the urgency for initiation of ART or the efficacy of ART and to determine the need for prophylaxis against opportunistic infections (strong recommendation, high quality evidence). CD4 cell counts should generally be monitored every 3–4 months. For patients on suppressive ART regimens whose CD4 counts have increased well above the threshold for opportunistic infection risk, the CD4 count can be monitored every 6–12 months unless there are changes in the patient’s clinical status [11] (strong recommendation, moderate quality evidence).

52. STD screening and tuberculosis screening tests should be repeated periodically depending on symptoms and signs, behavioral risk, and possible exposures (strong recommendation, moderate quality evidence).

53. Vaccinations for pneumococcal infection (strong recommendation, high quality evidence), influenza (strong recommendation, high quality evidence), varicella (strong recommendation, moderate quality evidence), and hepatitis A (strong recommendation, high quality evidence) and B (strong recommendation, high quality evidence) should be offered as indicated (Table 2). The likelihood of a response to any vaccine is greatest in patients with higher CD4 cell counts and in patients receiving suppressive ART.

II. What are the special considerations for women and the prevention of mother-to-child transmission?

Contraception and Preconception Care

Recommendation

54. All HIV-infected women of childbearing age should be asked about their plans and desires regarding pregnancy upon initiation of care and routinely thereafter (strong recommendation, low quality evidence).

Breast Cancer Screening

Recommendations

55. Mammography should be performed annually in women aged >50 years (strong recommendation, high quality evidence).

56. In women aged 40–49 years, providers should perform individualized assessment of risk for breast cancer and inform them of the potential benefits and risks of screening mammography (strong recommendation, high quality evidence).

Menopause

Recommendations

57. Hormone replacement therapy, particularly if prolonged, has been associated with a small increased risk of breast cancer and cardiovascular and thromboembolic morbidity, and its routine use is not currently recommended (strong recommendation, high quality evidence).

58. Hormone replacement therapy may be considered in women who experience severe menopausal symptoms (e.g., vasomotor symptoms and vaginal dryness) but should generally be used only for a limited period of time and at the lowest effective doses (weak recommendation, low quality evidence).

Mother-to-Child Transmission

Recommendations

59. To prevent infection of their fetus, pregnant women should be treated for HIV infection, regardless of their immunologic or virologic status (strong recommendation, high quality evidence).

60. Infants exposed to HIV in utero should receive antiretroviral postexposure prophylaxis and undergo HIV virologic diagnostic testing at 14–21 days of life, at 1–2 months of age, and at 4–6 months of age (strong recommendation, high quality evidence).

61. High-risk exposed infants should have virologic testing at birth (strong recommendation, moderate quality evidence).

III. What are the special considerations for children?

Recommendations

62. HIV-infected infants should undergo HIV resistance testing (strong recommendation, high quality evidence) and, because of the rapid progression of disease, should initiate therapy in the first year of life regardless of CD4 cell count, RNA level, or clinical status (strong recommendation, high quality evidence).

63. After the first year of life, initiation of therapy in HIV-infected children is based on age, CD4 count/percentage, viral load, and symptoms. ART should be initiated in all
symptomatic children (strong recommendation, high quality evidence).

(a) CD4 cell counts and viral loads should be monitored no less than every 3–4 months (strong recommendation, moderate quality evidence).

(b) Childhood vaccinations should be administered according to Advisory Committee on Immunization Practices schedules for HIV-infected infants and children (strong recommendation, high quality evidence).

Table 2. Routine Immunizations for HIV-Infected Adults

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Status</th>
<th>Dose/Regimen</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haemophilus influenzae type B, vaccine</td>
<td>Consider in selected settings; see comments</td>
<td>0.5 mL IM</td>
<td>Administer to asplenic patients</td>
</tr>
<tr>
<td>Hepatitis A vaccine</td>
<td>Recommended in selected settings; see comments</td>
<td>1 mL IM with revaccination in 6–12 mo for Havrix or 6–18 mo for Vaqta; also available in combination with hepatitis B vaccine as Twinrix administered as 3 or 4 doses</td>
<td>HAV vaccination is recommended for all susceptible men who have sex with men, as well as others with indications for HAV vaccine (eg, injection drug users, travelers to countries of high endemicity, persons with chronic liver disease, or who are infected with hepatitis B and/or C). Vaccination can be considered for all nonimmune patients</td>
</tr>
<tr>
<td>Hepatitis B vaccine</td>
<td>Recommended in selected settings; see comments</td>
<td>1 dose of 40 µg/mL (Recombivax HB) administered on a 3-dose schedule or 2 doses of 20 µg/mL (Engerix-B) administered simultaneously on a 4-dose schedule at 0, 1, 2, and 6 mo</td>
<td>Administer to patients without evidence of past or present hepatitis B infection. Vaccinated patients should be tested for HBsAb response 1–2 months or at the next scheduled clinic visit after the third dose</td>
</tr>
<tr>
<td>HPV vaccine</td>
<td>Ideally given prior to sexual activity. Indicated for females age 9–26 and males age 9–26</td>
<td>Gardasil 0.5 mL IM for 3 dose series given at 0, 2, and 6 mo</td>
<td>All patients. Especially important in patients at high risk for exposure to or morbidity from influenza.</td>
</tr>
<tr>
<td>Influenza vaccine</td>
<td>Inactivated influenza vaccine recommended; do not use live attenuated intranasal vaccine (FluMist)</td>
<td>0.5 mL IM annually</td>
<td>For travelers to an area endemic for polio</td>
</tr>
<tr>
<td>Pneumococcal vaccine</td>
<td>Recommended</td>
<td>Should receive a dose of PCV13 (Prevnar 13), followed by a dose of PPV23 (Pneumovax) at least 8 wk later. If previously vaccinated with PPV23, give PCV13 at least 1 y after PPV23.</td>
<td>Administer to patients with CD4 cell count ≥200/µL. A second PPV23 dose is recommended 5 y after the first PPV23 dose</td>
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<tr>
<td>Polio vaccine</td>
<td>OPV contraindicated; IPV should be given if indicated</td>
<td>0.5 mL SC; 3 doses over 6–12 mo for primary immunization</td>
<td>For travelers to an area endemic for polio</td>
</tr>
<tr>
<td>Tetanus toxoid</td>
<td>Same as for patient without HIV infection</td>
<td>Td 0.5 mL IM; Tdap 0.5–0.75 mL IM as per package insert</td>
<td>Substitute 1-time dose of Tdap vaccine at time of next booster, then Td every 10 y. Precautions with pregnancy. Td may be administered after 20 wk gestation or immediately postpartum</td>
</tr>
<tr>
<td>Varicella vaccine (primary)</td>
<td>Consider in selected settings; see comments</td>
<td>0.5 mL IM as 2 doses administered 3 mo apart</td>
<td>Administer to HIV-infected persons with a CD4 count ≥200 cells/µL who do not have evidence of immunity to varicella.</td>
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<tr>
<td>Zoster vaccine</td>
<td></td>
<td>Safety and efficacy in HIV-infected persons unknown; consider in patients &gt;60 y of age with CD4 counts ≥200 cells/µL.</td>
<td>Safety and efficacy in HIV-infected persons unknown; consider in patients &gt;60 y of age with CD4 counts ≥200 cells/µL.</td>
</tr>
</tbody>
</table>

Source: Adapted from the Advisory Committee on Immunization Practices [33].

Abbreviations: HAV, hepatitis A virus; HBsAg, hepatitis B surface antigen; HIV, human immunodeficiency virus; HPV, human papillomavirus; IM, intramuscular; IPV, inactivated polio vaccine; OPV, oral polio vaccine; PCV13, 13-valent pneumococcal conjugate vaccine; PPV23, 23-valent pneumococcal polysaccharide vaccine; SC, subcutaneous; Td, tetanus-diphtheria; Tdap, tetanus-diphtheria-pertussis.

64. HIV-infected infants and children should be managed by a specialist with knowledge of the unique therapeutic, pharmacologic, behavioral, and developmental issues associated with this disease (strong recommendation, low quality evidence).

IV. What are the special considerations for adolescents?

65. HIV-infected adolescents require an individual and developmental approach to therapy and care given by an HIV
It has been more than 30 years since the first case of AIDS was described. There have been dramatic changes in the management of human immunodeficiency virus (HIV) infection since the introduction of highly active antiretroviral therapy (ART) in 1996. There has also been a significant decrease in morbidity and mortality among persons living with HIV infection resulting from improved access to care, prophylaxis against opportunistic infections, antiretroviral therapy (ART), and preventive medicine interventions. A working group of clinicians and clinical scientists was chosen by the HIV Medicine Association (HIVMA) of the Infectious Diseases Society of America (IDSA) to develop guidelines addressing the primary care of HIV-infected persons. The purpose of these guidelines is to assist healthcare providers in their management of HIV-infected persons. Because of the improved survival among people living with HIV infection, it is imperative that in addition to screening for conditions related to HIV infection and its management, all such persons should receive other recommended preventive health interventions as determined on the basis of their age and sex.

It is not our intent to duplicate the extensive guidelines endorsed by the United States Public Health Service, the Department of Health and Human Services (DHHS), the Centers for Disease Control and Prevention (CDC), IDSA, or other accredited organizations. We have referred to these guidelines where applicable, so that this document may also serve as a "guide to the guidelines" (Table 1).

The following clinical questions are addressed in the guideline:

(I) What initial evaluation and immediate follow-up should be performed for HIV-infected patients?
(II) What are the special considerations for women and the prevention of mother-to-child transmission?
(III) What are the special considerations for children?
(IV) What are the special considerations for adolescents?
(V) What are the metabolic comorbidities associated with HIV and antiretroviral therapy?
(VI) How can patient adherence to HIV care be optimized?

PRACTICE GUIDELINES

“Practice guidelines are systematically developed statements to assist practitioners and patients in making decisions about appropriate healthcare for specific clinical circumstances. Attributes of good guidelines include validity, reliability, reproducibility, clinical applicability, clinical flexibility, clarity, multi-disciplinary process, review of evidence, and documentation” [12].

METHODS

Panel Composition
A panel of experts composed of specialists in internal medicine, pediatrics, and infectious diseases prepared these guidelines.

Literature Review and Analysis
For the 2013 update, the Expert Panel completed a review and analysis of literature on the management of persons with HIV published since 2009 and reviewed the older literature as well. Computerized literature searches of PubMed (for articles from
December 2008 through July 2013) were performed. Data published after July 2013 were also considered in the final preparation of the manuscript. Only English-language literature was reviewed.

**Process Overview**

In evaluating the evidence regarding the management of persons with HIV infection, the Panel followed a process used in the development of other IDSA guidelines. The Expert Panel employed the Grades of Recommendation, Assessment, Development and Evaluation (GRADE) method of assigning strength of recommendation and quality of the evidence to each recommendation (Table 3) [4].

**Consensus Development on the Basis of Evidence**

The Panel met on several occasions via teleconference and worked via email communications to complete the work of

<table>
<thead>
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<tr>
<td>Strong recommendation, high-quality evidence</td>
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<tr>
<td>Strong recommendation, moderate quality evidence</td>
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<tr>
<td>Strong recommendation, low-quality evidence</td>
</tr>
<tr>
<td>Strong recommendation, very-low-quality evidence (very rarely applicable)</td>
</tr>
<tr>
<td>Weak recommendation, high-quality evidence</td>
</tr>
<tr>
<td>Weak recommendation, moderate-quality evidence</td>
</tr>
<tr>
<td>Weak recommendation, low-quality evidence</td>
</tr>
<tr>
<td>Weak recommendation, very low-quality evidence</td>
</tr>
</tbody>
</table>

Based on the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system [3–8]. Abbreviation: RCT, randomized controlled trial.
these guidelines. The purpose of the teleconferences was to discuss the questions to be addressed, make writing assignments, and discuss recommendations. All members of the panel participated in the preparation and review of the draft guidelines. Feedback from external peer reviewers was obtained. These guidelines were reviewed and cleared by the IDSA Standards and Practice Guidelines Committee (SPGC) and the boards of the HIVMA and the IDSA prior to dissemination.

Guidelines and Conflict of Interest
All members of the Expert Panel complied with the IDSA policy on conflicts of interest, which requires disclosure of any financial or other interest that might be construed as constituting an actual, potential, or apparent conflict. Members of the Expert Panel were provided with the IDSA’s conflicts of interest disclosure statement and asked to identify ties to companies developing products that might be affected by promulgation of the guidelines. Information was requested regarding employment, consultancies, stock ownership, honoraria, research funding, expert testimony, and membership on company advisory committees. The Panel made decisions on a case-by-case basis as to whether an individual’s role should be limited as a result of a conflict. No limiting conflicts were identified.

Revision Dates
At annual intervals, the Expert Panel chair, the SPGC liaison advisor, and the chair of the SPGC will determine the need for revisions to the guidelines on the basis of an examination of current literature. If necessary, the entire Panel will be reconvened to discuss potential changes. When appropriate, the Panel will recommend revision of the guidelines to the SPGC and will submit revision to the boards of the HIVMA and IDSA for review and approval.

RECOMMENDATIONS FOR THE MANAGEMENT OF PERSONS INFECTED WITH HIV

I. What initial evaluation and immediate follow-up should be performed for HIV-infected patients?

Recommendations

1. A comprehensive present and past medical history, physical examination, medication/social/family history, and review of systems, including HIV-related information, should be obtained for all patients upon initiation of care (strong recommendation, moderate quality evidence).

Evidence Summary

Initial Assessment—History Taking

History of Present Illness

Providers should inquire about the date of diagnosis of HIV infection and, if possible, the approximate date of infection, which can sometimes be determined on the basis of prior negative test results, occurrence of symptoms suggestive of the acute retroviral infection, or timing of high-risk activities. It is critical to obtain a thorough medication history for patients who have already received antiretroviral therapy, preferably through a review of all relevant past medical records. Such a history should include nadir CD4 cell count, highest viral load, drug combinations taken, response to each regimen, including CD4 cell count and viral load, duration of treatment, reasons for treatment changes, drug toxicities, barriers to adherence if any, and prior drug resistance test results. In the course of taking a complete history, the provider can begin to assess the patient’s level of awareness about HIV infection and treatment, to evaluate his or her educational needs, and to determine what other ancillary and social supports might be necessary.

Past Medical and Surgical History

Patients should be asked about any prior HIV-associated complications and comorbidities, including opportunistic infections (OIs), malignancies, and other HIV-related conditions. Providers should inquire about any surgical procedures as well as all chronic medical conditions such as peripheral neuropathy, gastrointestinal disease, chronic viral hepatitis, hyperlipidemia, diabetes mellitus, cardiovascular disease (or risk), or kidney disease that might affect the choice of therapy or response to therapy. Providers should also inquire about prior history of mental illnesses, such as anxiety disorders, bipolar disorder, depression, violent behavior, and history of hospitalization due to mental health disorders. Other past medical conditions that may have implications for HIV-infected patients include a history of chickenpox or shingles; tuberculosis or tuberculosis exposure, including results of prior testing for latent Mycobacterium tuberculosis infection; sexually transmitted diseases (STDs); abnormal cervical or anal cytology; and gynecologic problems. It is important that the history also include questions about where the patient has traveled and lived. For example, patients reporting travel in areas of endemicity for histoplasmosis (Ohio and Mississippi River valleys) or coccidioidomycosis (southwestern deserts) may be at risk for reactivation disease, even after moving to areas in which these infections are not endemic. The status of adult immunizations as detailed in Table 4 should be elicited. A full birth history and review of maternal history and risk factors should be available for all children.

Medications and Allergies

Patients should be asked about all medications they take, including prescription and over-the-counter drugs, methadone, and dietary or herbal supplements, some of which have been shown to interact with antiretroviral drugs (ARVs). Patients should be asked if they have ever used ARVs for pre- or
postexposure prophylaxis or for use of a booster effect for recreational drug use. A discussion of allergies and intolerances should include questions about hypersensitivity reactions to antibiotics and ARVs.

Social and Family Histories
The social history should include a discussion of the use of tobacco, alcohol, and illicit drugs. Patients should be specifically asked whether they misuse prescription drugs as well as any substances (poppers, erectile dysfunction drugs) primarily used with sex. Active injection drug users should be asked about their drug-use practices, the source of their needles, and whether they share needles.

It is critical to obtain a sexual history in an open, nonjudgmental manner, asking about past and current practices. Risk reduction counseling can be introduced during this discussion. Counseling should focus on reduction of risk of HIV transmission to others, “superinfection,” and infection with other sexually transmitted pathogens. Transgendered patients should be co-managed by an expert if the primary care provider is unfamiliar with the complexities of medical and social issues [13]. Patients should also be asked about their partners, sexual practices (including

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Table 4. Initial Assessment: History—Present and Past

<table>
<thead>
<tr>
<th>Past history</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV diagnosis: how, where, when, and why was diagnosis was made</td>
</tr>
<tr>
<td>Duration of infection: dates of prior negative tests and/or diagnosis and/or symptoms of acute retroviral syndrome</td>
</tr>
<tr>
<td>HIV-related conditions: infections, malignancies, or other conditions potentially related to HIV (e.g., thrush, oral hairy cell leukoplakia, herpes zoster, cervical or anal cancer or dysplasia, Pneumocystis pneumonia, or other opportunistic infections, Kaposis sarcoma, lymphoma, neuropathy, anemia, neutropenia, thrombocytopenia [115], and neurocognitive impairment)</td>
</tr>
<tr>
<td>HIV medications: prior use of antiretroviral therapy including prevention for mother-to-child transmission or pre-/postexposure prophylaxis, including specific drugs, duration of therapy, complications or side effects, drug resistance, virologic response, and adherence</td>
</tr>
<tr>
<td>Comorbidities: history of and risk factors for coronary heart disease, dyslipidemia, diabetes mellitus, kidney disease, and osteoporosis</td>
</tr>
<tr>
<td>Psychiatric history: treatment for or symptoms of depression, anxiety, suicidal ideation, or posttraumatic stress disorder: psychiatric hospitalizations</td>
</tr>
<tr>
<td>Sexually transmitted diseases: gonorrhea, chlamydia, pelvic inflammatory disease, chancroid, syphilis, herpes simplex virus, viral hepatitis, HPV, and trichomoniasis, including history and outcome</td>
</tr>
<tr>
<td>Women: gynecologic and obstetric history, plans for future pregnancy, birth control practices, last Pap test, abnormal Pap test ever menstrual history, mammogram (if applicable)</td>
</tr>
<tr>
<td>Pediatric: maternal obstetric and birth history, exposure to perinatal antiretroviral, exposure to infectious diseases, growth and development</td>
</tr>
<tr>
<td>Healthcare maintenance:</td>
</tr>
<tr>
<td>○ Latent tuberculosis: history of tuberculosis or tuberculosis exposure and last screening test for latent tuberculosis, with treatment if applicable</td>
</tr>
<tr>
<td>○ Immunization history: childhood vaccination, dT or Tdap, hepatitis A and B, HPV, influenza meningococcal, pneumococcal, varicella zoster, and travel vaccinations</td>
</tr>
<tr>
<td>○ Last eye exam, including dilated funduscopic exam</td>
</tr>
<tr>
<td>○ Last dental visit</td>
</tr>
<tr>
<td>Past medical history: include any hospitalizations, surgeries, blood product receipt not mentioned above</td>
</tr>
<tr>
<td>Family medical history: diabetes, early heart disease, hypertension, cancer</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Social history</th>
</tr>
</thead>
<tbody>
<tr>
<td>Race and ethnicity</td>
</tr>
<tr>
<td>Sex and sexual identity</td>
</tr>
<tr>
<td>Health-related behaviors: tobacco, alcohol, and drug use</td>
</tr>
<tr>
<td>Patient birthplace, residence, and travel history</td>
</tr>
<tr>
<td>History of receipt of blood products, organ transplant, or semen donation</td>
</tr>
<tr>
<td>Employment history</td>
</tr>
<tr>
<td>Pets, diet, and exercise</td>
</tr>
<tr>
<td>Establish mode(s) of infection:</td>
</tr>
<tr>
<td>○ Sexual contacts (men, women, both), types of activity, condom use</td>
</tr>
<tr>
<td>○ History of injection drug use, shared needles/syringes.</td>
</tr>
<tr>
<td>○ History of transfusion or receipt of blood products, especially during 1975–1985. Artificial insemination by an unidentified donor</td>
</tr>
<tr>
<td>Review specific sexual practices, including exposure sites</td>
</tr>
<tr>
<td>Marital/relationship status, partner’s health and HIV status, and his or her access to healthcare, including HIV testing, and disclosure of HIV status to partner(s)</td>
</tr>
<tr>
<td>Social support and participation in support groups</td>
</tr>
<tr>
<td>For minors, review legal guardianship</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Allergies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dates and types of reactions.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Medications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current medications, including over-the-counter medications</td>
</tr>
<tr>
<td>Use of complementary or alternative therapy or treatment</td>
</tr>
</tbody>
</table>

Abbreviations: HPV, human papillomavirus; HIV, human immunodeficiency virus; dT, diphtheria-tetanus; dTap, tetanus, diphtheria, and pertussis.
all exposure sites, condom and contraceptive use), status of their partners, and whether their partner(s) have been informed of their HIV infection. Laws vary from state to state regarding the obligation of healthcare providers to notify sex partners, and clinicians should be aware of laws in their own jurisdiction.

Patients should also be asked about how they are coping with the diagnosis of HIV infection, whom they have informed of their HIV status, and what support they have been receiving from family and friends. If needed, patients should be offered assistance with the disclosure process. Assessing the stability of the patient’s housing status is critical, as well as work and educational histories, and whether these have been affected by the diagnosis of HIV infection. Other pertinent information includes insurance issues, financial status, marital and family status, and plans for having children. HIV-infected children may not reside with biologic parents, in which case establishing legal guardianship is critical.

**Family Medical History**

Family medical history has become more important now that HIV-infected patients are living longer and are at increased risk for age- and sex-specific conditions in addition to treatment-related complications. Patients should be asked about family history of conditions that might predispose them to malignancies, neurologic diseases, osteoporosis, and atherosclerotic disease (eg, hypertension, diabetes mellitus, hyperlipidemia) and whether there is a family history of early coronary heart disease (ie, myocardial infarction in a first-degree relative before the age of 55 years in male relatives and before the age of 65 years in female relatives).

**Review of Systems**

The review of systems should be comprehensive and include questioning about common HIV-related symptoms, including fever, night sweats, weight loss, visual changes, oral thrush or ulceration, swallowing difficulties, respiratory symptoms, chest pain, nausea, vomiting, abdominal pain, diarrhea, urinary symptoms, skin rashes or lesions, anogenital symptoms, and changes in neurological function or mental status. Patients should be questioned about how their current weight compares with baseline, along with a dietary assessment. For women, a menstrual history should be obtained.

**Depression, Posttraumatic Stress Disorder, and Domestic Violence Screening**

Depression is common among HIV-infected patients, and the review of systems should include questions focusing on changes in mood, libido, sleeping patterns, appetite, concentration, and memory [14]. As part of the initial evaluation and at periodic intervals thereafter, providers should assess the presence of depression, posttraumatic stress disorder, and domestic violence by means of direct questions or validated screening tools. Women with HIV infection have high rates of adult sexual and physical abuse and of childhood sexual abuse. The prevalence of depression among those with HIV infection is twice as high among women, compared with men, and is more prevalent in the setting of violence or victimization.

**Physical Examination**

A complete physical examination should be performed at the initial encounter. Please see Table 5 for particular emphases in the physical examination. In addition to full vital signs (including height and weight), head circumference should be measured in children aged <3 years and plotted against standard growth curves. Furthermore, developmental assessment is important in infants and children. For all patients, the overall body habitus should be assessed, looking for evidence of wasting, obesity, or, in patients who have received ART, evidence of drug-related lipohypertrophy (eg, dorsocervical fat pad, gynecomastia, or visceral abdominal fat accumulation) and/or lipoatrophy (eg, loss of subcutaneous fat in the face, extremities, or buttocks). All adult patients with advanced HIV disease (CD4 cell count <50 cells/µL), as well as infants and young children with profound immunodeficiency, should be referred to an ophthalmologist for a dilated examination. Although persistent generalized lymphadenopathy was historically common among untreated HIV-infected patients, it does not correlate with prognosis or disease progression. However, focal or rapidly progressive lymphadenopathy may require further evaluation, including biopsy. A comprehensive cardiopulmonary examination should be performed, including examination for evidence of peripheral vascular disease. Neurology and/or neuropsychology referral for assessment of neurocognitive disorders, dementia, and focal neuropathies may be indicated [15, 16]. In women, pelvic examination should include visual inspection of the vulva and perineum, bimanual and rectovaginal examination, and speculum examination. For men and women, anorectal examination is important to evaluate for anal warts, other STDs, and anal cancer, with screening for prostate abnormalities in men (as age appropriate).

**Baseline Laboratory Evaluation**

A number of initial laboratory studies are indicated for patients presenting with HIV infection (Table 6). The tests are used for determining HIV disease status, assessing baseline organ function, and screening for coinfections and comorbidities.

**HIV Disease Tests**

**Serological Assays for HIV**

**Recommendation**

2. Patients who have no documentation of their HIV serostatus or who were tested anonymously should have an HIV
serologic test performed upon initiation of care (strong recommendation, low quality evidence).

Evidence Summary
Serologic testing is especially important in patients who are asymptomatic and have a normal CD4 cell count and undetectable or very low viral load. In addition, patients may present to care with misinformation regarding previous test results or may be malingering to obtain other subsidized services that may be available for those infected with HIV. Providers should be familiar with the CDC’s HIV testing algorithms and interpretation of results based on algorithm and assays used [17, 18].

CD4 Cell Counts and Percentages

Recommendations
3. A CD4 cell count with percentage should be obtained upon initiation of care (strong recommendation, high quality evidence).

4. Measurement of the CD8 cell count and the ratio of CD4 cells to CD8 cells is unnecessary as the results are not used in clinical decision making (strong recommendation, high quality evidence).

Evidence Summary
The CD4 cell count is used to stage HIV disease, to help establish the risk of specific HIV-associated complications, to determine the need for prophylaxis against OIs, and to determine the urgency of and response to ART. It is important that the provider and patient be aware of the substantial variation in CD4 cell counts, especially during acute illness. CD4 cell counts may be affected by a variety of medications and intercurrent illnesses, so caution should be applied when interpreting CD4 cell counts during these situations. Although the absolute CD4 cell count is the number most often used in clinical practice, the CD4 cell percentage can also be used to assess immune function and is somewhat less variable than the absolute count. Total CD4 cell counts of 200 and 500 cells/µL generally correspond to CD4 cell percentages of 14% and 29%, respectively. In children aged <5 years, there is more variability in the absolute CD4 count; therefore, CD4 percentage is generally preferred for monitoring immune status [19].

Plasma HIV RNA Levels

Recommendation
5. A quantitative HIV RNA (viral load) level should be obtained upon initiation of care (strong recommendation, high quality evidence).

Evidence Summary
HIV RNA testing is used to assess prognosis, to define a baseline level so that the response to therapy can be measured, and
Table 6. Recommended Initial Laboratory and Other Studies in Patients Presenting With HIV Infection

<table>
<thead>
<tr>
<th>Test</th>
<th>Comment(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV disease specific tests</td>
<td></td>
</tr>
<tr>
<td>HIV serology</td>
<td>If diagnosis not previously confirmed and viral load low or undetectable</td>
</tr>
<tr>
<td>CD4 cell count and percentage</td>
<td>Assess urgency of antiretroviral therapy and need for OI prophylaxis</td>
</tr>
<tr>
<td>Plasma HIV RNA (viral load)</td>
<td></td>
</tr>
<tr>
<td>HIV resistance testing</td>
<td>Genotype preferred for antiretroviral-naive patients or patients not on therapy</td>
</tr>
<tr>
<td>HIV-related tests in selected patients</td>
<td></td>
</tr>
<tr>
<td>Coreceptor tropism assay</td>
<td>If use of CCR5 antagonist being considered</td>
</tr>
<tr>
<td>HLA B*5701</td>
<td>If use of abacavir being considered</td>
</tr>
<tr>
<td>Other laboratory tests</td>
<td></td>
</tr>
<tr>
<td>Complete blood cell count with differential</td>
<td></td>
</tr>
<tr>
<td>Alanine aminotransferase, aspartate</td>
<td>Assess for evidence of liver damage, hepatitis, or systemic infection</td>
</tr>
<tr>
<td>aminotransferase, total bilirubin, alkaline phosphatase</td>
<td>(eg, elevated alkaline phosphatase with some Ols)</td>
</tr>
<tr>
<td>Total protein/albumin</td>
<td>High total protein common with untreated HIV infection due to increased immunoglobulin fraction secondary to B-cell hyperplasia; low albumin may indicate nutritional deficiency or nephrotic syndrome</td>
</tr>
<tr>
<td>Electrolytes, blood urea nitrogen/creatinine</td>
<td>Assess kidney function; use creatinine to calculate estimated GFR. May consider calcium, magnesium, and phosphorous</td>
</tr>
<tr>
<td>Fasting lipid profile and blood glucose</td>
<td>Hemoglobin A1c may be measured</td>
</tr>
<tr>
<td>Urinalysis</td>
<td>Assess for evidence of proteinuria, hematuria</td>
</tr>
<tr>
<td>Coinfection and comorbidity laboratory tests</td>
<td></td>
</tr>
<tr>
<td>CMV screening</td>
<td>Anti-CMV IgG for patients at low risk of CMV infection</td>
</tr>
<tr>
<td>Gonorrhea, chlamydia screening</td>
<td>NAAT testing (preferred) or culture with sites based on exposure history</td>
</tr>
<tr>
<td>Syphilis screening</td>
<td>Using local protocol (either RPR or treponemal-specific antibody tests)</td>
</tr>
<tr>
<td>Screening for latent Toxoplasma gondii infection</td>
<td>Anti-Toxoplasma IgG</td>
</tr>
<tr>
<td>Screening for latent Mycobacterium tuberculosis infection</td>
<td>Tuberculin skin test or IGRA. IGRA preferred if history of BCG vaccination.</td>
</tr>
<tr>
<td>Varicella virus screening</td>
<td>Anti-varicella IgG if no known history of chickenpox or shingles</td>
</tr>
<tr>
<td>Viral hepatitis screening</td>
<td>HBsAg, HBsAb, anti-HBc, HCV antibody, HAV total or IgG antibody, (If HbsAg*, order HBV RNA level; if HCV Ab*, order HCV RNA level and HCV genotype)</td>
</tr>
<tr>
<td>Tests that may be performed under certain circumstances</td>
<td></td>
</tr>
<tr>
<td>Chest radiography</td>
<td>For patients with evidence of latent M. tuberculosis infection. Consider in patients with underlying lung disease for use as comparison in evaluation of future respiratory illness</td>
</tr>
<tr>
<td>Cytology: Pap test</td>
<td>Cervical; anal if indicated. Abnormal results require follow-up with colposcopy and high-resolution anoscopy, respectively</td>
</tr>
<tr>
<td>Glucose-6-phosphate dehydrogenase</td>
<td>Screen for deficiency in appropriate racial or ethnic groups to avoid use of oxidant drugs</td>
</tr>
<tr>
<td>HSV type-specific antibody screening (blood)</td>
<td>HSV-1 and HSV-2 type-specific antibody tests are available (not routinely recommended)</td>
</tr>
<tr>
<td>Serum testosterone level</td>
<td>In males with fatigue, weight loss, loss of libido, erectile dysfunction, or depression or who have evidence of reduced bone mineral density. Morning free testosterone preferred.</td>
</tr>
<tr>
<td>Trichomoniasis screening</td>
<td>In all HIV+ women</td>
</tr>
</tbody>
</table>

Abbreviations: anti-HBc, hepatitis B core antibody; CMV, cytomegalovirus; HAV, hepatitis A virus; HBsAb, hepatitis B surface antibody; HBsAg, hepatitis B surface antigen; HCV, hepatitis C virus; HSV, herpes simplex virus; HIV, human immunodeficiency virus; GFR, glomerular filtration rate; IgG, immunoglobulin G; IGRA, interferon-γ release assay; NAAT, nucleic acid amplification test; OI, opportunistic infection; RPR, rapid plasma reagin.

monitored for maintenance of suppression. Several viral load assays have been approved by the US Food and Drug Administration (FDA) for clinical use. Clinicians should be aware of changes in the type of assay used and the associated variability and the interpretation of results between assays. Thresholds for lower limits of detection for the most commonly used assays range from 20 to 80 copies/mL. Viral load should be measured during the initial evaluation of the untreated patient. HIV viral suppression is defined as a viral load persistently below the level of detection of the assay; however, DHHS guidelines define...
virologic failure as a confirmed viral load >200 copies/mL, allowing for assay variability and occasional blips [20]. The viral load may be transiently increased by vaccinations and intercurrent illnesses.

**HIV Resistance Testing**

**Recommendations**

6. Because drug-resistant virus can be transmitted from one person to another, all patients should be assessed for transmitted drug resistance with an HIV genotype test upon initiation of care (strong recommendation, high quality evidence). If therapy is deferred, repeat testing at the time of ART initiation should be considered because of the potential for superinfection (weak recommendation, low quality evidence).

7. Resistance testing is also indicated for patients who are experiencing virologic failure to guide modification of ART (strong recommendation, high quality evidence).

8. In persons failing integrase strand transfer inhibitor (INSTI)–based regimens, genotypic testing for INSTI resistance should be ordered (strong recommendation, high quality evidence).

**Evidence Summary**

All patients, including infants and children, should be tested for drug resistance at the time of initiation of care, regardless of whether ART will be initiated [19]. This test is especially important in newly infected patients because of the potential for transmitted viral resistance. Patients taking a failing antiretroviral regimen (HIV RNA >200 copies/mL) should undergo resistance testing to guide interventions to improve viral control. In addition, those with prior ART history, detectable viral load, and no prior documentation of resistance results should undergo resistance testing.

Baseline resistance tests are most useful when performed during acute or early infection. With time, resistant mutants may “back-mutate” to wild-type virus and may not be detected by standard genotype assays. However, replacement of mutant virus by wild-type virus can take years, which is why baseline HIV genotype testing is recommended for all patients at the time of HIV diagnosis, regardless of duration of infection and regardless of whether ART will be initiated. In patients with chronic HIV infection, a negative result may underestimate the true extent of resistance, because the resistant virus, although persistent, is present at levels too low for detection by standard resistance assays.

Routine baseline testing for resistance to integrase inhibitors is not currently recommended because of the low frequency of transmitted resistance. However, that may change with the increasing use of integrase inhibitors in clinical practice. Integrase inhibitor genotype assays are currently available, as are combined genotype assays that assess reverse transcriptase, protease, and integrase resistance. Baseline integrase genotypes should be considered in patients who have evidence of transmitted reverse transcriptase or protease mutations, or in patients who may have acquired HIV infection from an individual known to have been taking an integrase inhibitor–based regimen.

**Coreceptor Tropism Assay**

**Recommendation**

9. Tropism testing should be performed if the use of a CCR5 antagonist is being considered (strong recommendation, high quality evidence).

**Evidence Summary**

Coreceptor tropism testing is needed to determine which patients are appropriate candidates for therapy with a CCR5 antagonist [20, 21]. CCR5 antagonists should not be used in patients infected with X4- or dual/mixed-tropic (D/M) virus. Some of the initial safety concerns about the possibility of more rapid progression of disease attributable to selection of X4-tropic virus have been allayed by data demonstrating no decrease in CD4 cell count despite selection of X4 virus when maraviroc was given to patients with D/M virus [22]. However, the use of a CCR5 inhibitor in this population could increase the risk of virologic failure and resistance to the other drugs in the antiretroviral regimen. Tropism screening may fail to detect X4- or D/M virus present at very low levels, and patients may experience treatment failure with CCR5 antagonists because of the presence of preexisting X4 or D/M virus not detected by the tropism assay.

At the present time, tropism testing is recommended for patients who are being considered for treatment with a CCR5 antagonist–containing antiretroviral regimen. Routine tropism testing is not recommended prior to initiation of other regimens because of cost and lack of demonstrated benefit. Patients who exhibit virologic failure while taking a CCR5 antagonist may also be considered for tropism testing.

**Laboratory Tests**

**Complete Blood Count and Chemistry Panel**

**Recommendation**

10. A complete blood count with differential white blood cell count and chemistry panel should be obtained upon initiation of care (strong recommendation, high quality evidence).

**Evidence Summary**

Anemia, leukopenia, and thrombocytopenia are common among HIV-infected persons. The complete blood count is also used to calculate the total CD4 cell count. A chemistry panel is an important tool to assess renal and hepatic function and to look for evidence of preexisting liver injury or hepatitis. A fasting glucose and/or hemoglobin A1c (HbA1c) is recommended to screen for glucose intolerance and diabetes,
especially because of the increased prevalence in this population [23]. In young children, fasting blood studies are more problematic because of feeding schedules, and clinicians may obtain fasting levels when nonfasting levels are abnormal [19]. See Section V for further discussion of glucose abnormalities. The complete blood count and the chemistry panel also provide baseline information that is necessary before the initiation of therapeutic agents that may have myelosuppressive, nephrotoxic, or hepatotoxic effects or those that require dosage adjustment in patients with renal or hepatic dysfunction.

Glucose-6-Phosphate Dehydrogenase

**Recommendation**

11. Screening for glucose-6-phosphate dehydrogenase (G6PD) deficiency is recommended upon entry into care or before starting therapy with an oxidant drug in patients with a predisposing racial or ethnic background (strong recommendation, moderate quality evidence).

**Evidence Summary**

G6PD deficiency is a genetic condition that may result in hemolysis after exposure to oxidant drugs. The drugs most commonly used to treat HIV-infected patients that can lead to hemolysis in the presence of G6PD deficiency are dapsone, primaquine, and sulfonamides. Although there are many variants of G6PD deficiency, the most common variants are GdA−, which is found in 10%–15% of black men and women, and Gdmed, which is found predominantly in men from the Mediterranean, India, and Southeast Asia [24]. The hemolysis associated with Gdmed can be life-threatening, whereas patients with the GdA− variant have milder, more self-limited hemolysis that may not preclude the use of oxidant drugs.

Fasting Lipid Profile

**Recommendation**

12. Because many antiretroviral drugs, HIV infection itself, and host factors are associated with increased cholesterol and triglyceride levels, a fasting lipid profile should be obtained upon initiation of care (strong recommendation, high quality evidence).

**Evidence Summary**

The frequency of follow-up testing and response to therapy should be based on current National Cholesterol Education Program Guidelines [25]. See Section V for further discussion regarding dyslipidemia in HIV-infected patients.

HLA B*5701 Screening

**Recommendations**

13. HLA-B*5701 testing should be performed before initiating abacavir therapy (strong recommendation, high quality evidence).

14. Patients who are positive for the HLA B*5701 haplotype are at high risk for hypersensitivity reaction and should not be treated with abacavir (strong recommendation, high quality evidence).

**Evidence Summary**

Screening for the HLA B*5701 haplotype is recommended in patients being considered for abacavir therapy to identify those who are at high risk for the abacavir hypersensitivity reaction [20]. A negative test result does not rule out the possibility of a hypersensitivity reaction but makes it extremely unlikely. Patients who have negative test results should still be counseled about a hypersensitivity reaction before being treated with abacavir. If HLA B*5701 screening is not available or a patient declines testing, it is reasonable to initiate abacavir with appropriate counseling and monitoring for symptoms or signs of a hypersensitivity reaction [20].

Urinalysis and Calculated Creatinine Clearance

**Recommendations**

15. A baseline urinalysis and calculated creatinine clearance or estimated glomerular filtration rate (GFR) should be obtained, especially in black HIV-infected patients and those with advanced disease or comorbid conditions, because of an increased risk of nephropathy (strong recommendation, high quality evidence).

16. Urinalysis and calculated creatinine clearance assay should also be performed prior to initiating drugs such as tenofovir or indinavir that have the potential for nephrotoxicity (strong recommendation, moderate quality evidence).

**Evidence Summary**

Kidney function is abnormal in up to 30% of HIV-infected patients, and HIV-associated nephropathy is a relatively common cause of end-stage renal disease in black HIV-infected patients [26]. The GFR should be estimated to assist in prescribing antiretroviral agents and other commonly used medications that require renal dosing. Medications should be dosed based on renal function according to their package inserts. Clinicians should be aware that some medications such as cobicistat, dolutegravir, and trimethoprim may effect creatinine secretion and elevate serum creatinine without affecting renal function. In addition, a screening urinalysis for proteinuria should be considered at initiation of care and annually thereafter, especially in patients who are at increased risk for developing kidney disease (eg, black patients, those with CD4 cell count <200 cells/µL or viral load >4000 copies/mL, and those with diabetes mellitus, hypertension, or hepatitis C virus [HCV] coinfection). Patients with proteinuria of grade ≥1+ by dipstick analysis or reduced kidney function should be referred to a nephrologist for consultation and should undergo additional studies, including quantification of proteinuria, renal function. 

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ultrasound, and possible renal biopsy. Biannual monitoring for renal function and urinary abnormalities is warranted for patients receiving tenofovir or indinavir [26].

Coinfection and Comorbidity Laboratory Tests

**Tuberculosis Screening**

**Recommendations**

17. Upon initiation of care, HIV-infected patients without a history of tuberculosis or a prior positive tuberculosis screening test should be tested for M. tuberculosis infection by either a tuberculin skin test (TST) or by an interferon-γ release assay (IGRA) (strong recommendation, high quality evidence). Those with positive test results should be treated for latent M. tuberculosis infection after active tuberculosis has been excluded [9, 10] (strong recommendation, high quality evidence).

18. Repeat testing is recommended in patients with advanced HIV disease who initially had negative TST or IGRA results but subsequently experienced an increase in the CD4 cell count to >200 cells/µL on ART and who may thus have developed sufficient immunocompetence to mount a positive reaction (strong recommendation, high quality evidence).

19. HIV-infected patients who are close contacts of persons with infectious tuberculosis should be treated for latent M. tuberculosis infection regardless of their TST or IGRA results, age, or prior courses of tuberculosis treatment; active tuberculosis should be excluded first (strong recommendation, high quality evidence).

**Evidence Summary**

All HIV-infected patients should be tested for M. tuberculosis infection by TST or IGRA upon initiation of care [10, 20]. For an HIV-infected person, induration of >5 mm by TST is considered to be a positive result and should prompt chest radiography and other evaluation, as warranted, to rule out active tuberculosis [27]. Annual testing should be considered for those who have negative results by TST but are at ongoing risk for exposure [10, 28]. A TST or IGRA should be performed any time there is concern of a recent exposure or after increase of CD4 cell count to >200 cells/µL following initiation of ART. Routine cutaneous anergy testing is not recommended because of lack of standardization of reagents and poor predictive value, and because prophylaxis provided to anergic persons has been shown to prevent few cases of tuberculosis [29]. The QuantiFERON-TB Gold test, the QuantiFERON-TB Gold In-tube test (Cellestis Limited), and the T-SPOT TB test (Oxford Immunotech) are approved by the FDA as aids for detecting latent M. tuberculosis infection. A large meta-analysis suggests that IGRA perform similarly to TST at identifying HIV-infected individuals with latent tuberculosis infection [30]. However, prior vaccination with bacillus Calmette-Guérin (BCG) may result in a positive TST result, whereas there is less cross-reactivity with IGRA. IGRA that are reported as weakly positive should be repeated, as follow-up testing may be negative. The CDC issued updated recommendations in 2010 stating that use of an IGRA was preferred over TST in patients with a history of BCG vaccination and in patients with a low likelihood of returning to have their skin test read. Advanced immunosuppression may be associated with false-negative results in all types of immunologically based tests used for detection of M. tuberculosis infection. The routine use of IGRA assays in children, especially those aged <5 years, is currently not recommended due to limited data and some evidence of lower sensitivity [9].

**Serologic Testing for Toxoplasma gondii**

**Recommendations**

20. All HIV-infected patients should be tested for prior exposure to T. gondii by measuring anti-Toxoplasma IgG upon initiation of care (strong recommendation, moderate quality evidence).

21. Toxoplasma-seronegative adults, representing 70%–90% of the US population, should be counseled on how to avoid new infection (weak recommendation, moderate quality evidence).

**Evidence Summary**

If the anti-Toxoplasma IgG assay result is positive, the patient should be managed according to the published guidelines [10]. Although serologic tests for Toxoplasma can never be used to diagnose or exclude toxoplasmosis, a seronegative patient with a space-occupying lesion of the central nervous system is less likely to have toxoplasmosis than a seropositive patient. HIV-infected pregnant women with a positive Toxoplasma serology result have an increased likelihood of maternal reactivation and congenital transmission. Infants born to women who are seropositive for Toxoplasma should be evaluated for congenital toxoplasmosis [31]. Seronegative patients should be counseled on avoidance of exposure to T. gondii through proper cooking of meat and appropriate precautions with handling of cat litter and gardening. Prophylaxis should be restarted if the CD4 cell count decreases to 100 cells/µL.

**Viral Hepatitis Screening and Vaccination Recommendations**

**Recommendations**

22. HIV-infected patients should be screened for evidence of hepatitis B virus (HBV) infection upon initiation of care by detection of hepatitis B surface antigen (HBsAg), hepatitis B surface antibody (HBsAb), and antibody to hepatitis B total core antigen (anti-HBc or HBcAb) (strong recommendation, high quality evidence), and those who are susceptible to infection should be vaccinated against HBV (strong recommendation, high quality evidence). HBsAb should be
repeated 1–2 months or at the next scheduled visit after the third vaccine was given to assess for immunogenicity. A second series of vaccine is recommended for those whose HBsAb levels are negative or <10 IU/mL after primary vaccine series (strong recommendation, high quality evidence).

23. Vaccination should be recommended for nonimmune sexual partners of patients who are positive for HBsAg (strong recommendation, high quality evidence).

24. Patients who are negative for HBsAg and HBsAb but positive for anti-HBc should be screened for chronic HBV infection by determination of HBV DNA; those without evidence of chronic infection should consider vaccination (strong recommendation, low quality evidence).

25. HIV-infected patients should be screened for HCV infection upon initiation of care by a test for HCV antibody and annually thereafter for those at risk (strong recommendation, high quality evidence).

26. HCV RNA should be ordered on all those with a positive HCV antibody test to assess for active HCV disease (strong recommendation, high quality evidence).

27. Infants born to HBV- and/or HCV-infected women should be tested for HBV and HCV transmission, respectively (strong recommendation, high quality evidence).

28. Hepatitis A vaccination is recommended for all susceptible men who have sex with men (MSM), as well as other susceptible individuals with indications for hepatitis A vaccine (eg, injection drug users, persons with chronic liver disease, travelers to countries with high endemicity, or patients who are infected with hepatitis B and/or C) (strong recommendation, high quality evidence). Hepatitis A total or IgG antibody should be repeated 1–2 months or at the next scheduled visit after the second vaccine to assess for immunogenicity. A repeat vaccine series is recommended in those who remain seronegative (strong recommendation, high quality evidence).

29. Hepatitis A vaccine may be considered for all other nonimmune patients (negative anti–hepatitis A virus [HAV] total or IgG antibody) (weak recommendation, low quality evidence).

Evidence Summary
Screening and prevention of HBV and HAV are critical in the management of HIV. HIV-infected persons who are coinfectected with HBV and/or HCV should be managed according to published guidelines [10, 20, 32].

Prevaccination screening for hepatitis A virus infection is cost-effective when there is a seroprevalence of >30% in the patient population. Some experts recommend a double dose (40 µg) of HBV vaccine, similar to recommendations for other immunocompromised patients [33]. Responses to both HAV and HBV vaccines are reduced in patients with CD4 <200 cells/µL and detectable HIV RNA level. Decisions to delay HAV and HBV vaccination until immunologic and virologic response on ART should be individualized based on potential benefits of vaccine vs the patient’s risk of exposure to HAV and HBV infection. HBV vaccination should be administered to those persons who have a positive anti-HBc with a negative HBsAg and HBsAb and who do not have detectable HBV DNA [34]. Patients who fail to respond to HBV vaccine should be revaccinated with a complete series again with consideration of using the 40-µg dose and after virologic suppression on ART [10].

All infants born to HBsAg-positive women should receive hepatitis B immune globulin and hepatitis B immunization, preferably in the first 12 hours of life. Routine hepatitis A and hepatitis B vaccination is recommended for all infants [31, 35].

HCV RNA should also be measured in HCV-seronegative patients with a history of injection drug use or with unexplained increased serum transaminases, because approximately 6% of HIV/HCV-coinfected persons do not develop HCV antibodies [36]. The rate of mother-to-infant HCV transmission is increased among women who are coinfected with HIV and is estimated to be 3-fold higher, according to multiple studies [37]. Infants can be tested for HCV RNA after 2 months of age or HCV antibody after 18 months of age [31].

Screening and Vaccination Recommendations for Herpes Viruses

Recommendations

30. Patients at lower risk of cytomegalovirus (CMV) infection (eg, populations other than MSM or injection drug users, both of which may be assumed to be seropositive) should be tested for latent CMV infection with an anti-CMV IgG upon initiation of care (strong recommendation, moderate quality evidence).

31. Patients who are susceptible to varicella zoster virus (VZV) (those who have not been vaccinated, have no history of varicella or herpes zoster, or are seronegative for VZV) should receive postexposure prophylaxis with varicella zoster immune globulin (VariZIG) as soon as possible (but within 10 days) after exposure to a person with varicella or shingles (strong recommendation, moderate quality evidence).

32. Varicella primary vaccination may be considered in HIV-infected, VZV-seronegative persons aged >8 years with CD4 cell counts >200 cells/µL (moderate recommendation, low quality evidence) and in HIV-infected children aged 1–8 years with CD4 cell percentages >15% (strong recommendation, moderate quality evidence).

Evidence Summary
Although the seroprevalence of CMV among HIV-infected persons is high, the identification of seronegativity would prompt the use of CMV-negative or leukocyte-reduced blood products when transfusions are needed, thus reducing the risk
of iatrogenic infection [36, 38]. Persons who are seronegative for CMV should be reminded that CMV may be sexually transmitted, providing another reason to practice safer sex. It may also be valuable to determine anti-varicella IgG levels for the minority of patients who are unable to give a history of varicella or shingles. Data on the use of varicella vaccine in HIV-infected adolescents and adults are lacking. However, on the basis of expert opinion, the safety of varicella vaccine in HIV-infected persons aged >8 years with comparable levels of immune function is likely to be similar to that of children aged <8 years [39]. Varicella vaccination may be considered (2 doses of single antigen varicella vaccine, not measles/mumps/rubella/varicella, administered 3 months apart) for HIV-infected persons with a CD4 cell count >200 cells/µL who do not have evidence of immunity to varicella. Persons without evidence of immunity who have no history of varicella or shingles and no history of vaccination against VZV and who are at risk of developing severe disease or complications should receive VariZIG within 10 days after exposure [31, 39, 40]. VariZIG can be obtained only under a treatment Investigational New Drug protocol (contact FFF Enterprises at 1-800-843-7477). VariZIG is not indicated for persons who received 2 doses of varicella vaccine and became immunocompromised later in life [31, 33, 39]. At this time, zoster vaccine for prevention of shingles in HIV-infected adults is not routinely recommended. However, administration of 2 doses of zoster vaccine in HIV-infected adults with CD4 ≥200 cells/µL and complete virologic suppression on ART was shown to be safe, and preliminary data suggest it was immunogenic [41]. Routine screening for HSV is not recommended. Counseling infected persons and their sex partners may help reduce the risk of HSV sexual and perinatal transmission.

Screening for Syphilis

Recommendations

33. All patients should be screened for syphilis upon initiation of care and periodically thereafter, depending on risk (strong recommendation, high quality evidence).

34. A lumbar puncture should always be performed for patients with a reactive syphilis serology who have neurologic or ocular symptoms or signs, irrespective of past syphilis treatment history (strong recommendation, high quality evidence).

35. A lumbar puncture should be performed in patients who experience serologic treatment failure (ie, whose nontreponemal titers fail to decline 4-fold after stage-appropriate therapy, or whose titers increase 4-fold if reinfection is ruled out) (weak recommendation, low quality evidence).

Evidence Summary

Serologic testing for syphilis should be performed at baseline and periodically thereafter, depending on the patient’s risk behavior or the presence of other new STDs [31, 36, 42]. Routine serologic screening for syphilis is recommended at least annually for sexually active HIV-infected persons, with more frequent screening (every 3–6 months) in those with multiple partners, a history of unprotected intercourse, a history of sex in conjunction with illicit drug use, methamphetamine use, or sexual partners who participate in such activities [31, 36, 42].

The traditional approach to syphilis testing has been to start with a nontreponemal test (eg, rapid plasma regain [RPR] or Venereal Disease Research Laboratory [VDRL]) followed by a treponemal test (eg, fluorescent treponemal antibody absorption, microhemagglutination assay for Treponema pallidum, or T. pallidum particle agglutination assay) if the first test is reactive. Many laboratories now use a reverse testing algorithm, initially screening for Treponema-specific antibodies (using an enzyme immunoassay or a chemiluminescent assay), followed by a nontreponemal test titered to endpoint dilution if the initial treponemal test is reactive. Biologic false-positive RPR and VDRL test results are generally of low titer (ie, <1:8). Expert opinion varies on the need for lumbar puncture in neurologically asymptomatic HIV-infected patients with syphilis. There is a higher incidence of cerebrospinal fluid abnormalities among HIV-infected patients when the nontreponemal test result is positive at a high titer (ie, ≥1:32) or when the CD4 cell count is ≤350 cells/µL, regardless of syphilis stage.

Screening for Other STDs (Refer to Section II for Information on Routine STD Screening)

Recommendation

36. All women should be screened for trichomoniasis, and all women aged ≤25 years should be screened for Chlamydia trachomatis infection (strong recommendation, high quality evidence).

37. Men and women should be screened for gonorrhea and chlamydia infection at initial presentation and then annually if at risk for infection (strong recommendation, high quality evidence).

38. Retesting in 3 months is indicated in men and women found to be positive for gonorrhea and chlamydial infections and women found to be positive for trichomoniasis on initial screening, because of high reinfection rates (strong recommendation, moderate quality evidence).

39. All of these conditions should be screened for periodically thereafter, depending on the population, reported behaviors, the presence of other STDs in the patient or his/her partner(s), and the prevalence of STDs in the community (strong recommendation, low quality evidence).

Evidence Summary

Many STDs are asymptomatic. Annual screening for trichomoniasis is recommended for all women. Annual C. trachomatis screening for all women aged ≤25 years, for all sexually active
MSM, and for high-risk women aged >25 years is recommended. Annual screening for gonorrhea is recommended for all sexually active MSM, and targeted screening is recommended for high-risk women (eg, women with previous gonorrhea infection, other STDs, new or multiple sex partners, and inconsistent condom use; those who engage in commercial sex work and drug use; women in certain demographic groups; and those living in communities with a high prevalence of disease). Bimanual examination should be performed to assess for cervical motion, uterine, or adnexal tenderness suggestive of pelvic inflammatory disease. Nucleic acid amplification tests (NAATs) have the highest sensitivity for detecting gonorrhea, chlamydia, and trichomoniasis. Vaginal swabs in women and urine in men are the preferred specimens for genital testing with NAATs. Other specimens (eg, urethral swabs, endocervical swabs) are also appropriate. Anorectal testing for gonorrhea and chlamydia should be performed on the basis of report of receptive anal intercourse. A test for pharyngeal gonorrhea should be considered if the patient reports a history of receptive oral sex. Testing for oropharyngeal chlamydia is not routinely recommended because its prevalence is generally low. NAATs, although not FDA approved or universally available, are preferred for extra genital testing because of enhanced sensitivity. All patients treated for gonorrhea and chlamydia and all women treated for trichomoniasis should be retested 3 months later because short-term reinfection rates are high. Periodic follow-up screening should be considered depending on the patient’s reported risk behaviors. For example, more frequent STD screening (ie, at 3- to 6-month intervals) is indicated for MSM who have multiple or anonymous partners. In addition, MSM who have sex in conjunction with illicit drug use (particularly methamphetamine use) or whose sex partners participate in these activities should be screened more frequently. Whenever a person has received a diagnosis of a specific STD for which there is curative treatment, immediate therapy should be given and their sexual contacts should be evaluated and presumptively treated.

Cervical Cancer Screening and Prevention

Recommendations

40. HIV-infected women should have a cervical Pap test performed upon initiation of care, and this test should be repeated at 6 months and annually thereafter if results are normal (strong recommendation, moderate quality evidence).

41. Women with atypical squamous cells (both ASC-US [atypical squamous cells of undetermined significance] and ASC-H [ASC, cannot rule out high-grade squamous intraepithelial lesion]), atypical glandular cells, low-grade or high-grade squamous intraepithelial lesion, or squamous carcinoma noted by Pap testing should undergo colposcopy and directed biopsy, with further treatment as indicated by results of evaluation (strong recommendation, high quality evidence).

Evidence Summary

Abnormal cervical cytology is 10–11 times more common in HIV-infected women compared with the general female population and is associated with the presence of human papillomavirus (HPV) infection and the degree of immune dysfunction. More frequent Pap tests should be considered in the following circumstances: if there is a previous history of an abnormal Pap test; after treatment for cervical dysplasia; in women with symptomatic HIV infection; and in women with HPV infection. HIV-infected women who have had a hysterectomy, particularly if they have had a history of abnormal cervical cytology before or at the time of the procedure, are at increased risk for squamous intraepithelial lesion on vaginal cytologic testing and should undergo regular screening with Pap tests [43]. Although the appropriate interval for screening has not been established, it is reasonable to follow guidelines similar to those for women who have not undergone a hysterectomy [44]. Pap tests should be reported according to the Bethesda System [45]. The results should include a statement on specimen adequacy and a general categorization (negative for intraepithelial lesion or malignancy, epithelial cell abnormality, or other). Specimens that are reported to be unsatisfactory for evaluation should be obtained again. The presence of epithelial cell abnormalities, including atypical squamous cells, squamous intraepithelial lesion, glandular cell abnormalities, and squamous cell carcinoma, warrants further evaluation. Pap test screening techniques that use liquid-based media appear to increase sensitivity, decrease the number of tests with inadequate sampling, and reduce but not eliminate false-negative results; they also offer the possibility of direct testing for HPV and other STDs on collected specimens. The role of HPV testing as an adjunct to the routine Pap test in HIV-infected women has not been defined. However, recent evidence that the absence of oncogenic HPV is associated with a low incidence of squamous intraepithelial lesions over a 3-year period in HIV-infected women with CD4 cell counts >500 cells/µL, comparable to that described in HIV-seronegative women, suggest that the same cervical cancer screening practices may be appropriate in both groups [46]. Consideration should be given to increasing the screening interval to 3 years if both Pap and HPV testing results are negative, which is now an option for HIV-negative women aged >30 years [47].

Screening for Anal HPV

Recommendation

42. HIV-infected men and women with HPV infection are at increased risk for anal dysplasia and cancer. MSM, women with a history of receptive anal intercourse or
abnormal cervical Pap test results, and all HIV-infected persons with genital warts should have anal Pap tests (weak recommendation, moderate quality evidence).

43. HPV vaccination is recommended for all females aged 9–26 years and all males aged 9–21 years. Males aged 22–26 years should also be vaccinated if not vaccinated at younger ages (strong recommendation, high quality evidence).

Evidence Summary

HIV-infected MSM with HPV infection are at increased risk for anal dysplasia and cancer. HPV-related anal dysplasia is seen at a lower frequency among heterosexual men. If anal cytologic screening (ie, anal Pap smears) is performed and indicates abnormal findings, then high-resolution anoscopy should be performed with biopsy of abnormal areas and appropriate therapy based on biopsy results [10, 14, 48, 49].

HPV PREVENTION

A preventive quadrivalent HPV vaccine is now available and routinely recommended in a 3-dose schedule for all females aged 9–26 years and all males aged 9–21 years. Males aged 22–26 years should also be vaccinated if not vaccinated at younger ages [33]. This preparation is safe and highly effective in preventing infection with the HPV subtypes that are most often found in genital warts and that are responsible for approximately 70% of cervical cancers and most anal cancers. There is no evidence that this vaccine has a therapeutic effect on preexisting cervical or anal dysplasia. One small trial in HIV-infected boys and girls found the vaccine to be safe and immunogenic [50], as did a study in HIV-infected men [51]. Although efficacy data in HIV-infected patients are lacking, the CDC Advisory Committee on Immunization Practices [33] has recommended that vaccination be given to all HIV-infected males and females in a 3-dose series at 11 or 12 years of age, and for those 13–26 years of age if not previously vaccinated.

Serum Testosterone Level

Recommendations

44. Morning serum testosterone levels are recommended in adult men with decreased libido, erectile dysfunction, reduced bone mass or low trauma fractures, hot flashes, or sweats, and should be considered in the setting of less specific symptoms such as fatigue and depression (strong recommendation, moderate quality evidence).

45. Obtaining testosterone levels in women in nonresearch settings is not recommended (strong recommendation, low quality evidence).

Evidence Summary

HIV-infected men, especially those with advanced disease, are at risk for hypogonadism. Interpretation of testosterone values must be made in clinical context, as all currently available assays (including measures of total, free, and bioavailable testosterone) are associated with technical issues that may result in significant variability. Experts are in agreement that testing should be performed on a specimen obtained in the morning (ideally before 10 AM) and should be confirmed with repeat testing if the result is below the lower limit of normal, but differ in their recommendations regarding the optimal assay to use for initial testing in the setting of HIV. Because testosterone circulates primarily bound to plasma proteins (including sex hormone–binding globulin and albumin), if total testosterone is employed for initial testing, a determination of sex hormone binding globulin and/or free testosterone is strongly recommended when alterations of binding proteins are suspected (eg, patients with cirrhosis and hepatitis, hyper- or hypothyroidism, nephrotic syndrome). Free testosterone may be obtained by equilibrium dialysis (most reliable but most expensive), or determined using the free testosterone calculator (available at http://www.issam.ch/freetesto.htm); so-called “direct” free testosterone (analogue) assays are unreliable and should not be used. If a diagnosis of hypogonadism is established, measurement of luteinizing hormone and follicle-stimulating hormone is recommended to determine whether the source of dysfunction is primary (testicular) or central (pituitary or hypothalamic) in origin. Hypogonadism should be treated by clinicians familiar with monitoring patients on androgen replacement therapy.

Chest Radiography

Recommendation

46. A baseline chest radiograph should be obtained in all HIV-infected patients with a positive tuberculosis screening test result to rule out active tuberculosis; it may also be useful in other patients who are likely to have preexisting lung abnormalities (strong recommendation, moderate quality evidence).

Evidence Summary

HIV-infected patients are susceptible to a variety of pulmonary complications. Injection drug users are especially likely to have radiographic abnormalities that may be mistaken for infiltrates. A radiograph obtained at baseline in persons with a history of pulmonary disease may be useful for comparison in the evaluation of future respiratory complaints.

Other Laboratory Tests

Recommendation

47. Routine testing for cryptococcal infection with serum cryptococcal antigen or for disseminated Mycobacterium avium complex (MAC) infection by culture of blood for acid-fast bacilli (AFB) are not recommended, but may be considered in selected patients with CD4 cell counts...
<50 cells/µL (strong recommendation, moderate quality evidence).

Evidence Summary
Specific testing for cryptococcosis or MAC is useful for the diagnosis of infection in patients with advanced immunodeficiency who have suggestive clinical findings. Disseminated MAC disease should be excluded by clinical assessment, which may include blood culture for AFB prior to initiation of prophylaxis with macrolides.

Other tests may be indicated depending on the age and sex of the patient and/or symptoms. Patients with HIV infection may be at higher risk for developing age- and sex-specific malignancies; therefore, preventive medicine screening should be performed at recommended intervals. There are no data supporting the use of inflammatory biomarkers for risk assessment of co-morbidities.

Behavioral Intervention
Recommendations
48. General messages regarding risk reduction should be provided at all healthcare encounters, regardless of risk behaviors reported by the patient or perceived risk on the part of the healthcare provider. Such messages can be delivered by the provider, by others in the healthcare setting, or by educational materials (eg, pamphlets, posters, and videos) in the healthcare setting (strong recommendation, low quality evidence).

49. Tailored messages are critical for patients who report persistent high-risk behavior or who have symptoms or signs of STDs. In nearly all situations, the provider should offer brief counseling; in general, persons exhibiting risk behavior should also be referred to programs capable of offering more extensive intervention programs (strong recommendation, moderate quality evidence).

Evidence Summary
More details concerning behavioral intervention in the healthcare setting, including criteria for referrals and information about making referrals, can be found in the HIV prevention guidelines [36].

Schedule-of-Care Evaluation for HIV-Infected Patients
Adults
Recommendations
50. Viral load is generally monitored every 3–4 months in untreated patients and patients on stable ART. This interval may be prolonged to 6 months for adherent patients whose viral load has been suppressed for more than 2–3 years and whose clinical and immunologic status is stable. Viral load should be monitored more frequently after initiation or change in ART: preferably within 2–4 weeks, and not more than 8 weeks, after initiation or modification, with repeat testing every 4–8 weeks until viral load becomes undetectable (strong recommendation, moderate quality evidence).

51. CD4 cell counts should be monitored both to assess the urgency for initiation of ART or the efficacy of ART and to determine the need for prophylaxis against OIs (strong recommendation, high quality evidence). CD4 cell counts should generally be monitored every 3–4 months. For patients on suppressive ART regimens whose CD4 counts have increased well above the threshold for OI risk, the CD4 count can be monitored every 6–12 months unless there are changes in the patient’s clinical status [11] (strong recommendation, moderate quality evidence).

52. STD screening and tuberculosis screening tests should be repeated periodically depending on symptoms and signs, behavioral risk, and possible exposures (strong recommendation, moderate quality evidence).

53. Vaccinations for pneumococcal infection (strong recommendation, high quality evidence), influenza (strong recommendation, high quality evidence), varicella (strong recommendation, moderate quality evidence), and hepatitis A (strong recommendation, high quality evidence) and B (strong recommendation, high quality evidence) should be offered as indicated (Table 2). The likelihood of a response to any vaccine is greatest in patients with higher CD4 cell counts and in patients receiving suppressive ART.

Evidence Summary
The frequency of evaluation depends in part on the stage of HIV disease and in part on the rate at which it is progressing. Patients may need to be seen more frequently depending on their need for ancillary services, such as treatment adherence counseling, mental health services, HIV education, case management services, harm reduction counseling, and others. Patients who are engaged in care are more likely to remain adherent to their medication and have improved health outcomes. See Tables 2 and 7 for recommendations on routine immunizations and health maintenance evaluation. If an HIV-infected patient is traveling internationally, required vaccinations should be carefully considered before offering routine live virus vaccines [52]. Complete blood count and chemistry panels should be monitored on a regular basis to assess medication toxicity if the patient is given prophylaxis for OIs and/or ART and to monitor potential comorbid conditions (eg, chronic kidney disease or hepatitis). Once ART has been initiated, the response to therapy should be monitored more frequently, preferably every 2–4 weeks (and at least within 8 weeks) until the viral load is below limits of quantification. After the viral load has become undetectable, laboratory tests...
can then be obtained at 3- to 6-month intervals, to monitor for drug toxicity and to assess response to therapy [20]. Patients well controlled on ART for an extended period of time may require less frequent testing (see DHHS guidelines for further details). Serologic testing for viral hepatitis should be repeated if suspected exposure occurs or there are newly elevated transaminase levels in a patient who was not previously immune. Patients with CD4 cell counts <50 cells/µL should undergo regular (every 6–12 months) dilated funduscopic examinations to evaluate for HIV-related complications such as CMV retinitis. All patients should have semiannual oral health examinations and regular screening for depression.

II. What are the special considerations for women and the prevention of mother-to-child transmission?

Women with HIV infection have the same reproductive health needs and concerns as do women without HIV infection. In addition, they may have gynecologic problems that are associated epidemiologically with HIV infection because of common risk behaviors. Certain gynecologic problems may be more common or severe because of HIV-associated immunosuppression. Both the incidence and prevalence of gynecologic problems are high among HIV-infected women throughout their disease course [53].

As part of the initial assessment, a comprehensive gynecologic and obstetrical history should be obtained, including menstrual history, sexual practices, contraception history and current use, male or female condom use and consistency of use, previous STDs and other genital tract infections, prior abnormal Pap test results including subsequent evaluation and treatment, history of gynecologic conditions (eg, uterine fibroids, endometriosis, and infertility) or surgery, and current gynecologic symptoms (eg, abnormal vaginal discharge, abnormal vaginal bleeding, amenorrhea, and pelvic pain).

Contraception and Preconception Care

Recommendation

54. All HIV-infected women of childbearing age should be asked about their plans and desires regarding pregnancy upon initiation of care and routinely thereafter (strong recommendation, low quality evidence).

Evidence Summary

An in-depth discussion about childbearing is indicated if the patient expresses desire for future pregnancy, is not trying to conceive but is not using appropriate contraception, or expresses uncertainty about reproductive plans. The goal is to ensure informed decisions about contraception with prevention of unintended pregnancy and to offer preconception counseling if pregnancy is desired. Patients should explicitly be asked to communicate with their provider if their plans change, when they are ready to consider pregnancy, or when they have questions related to reproduction. In women who are at risk for pregnancy (ie, are trying to conceive or are not using effective and consistent contraception), providers should carefully review all medications and avoid drugs with potential reproductive toxicity. The time of greatest risk to the fetus is early in pregnancy, often before it has been recognized.

Women who do not wish to become pregnant should be advised to use effective contraception. Condom use should be recommended with each sexual act, which provides dual protection against pregnancy, STDs, and potential superinfection with HIV. However, condoms are associated with higher rates of failure than other contraceptive methods, and women should be counseled about the greater effectiveness of using a second method of protection as well. Combined estrogen–progestin hormonal contraceptives (birth control pill, transdermal patch, and vaginal ring) have interactions with several ARVs, which may decrease their effectiveness or increase the risk of adverse effects. Contraindications to combined hormonal methods, such as diabetes mellitus, hyperlipidemia, and chronic liver disease, may be more prevalent among HIV-infected women. The use of intrauterine devices (IUDs) in HIV-infected women remains controversial; they should be avoided in women at increased risk for other STDs. However, in low-risk women, the benefits may outweigh the risks, and a levonorgestrel-releasing IUD may have additional benefits in terms of reduction in menstrual blood loss. Spermicides have been associated with an increased risk of HIV seroconversion and are not recommended for the prevention of HIV transmission or acquisition.

Safer conception for serodiscordant couples starts with treatment of the HIV-infected partner with suppressive ART. Women who desire conception in a serodiscordant couple should be referred to a provider with expertise in this area. The use of home artificial insemination (vaginal insertion of ejaculate with a syringe) effectively avoids risk to an uninfected male partner, with otherwise consistent condom use. When the man is HIV-infected and his female partner is uninfected, the following interventions may reduce risk of transmission: (1) Each partner should be screened and treated for STDs to minimize genital ulcers and genital tract HIV load; (2) semen analysis should be performed to exclude abnormalities that might preclude conception; (3) the male partner should be receiving ART and have an undetectable viral load; (4) preexposure prophylaxis with ARVs may be considered for the woman; and (5) the use of ovulation predictors should be considered to optimize timing of intercourse with unprotected sex limited to when conception is likely to occur. Alternatively, such couples could be referred to centers with assisted reproductive technology.

HIV-infected women should be instructed not to breastfeed, to minimize the risk of viral transmission to their infant.
Breast Cancer Screening

Recommendations

55. Mammography should be performed annually in women aged >50 years (strong recommendation, high quality evidence).
56. In women aged 40–49 years, providers should perform individualized assessment of risk for breast cancer and inform them of the potential benefits and risks of screening mammography (strong recommendation, high quality evidence).

Evidence Summary

Breast cancer is the second leading cause of cancer-related death in women in the United States. It does not appear to be increased in prevalence among women with HIV infection, although unusual clinical presentations and rapid progression have been reported, suggesting that breast cancer may behave more aggressively in this setting [54, 55]. At present, screening mammography for HIV-infected women should follow standard guidelines [56, 57].

Menopause

Recommendations

57. Hormone replacement therapy, particularly if prolonged, has been associated with a small increased risk of breast cancer and cardiovascular and thromboembolic morbidity, and its routine use is not currently recommended (strong recommendation, high quality evidence).
58. Hormone replacement therapy may be considered in women who experience severe menopausal symptoms (eg, vasomotor symptoms and vaginal dryness) but should generally be used only for a limited period of time and at the lowest effective doses (weak recommendation, low quality evidence).

Evidence Summary

It is now common for HIV-infected women to live past natural menopause or to become infected at a later age, and some may undergo surgical menopause. In addition, there is evidence that HIV-infected women may be more likely to undergo premature physiologic menopause. Menopausal women are at increased risk of premature bone loss (osteopenia and osteoporosis), which may be exacerbated by HIV infection and use of ART, and should have bone mineral density screening.

Mother-to-Child Transmission

Recommendations

59. To prevent infection of their fetus, pregnant women should be treated for HIV infection, regardless of their immunologic or virologic status (strong recommendation, high quality evidence).
60. Infants exposed to HIV in utero should receive antiretroviral postexposure prophylaxis and undergo HIV virologic diagnostic testing at 14–21 days of life, at 1–2 months of age, and at 4–6 months of age (strong recommendation, high quality evidence).
61. High-risk exposed infants should have virologic testing at birth (strong recommendation, moderate quality evidence).

Evidence Summary

Perinatal HIV infection is preventable if pregnant women are identified through antenatal testing and receive ART as outlined in the Public Health Service Task Force Recommendations for the Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV-1 Transmission in the United States [58]. The transmission rate has been reported to be <1% in women who achieve undetectable viral loads while receiving treatment. If the rapid test is positive in women during labor, HIV antiretroviral prophylaxis should be initiated immediately without waiting for confirmatory tests. The use of postexposure prophylaxis in the neonate, instituted as soon as possible after birth, ideally within 12 hours, even without antenatal treatment, can still significantly decrease HIV transmission [59].

HIV-infected neonates are usually asymptomatic, although a number of perinatal conditions may occur because of other maternal comorbidities. Prior to discharge from the nursery, the infant should undergo a thorough medical evaluation. The infant’s family should be advised about avoidance of breastfeeding and educated regarding antiretroviral prophylaxis and the need for medical follow-up [60]. A number of diagnostic issues distinguish perinatal HIV infection from adult disease. Because maternal IgG crosses the placenta, term newborn infants usually have positive serology independent of their infection status. Positive enzyme-linked immunosorbent assay and Western blot assay results can remain until 18 months of age. Diagnosis of active HIV infection in the infant can be established by a polymerase chain reaction (PCR) assay for HIV DNA or RNA; a positive result should be immediately repeated. Because the majority of transmissions occur around the time of birth, the sensitivity of virologic tests improves from 50% at birth to >90% at 2–4 weeks of age. To maximize opportunities for early intervention, high-risk infants should be tested at birth; these include infants whose mothers seroconverted during pregnancy or were untreated for their HIV [61]. Infants should receive *Pneumocystis* prophylaxis until infection has been ruled out [31]. Infection is definitively ruled out if the PCR is negative at >1 and >4 months of age and the infant is asymptomatic [62]. Many experts confirm the absence of HIV infection with a negative HIV antibody assay result at 12–18 months of age.
III. What are the special considerations for children?

Recommendations

62. HIV-infected infants should undergo HIV resistance testing (strong recommendation, high quality evidence) and, because of the rapid progression of disease, should initiate therapy in the first year of life regardless of CD4 cell count, RNA level, or clinical status (strong recommendation, high quality evidence).

63. After the first year of life, initiation of therapy in HIV-infected children is based on age, CD4 count/percentage, viral load, and symptoms. ART should be initiated in all symptomatic children (strong recommendation, high quality evidence).

(a) CD4 cell counts and viral loads should be monitored no less than every 3–4 months (strong recommendation, moderate quality evidence).

(b) Childhood vaccinations should be administered according to Advisory Committee on Immunization Practices schedules for HIV-infected infants and children (strong recommendation, high quality evidence).

64. HIV-infected infants and children should be managed by a specialist with knowledge of the unique therapeutic, pharmacologic, behavioral, and developmental issues associated with this disease (strong recommendation, low quality evidence).

Evidence Summary

Infants determined to be infected with HIV should be started on ART according to US Public Health Service guidelines [19]. All infants should also receive Pneumocystis prophylaxis in the first year. In general, perinatally infected infants have higher viral loads than infected adults, and the viral load can remain high throughout the first year. There are age-specific differences in CD4 cell counts, with infants having higher normal absolute lymphocyte counts than adults. In young children, CD4 percentages are less variable than absolute counts. After the first year of life, the benefits of universal treatment are less definitive and the decision to start ART includes a number of factors including age, immune status, viral load, and symptoms. All symptomatic children should be treated. There are guidelines and prognostic tables that aid clinicians in this decision, but assessing family readiness is also essential [19, 63].

Frequent clinical visits are required to assure that growth and development are on schedule, that appropriate adjustment of dosages are made, and that the infant is tolerating the medications. Vaccination status should be reviewed at each visit. HIV-infected infants and children can safely receive most childhood vaccines, although effective response depends on the degree of immunosuppression. Varicella and the measles, mumps, and rubella vaccines should not be administered to severely immunocompromised children (ie, those with CD4 cell percentages <15%). All HIV-infected children should be vaccinated against pneumococcus and receive yearly trivalent inactivated influenza vaccine. Once the child’s HIV medication is stable, the frequency of laboratory testing is similar to that for adults.

Infants and children with undiagnosed HIV infection are more likely to present with common bacterial infections, chronic diarrhea with failure to thrive, or delays in development, than with the conditions defined in categories B or C that are seen in adults [64]. This population has higher rates of serious bacterial infections, such as pneumococcal disease, herpes zoster, and tuberculosis [65], in addition to asthma and chronic lung and skin disease. Up to 20% of perinatal infections present after 6 years of age in populations that lack access to prenatal or newborn screening. These cases can present diagnostic challenges, presenting with immune thrombocytopenic purpura, anemia, recurrent parotitis, chronic diarrhea, encephalopathy, or stroke. Unfortunately, HIV transmission attributable to sexual abuse occurs in children, so children with signs and symptoms of HIV should be tested for HIV even if their initial testing result as an infant was negative.

IV. What are the special considerations for adolescents?

Recommendations

65. HIV-infected adolescents require an individual and developmental approach to therapy and care given by an HIV specialist with expertise in this population (strong recommendation, low quality evidence).

66. Adolescents infected with HIV should have a coordinated, deliberate transition to adult care (strong recommendation, low quality evidence).

Evidence Summary

HIV-infected adolescents—both perinatally and behaviorally infected youth—present many challenges [66–68].

The mean age of the US cohort of perinatally infected children is the mid-teens, and many have reached adulthood [69]. Youth infected with HIV have to cope with many issues, including social stigma, poorer adherence to ART, loss of family members, distortion of body image, and negotiation of sexual activity. In many studies, rates of cognitive, psychiatric, and behavioral problems are higher in perinatally infected children [70]. Disclosure of diagnosis can be overwhelming to caregivers but should occur early, in late childhood [66–68]. Puberty can affect drug metabolism; thus, decisions regarding dosing should consider Tanner staging. Long-term treatment from infancy may result in increased end-organ toxicity and requires careful monitoring. Special attention should be paid to risk reduction counseling and secondary prevention in early adolescence [71, 72].

Behaviorally infected youth have similar issues including high rates of substance abuse, STDs, and psychiatric comorbidity.
The resilience of their immune system and the recent occurrence of their infection offer opportunity for early therapy and secondary prevention if comorbid behavioral issues are addressed. The transition of care to adult providers should be a deliberate, comprehensive, and coordinated process involving the healthcare team and the patient. Care must be given to attend to the diverse needs of the adolescent that extend beyond medical care, including employment, independent living, and intimate relationships. Over time, youth need to learn to negotiate the healthcare system and assume increasing responsibility for their healthcare. The national AIDS Education and Training Centers (AETC) provides a resource book on transition, as do several other sources [73–75].

V. What are the metabolic comorbidities associated with HIV and antiretroviral therapy?

The previously reported adverse effects that complicated the management of HIV infection, including hyperlipidemia, diabetes, body morphology changes (lipohypertrophy and lipoatrophy), and lactic acidosis, are much less frequent with the use of antiretroviral therapy. The metabolic comorbidities associated with HIV and antiretroviral therapy are discussed in detail below.

### Table 7. Routine Healthcare Maintenance in the HIV-Infected Adult

<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></td>
</tr>
<tr>
<td>Digital rectal exam</td>
<td>Consider annually in all patients</td>
<td>Inspect for anal warts, malignancy, prostate abnormalities in men</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>Examine with tonometry is advised every 2–3 y in all patients ≥50 y</td>
</tr>
<tr>
<td>Depression screening</td>
<td>Perform annually in all patients</td>
<td>Use conventional mental health interview or standardized test</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. 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 lipid profile</td>
<td>Perform every 6–12 mo in all patients</td>
<td>Consider testing 1–3 mo after starting or modifying antiretroviral therapy</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 for STDs</td>
</tr>
<tr>
<td>Gonorrhea and chlamydia testing</td>
<td>Perform annually in patients at risk for STDs (see text for details)</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>Hepatitis C testing</td>
<td>Perform annually in patients at risk, eg, injection drug users and MSM</td>
<td>More frequent testing may be indicated in patients at high risk, especially if increase in serum transaminases</td>
</tr>
<tr>
<td>Trichomoniasis</td>
<td>Perform annually in all women</td>
<td>Repeat testing 3 mo later if positive</td>
</tr>
<tr>
<td>TST or IGRA</td>
<td>Perform at baseline and annually in patients at risk for tuberculosis</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>Colorectal cancer screening</td>
<td>Perform at age 50 y in asymptomatic patients at average risk</td>
<td>More frequent testing is indicated in patients with a history of adenomatous polyposis; testing at an earlier age may be advised in patients with a strong family history of colon cancer</td>
</tr>
<tr>
<td>Mammography</td>
<td>Perform annually in all women age ≥50 y</td>
<td>Some authorities advise initiation of screening starting at age 40 y based on an individual risk/benefit assessment</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></td>
</tr>
<tr>
<td>Bone densitometry</td>
<td>Perform baseline exam in postmenopausal women and men age ≥50 y</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>Abdominal ultrasonography</td>
<td>Perform once in men aged 65–75 y who have ever smoked</td>
<td>Screening test for abdominal aortic aneurysm</td>
</tr>
<tr>
<td>Patient education</td>
<td>Address regularly in all patients</td>
<td>Issues may include sexual behavior, alcohol and drug counseling, dietary teaching, weight reduction, smoking cessation, and seat belt use.</td>
</tr>
</tbody>
</table>

For information on digital prostate exam, prostatic specific antigen, colonoscopy and mammography, see the United States Preventive Services Task Force (http://www.ahrq.gov/clinic/USptf/). Abbreviations: HbA1 c, hemoglobin A1c; HIV, human immunodeficiency virus; IGRA, interferon-γ release assay; MSM, men who have sex with men; STD, sexually transmitted disease; TST, tuberculin skin test.
of the newer agents. Concern has heightened about long-term cardiovascular morbidity in patients who experience dyslipidemia and/or glucose intolerance, as well as other common comorbidities associated with age. In general, it appears that the benefits of ART used in accordance with published guidelines outweigh the risk of cardiovascular disease and other comorbidities associated with long-term exposure [76, 77]. Guidelines and expert recommendations have been developed to assist providers in the identification and management of lipid abnormalities, metabolic complications, and bone disorders [25, 78, 79].

**Recommendations**

67. Fasting blood glucose (FBG) and/or hemoglobin A1c (HbA1c) should be obtained prior to and within 1–3 months after starting ART. Patients with diabetes mellitus should have an HbA1c level monitored every 6 months with a goal of <7%, in accordance with the American Diabetes Association Guidelines (strong recommendation, moderate quality evidence).

68. Fasting lipid levels should be obtained prior to and within 1–3 months after starting ART. Patients with abnormal lipid levels should be managed according to the National Cholesterol Education Program Guidelines (strong recommendation, moderate quality evidence).

69. Baseline bone densitometry (DXA) screening for osteoporosis in HIV-infected patients should be performed in postmenopausal women and men aged ≥50 years (strong recommendation, moderate quality evidence).

**Evidence Summary**

The HbA1c is a preferred alternative for diagnosing diabetes, especially given the difficulty of obtaining fasting blood samples. The American Diabetes Association (ADA)

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**Table 8. Effect of Protease Inhibitors and Nonnucleoside Reverse Transcriptase Inhibitors on Statins**

<table>
<thead>
<tr>
<th>Statin</th>
<th>Protease Inhibitors</th>
<th>ART Drug Class</th>
<th>NNRTI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atorvastatin</td>
<td>Caution (moderately increase atorvastatin’s AUC)</td>
<td>Acceptable with appropriate dosing and monitoring Efaviren [116] and etravirine [117] decrease atorvastatin’s AUC No data for nevirapine May need higher atorvastatin starting dose</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Use lowest starting atorvastatin dose</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluvastatin</td>
<td>Not recommended with nelfinavir</td>
<td>Acceptable with appropriate dosing and monitoring Etravirine may increase fluvastatin’s AUC [117] May need lower fluvastatin starting dose with etravirine</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Use of other protease inhibitors is allowed with appropriate dosing and monitoring</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lovastatin</td>
<td>Contraindicated (greatly increase lovastatin’s AUC [118])</td>
<td>Acceptable with appropriate dosing and monitoring Decreases simvastatin’s AUC, so may need higher lovastatin starting dose</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pitavastatin</td>
<td>Acceptable with appropriate dosing and monitoring No significant change in pitavastatin’s AUC with lopinavir/ritonavir [119] Pitavastatin’s mean AUC decreased 26% with darunavir [120]</td>
<td>No data for NNRTIs</td>
<td></td>
</tr>
<tr>
<td>Pravastatin</td>
<td>Acceptable with appropriate dosing and monitoring, except with darunavir Decrease in pravastatin’s AUC, except with darunavir, which increases pravastatin’s AUC by 81% [121]</td>
<td>Acceptable with appropriate dosing and monitoring Efaviren decreases pravastatin’s AUC [116], but no change with etravirine [117] No data for nevirapine and rilpavirine May need higher pravastatin starting dose with efavirenz</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rosuvastatin</td>
<td>Acceptable with appropriate dosing and monitoring; lopinavir/ritonavir and tipranavir + ritonavir increase rosuvastatin’s AUC [122] May need to start rosuvastatin at lower dose with lopinavir/ritonavir Superior to pravastatin in HIV patients in one study [123]</td>
<td>Acceptable with appropriate dosing and monitoring</td>
<td></td>
</tr>
<tr>
<td>Simvastatin</td>
<td>Contraindicated (greatly increase simvastatin’s AUC [117, 120])</td>
<td>Acceptable with appropriate dosing and monitoring Efaviren [116] and etravirine [117] decrease simvastatin’s AUC No data for nevirapine May need higher simvastatin starting dose</td>
<td></td>
</tr>
</tbody>
</table>

**Abbreviations:** ART, antiretroviral therapy; AUC, area under the curve; HIV, human immunodeficiency virus; NNRTI, nonnucleoside reverse transcriptase inhibitor.
established the diagnostic criteria of diabetes mellitus of a fasting plasma glucose level of ≥126 mg/dL (7.0 mmol/L) or a 2-hour plasma glucose level of ≥200 mg/dL (11.1 mmol/L) during an oral glucose tolerance test (OGTT) conducted with a standard loading dose of 75 g, or an HbA1c ≥6.5% [80]; however, using the National Health and Nutrition Examination Survey cutoff of ≥5.8% improves the sensitivity for diagnosis for patients on ARVs [81]. As of 2011, the ADA altered its recommendations to say that in cases of HbA1c and FBG discordance, the abnormal laboratory test should be repeated, and the diagnosis of diabetes should be made only if repeat testing is again above the diagnostic cut-point [78].

In most cases, blood glucose abnormalities can be effectively managed by lifestyle changes that include weight loss, increased exercise, and dietary modification. However, if therapeutic intervention is needed, insulin-sensitizing agents are preferred. Patients should be managed according to the ADA guidelines [78, 82]. There are no data suggesting that switching ARVs is beneficial in patients with impaired glucose tolerance associated with HIV infection itself or traditional risk factors.

Similar to the reports on insulin resistance, dyslipidemia has been associated with traditional risk factors, HIV infection itself, and ARVs. It is recommended that all patients be assessed for coronary heart disease risk, and those with ≥2 risk factors should be further evaluated and managed according to the National Cholesterol Education Program guidelines [25]. As HIV itself may be considered an independent risk factor for heart disease, many experts favor more aggressive management of lipids. Caution should be used when prescribing statins with protease inhibitors (PIs) and nonnucleoside reverse transcriptase inhibitors due to potential serious drug–drug interactions (Table 8). Most PIs inhibit the metabolism of statins, thereby increasing potential for statin toxicity. However, there are exceptions such as pitavastatin and pravastatin, which are metabolized by glucuronidation, thereby having little effects when coadministered with a PI. In addition, atorvastatin and rosuvastatin may be used in patients on a PI but should be initiated at low doses and titrated carefully according to tolerability and effect. Efavirenz induces statin metabolism, resulting in lowering of statin levels. Nevirapine, etravirine, and rilpivirine have not been extensively studied. Cobicistat is expected to have similar interactions as ritonavir with statins; however, these interactions have not been formally studied. There may be other pathways effecting drug metabolism leading to unexpected interactions, and it is advised to refer to the package insert of the ARV before prescribing lipid-lowering agents. All patients should be encouraged to stop smoking regardless of cardiovascular risk, and hypertension and diabetes mellitus should be managed as appropriate.

Baseline bone densitometry by dual-energy X-ray absorptiometry (DXA) should be performed in all postmenopausal women and men aged ≥50 years. If the DXA demonstrates osteopenia or if the patient has a history of fragility or fracture, intervention with vitamin D, calcium, and a bisphosphonate or other medical therapy may be warranted. Bisphosphonates appear to be effective in improving bone density in small studies of HIV-infected patients, but the data are limited [79, 83, 84]. It is important to exclude osteomalacia prior to initiating a bisphosphonate, as this could lead to increased fragility and fracture. Common reasons for osteomalacia in this population are tenofovir-induced renal phosphate wasting and vitamin D deficiency, which has been reported in 40%–80% of HIV-infected persons. The spectrum and severity of metabolic complications associated with vitamin D deficiency in HIV-infected adults remain to be better characterized. Patients with vitamin D deficiency and osteopenia by DXA should be treated with vitamin D and calcium without bisphosphonates until the vitamin D deficiency has resolved. A follow-up DXA should be repeated 1 year later to monitor the response to therapy.

Patients should be reminded of the health benefits of regular exercise in addition to adequate calcium and vitamin D intake. They should also be counseled about the risks of cigarette smoking and excessive alcohol consumption. Secondary causes of decreased bone density, such as hypogonadism, alcoholism, glucocorticoid exposure, and vitamin D deficiency, should be investigated and treated accordingly.

Routine radiographic monitoring for avascular necrosis in asymptomatic persons is not recommended, but for patients presenting with persistent hip pain who have normal standard radiologic studies, magnetic resonance imaging is the preferred method of diagnosis, and both sides should be imaged. Most patients with symptomatic avascular necrosis will ultimately require surgical intervention (eg, hip replacement).

VI. How can patient adherence to HIV care be optimized?

Recommendations

70. All HIV-infected patients should be provided timely access to routine and urgent primary medical care (strong recommendation, moderate quality evidence).

71. HIV care sites should make every effort to provide care in a way that is linguistically and culturally appropriate and competent (strong recommendation, moderate quality evidence).

72. HIV care sites should utilize a multidisciplinary model but identify a primary provider for each patient and support the development of trusting long-term patient–provider relationships (strong recommendation, moderate quality evidence).

73. All patients should be evaluated for depression and substance abuse, and if present, a management plan that addresses these problems should be developed and implemented in collaboration with appropriate providers (strong recommendation, high quality evidence).
Evidence Summary
The long-term effectiveness of ART is dependent on durable suppression of viral replication. Providers should emphasize that adherence to ARVs not only improves the patient’s health, but has been shown to be an effective way to prevent HIV transmission to others [85]. Unfortunately, not all patients achieve this goal [86, 87]. The primary reason for treatment failure, particularly among patients taking initial regimens, is suboptimal adherence to treatment regimens [88, 89]. Adherence to care not only means medication adherence, but also adherence with medical visits and engagement in care [87, 90]. Low adherence to visits and poor engagement in care has been found to be a predictor of higher mortality among persons with HIV/AIDS (approximately 50% higher mortality rate) [91]. Thus, it is critically important that HIV providers and clinics have a strategy to effectively engage and retain patients in care. Access to timely quality care is also critical; long waiting time for an initial appointment for HIV care has been shown to be one predictor of failure to engage in care [92].

The quality of the patient–provider relationship is often cited as one of the most important factors in a patient’s engagement in care. Having a provider with whom the patient feels comfortable and can communicate effectively and frankly is key to developing this type of relationship [93, 94]. The site should provide a setting in which provider accessibility and scheduling and a team approach to care make these goals achievable. In addition, the multidisciplinary care model often helps retain patients in care, identify unmet care needs, and improve adherence to medications. Having an HIV team that includes a case manager has been frequently shown to enhance adherence to care and engagement [95]. Culturally and linguistically competent care is critical to successfully engage and retain patients in care; a broad range of components, from having staff of the same race, culture, or lifestyle to having art and reading material in the clinic that reflects the culture of the local community, may be useful in facilitating this goal [96, 97]. The assessment of nonadherence also should include social and economic factors. Lack of adequate food or safe housing can impact a patient’s ability to remain adherent to their treatment regimen. Early assessment by a qualified social worker or case manager is essential to successful care later on [98–100].

Depression and substance abuse are highly prevalent in persons living with HIV infection. These 2 comorbid conditions have been found to be important barriers to consistent adherence to ART and HIV care [101]. Treatment of depression can improve medication adherence, so it is essential that patients with depression be identified and treated [102]. A variety of management strategies, including directly observed therapy, have been found to enable successful HIV treatment of active substance abusers [103]. Regular assessment of depression and substance use (including nonclinical levels of use) is essential.

PERFORMANCE MEASURES
HIV quality-of-care performance metrics have been developed by a national expert panel [104] endorsed by the National Quality Forum and adopted by many care organizations. Some states and federal agencies (eg, Health Resources and Services Administration [HRSA], the New York State AIDS Institute) have additional performance measures. There is now an increasing national effort to harmonize these measures across multiple platforms and simplify reporting requirements. HIV performance measures are in use through the American Medical Association–convened Physician Consortium for Performance Improvement, the HRSA, and the New York State AIDS Institute.

Notes
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Disclaimer. Guidelines cannot always account for individual variation among patients. They are not intended to supplant physician judgment with respect to particular patients or special clinical situations. The Infectious Diseases Society of America considers adherence to this guideline to be voluntary, with the ultimate determination regarding their application to be made by the physician in light of each patient’s individual circumstances.

Potential conflicts of interest. The following list is a reflection of what has been reported to IDSA. To provide thorough transparency, IDSA requires full disclosure of all relationships, regardless of relevancy to the guideline topic. Evaluation of such relationships as potential conflicts of interest (COI) is determined by a review process that includes assessment by the SPGC Chair, the SPGC liaison to the development panel, and the Board of Directors liaison to the SPGC and, if necessary, the COI Task Force of the Board. This assessment of disclosed relationships for possible COI will be based on the relative weight of the financial relationship (ie, monetary amount) and the relevance of the relationship (ie, the degree to which an association might reasonably be interpreted by an independent observer as related to the topic or recommendation of consideration). The reader of these guidelines should be mindful of this when the list of disclosures is reviewed. For activities outside of the submitted work, J. A. A. served on the advisory board for Abbvie, Janssen (Tibotec), Merck, and ViiV, and received research grants from the National Institutes of Health, Kowa, Gilead, and Wyeth/Pfizer. For activities outside of the submitted work, J. E. G. has received personal fees from Gilead, Bristol-Myers Squibb, Vertex Pharmaceuticals, and ViiV. Also outside of the submitted work, he has received personal fees from Gilead, Bristol-Myers Squibb, Janssen, Merck, ViiV, and GlaxoSmithKline. He is also a member of the Department of Health and Human Services panel for adult and adolescent antiretroviral therapy guidelines. For activities outside of the submitted work, B. S. Z. received grants from Gilead, ViiV, GlaxoSmithKline, and Siemens. All other authors report no potential conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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