



**Medical Education Collaborative**

## **EVALUATION AND MANAGEMENT OF THE NEWLY DIAGNOSED HIV-POSITIVE PATIENT**

### **Faculty**

**Joel E. Gallant, MD, MPH**

Associate Professor of Medicine and Epidemiology  
Division of Infectious Diseases  
Johns Hopkins University School of Medicine  
Baltimore, Maryland

### **Release Date**

Release Date: February 1, 2005; Valid for credit through January 31, 2006.

### **Disclosures**

Dr. Gallant has no significant financial relationships to disclose.

In this activity, Dr. Gallant does not discuss any investigational agents, but he does discuss the unlabeled use of trimethoprim-sulfamethoxazole in the prevention of *toxoplasma gondii* infection, fluconazole in the prevention of *cryptococcus neoformans* infection, and itraconazole in the prevention of *histoplasma capsulatum* infection. Of note, all 3 agents are FDA approved for the treatment of these infections.

### **Target Audience**

This activity is intended for healthcare providers involved in the management of HIV-infected patients.

## **Learning Objectives**

Upon completion of this activity, participants should be able to:

- List the appropriate examinations and laboratory tests that should be performed at first encounter with a newly diagnosed HIV-positive patient
- Outline current recommendations for vaccination, prophylaxis and antiretroviral treatment of newly diagnosed HIV-positive patients
- Discuss other special considerations that should be addressed at the first encounter, including education and counseling, mental health and substance abuse issues.

## **Credit Hours Available**

Medical Education Collaborative designates this educational activity for a maximum of 1.0 category 1 credits toward the AMA Physician's Recognition Award. Each physician should claim only those hours of credit that he/she actually spent in the activity.

## **Instructions for Credit**

Participation in this self-study activity should be completed in approximately 1 hour. To successfully complete this activity and receive credit, participants must follow these steps during the period from February 1, 2005 through January 31, 2006:

1. Register online at <http://clinicaloptions.com>
2. Read the target audience, learning objectives, and faculty disclosures.
3. Study the educational activity online or printed out.
4. Submit answers to the post-test questions and evaluation questions online.

You must complete the post-test and respond to all evaluation questions to receive a certificate. After submitting the evaluation, you may access your online certificate by selecting the certificate link on the post-test confirmation page. Records of all CME activities completed can be found on the "My CME" page. There are no costs/fees for this activity.

## Accreditation

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**This activity is supported by an educational grant from:**



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## Contents

- History
- Physical Examination
- Baseline Laboratory Evaluation Overview
- Baseline Laboratory Testing: Chemistry and Metabolic Tests (Checklist)
- Baseline Laboratory Testing: Serologic Tests (Checklist)
- Baseline Laboratory Testing: Other Infections and Cancers (Checklist)
- Unnecessary Tests
- Vaccinations
- Special Considerations: Education and Counseling
- Special Considerations: Prophylaxis
- Other Special Considerations for the First Encounter
- Conclusions

## History

While the initial evaluation of a patient with newly diagnosed HIV infection is similar in many ways to the evaluation of patients with other chronic diseases, there are many additional components to the history and physical examination, numerous additional laboratory tests indicated at baseline, and a number of special considerations that affect the content of the first encounter.

## Medical History

The initial evaluation of a newly diagnosed HIV-positive patient should include a complete medical history (Table 1). Whenever possible, the approximate time and source of infection should be determined. Patients should be asked about prior negative HIV serologies, their beliefs as to the approximate time of infection, and the presumed source. If the patient knows the source, further questioning may elicit information relevant to the likelihood of transmission of drug-resistant virus. The patient should also be asked about his or her sexual and/or drug-using contacts since the time of onset of infection, and whether those contacts have been notified.

## Factors to Assess During the Initial Encounter

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- Approximate time and source of infection
  - Risk of coinfection or latent infection (HSV, VZV, M.Tb, HBV, HCV, HPV)
  - Sexual and/or drug-using contacts
  - Where the patient has lived and traveled
  - Prior sexually transmitted diseases
  - Current sexual activity
  - Substance abuse history
  - Family medical history
  - Cardiovascular risk factors
  - Symptoms that could indicate progressive HIV disease
    - Fevers, night sweats, involuntary weight loss, diarrhea, and oral or cutaneous manifestations of HIV disease
  - Current medications (including over-the-counter medications, methadone, and dietary or herbal supplements)
  - Depression screening
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\**HSV, herpes simplex virus; VZV, varicella zoster virus;*  
*M.Tb, Mycobacterium tuberculosis;*  
*HBV, hepatitis B virus, HCV, hepatitis C virus;*  
*HPV, human papillomavirus*

Other elements of the patient's history that are of particular importance with HIV-infected patients include questions pertaining to the risk of coinfection or latent infection with pathogens that may result in disease reactivation. Examples of questions that should be asked include:

- *“Have you ever had herpes or cold sores?”*
- *“Have you ever had chickenpox or shingles?”*
- *“Have you ever been exposed to tuberculosis? Have you ever had a positive TB skin test? When was your last test?”*
- *“Have you ever had hepatitis? Have you been vaccinated against hepatitis?”*
- *“Have you ever had genital/anal warts? Have you ever had an abnormal cervical/anal Pap smear? When was the last Pap smear?”*

The history should also include questions about where the patient has lived and traveled. For example, patients reporting travel in areas endemic for histoplasmosis (Ohio and Mississippi River valleys) or coccidioidomycosis (Southwestern deserts) and those traveling abroad may be at risk for disease reactivation, even after moving or returning to nonendemic areas.

A thorough sexual history should be taken, with questions about prior sexually transmitted diseases and current sexual activity, including use of condoms and other forms of birth control. An understanding of the patient's sexual behavior is critical for effective risk-reduction counseling. Patients who report a decrease in libido or sexual performance should be screened for depression and hypogonadism. Patients should also be asked about substance use, including questions about drug- or alcohol-related behavior that might directly or indirectly facilitate further transmission of HIV infection.

Family medical history was rarely important in the pre-HAART era; however, such information is now of much greater importance, since patients on HAART may be at increased risk of hyperlipidemia, diabetes, and eventually coronary artery disease. A thorough assessment of cardiovascular risk factors has therefore become essential for HIV-infected patients.

The review of systems should include questions about symptoms that could indicate progressive HIV disease, such as fevers, night sweats, involuntary weight loss, diarrhea, and oral or cutaneous manifestations of HIV disease. Symptomatic patients generally merit antiretroviral therapy, regardless of what their CD4+ cell count or viral load is.

Patients should be asked about the medications they take, including over-the-counter medications, medications taken infrequently, methadone, and dietary or herbal supplements--a number of which have been shown to interact with antiretroviral agents.

It is important to realize that newly diagnosed patients may be experiencing significant coping difficulties or clinical depression. Screening for depression is a vital part of the initial history, in part because untreated depression is a strong predictor of nonadherence to medical follow-up and antiretroviral therapy.

## Physical Examination

A complete physical examination should be performed as part of the initial evaluation. Funduscopic examination is particularly important in patients with advanced HIV disease (eg, CD4+ cell count < 100 cells/mm<sup>3</sup>) since these patients are at increased risk of cytomegalovirus (CMV) retinitis and other HIV-related ocular complications. Special attention should be paid to the oropharynx, where the presence of candidiasis or oral hairy leukoplakia may indicate significant immunosuppression. Generalized lymphadenopathy, while common among HIV-infected patients, is not helpful in assessing immune status or need for therapy. However, asymmetric or rapidly enlarging lymph nodes may reflect underlying infection or malignancy. Examination of the genitals and anus should be performed to look for internal or external lesions such as herpes or condylomata. The neurologic examination should include an assessment of lower-extremity peripheral nerve function, which can be quickly evaluated by measuring vibratory sensation in the toes and by checking ankle reflexes. A thorough skin examination should be performed to look for evidence of any significant skin lesions and cutaneous manifestations of opportunistic infections. Lesions that occur with increased frequency among HIV-infected individuals include seborrheic dermatitis, psoriasis, folliculitis, Kaposi's sarcoma, common warts, and molluscum contagiosum.

*View the “Physical Examination Checklist” at the end of this document >>*

## Baseline Laboratory Evaluation Overview

The initial evaluation of an HIV-infected patient should include a variety of baseline laboratory tests. The indications and rationale for such tests are discussed in the next few pages. It cannot be ignored that many HIV-infected patients are uninsured when they first present for care, and the full panel of baseline tests is expensive. In practice, some of the tests discussed, especially serologic tests used to determine the need for opportunistic infection prophylaxis or vaccination, can be deferred until funding is available or until they are clinically indicated.

## Baseline Laboratory Testing: HIV-Related and Hematologic Tests

*View the “Baseline Laboratory Test Checklist, Part 1: HIV Related and Hematologic Tests” at the end of this document >>*

CD4+ cell count: The CD4+ cell count is the most important test for assessing the patient's disease state and indications for antiretroviral therapy. It should be performed at baseline and routinely, every 3-6 months, depending on rate of CD4+ cell count decline in untreated patients. It is not necessary to measure the CD8+ cell count or the CD4/CD8 ratio, since clinical decisions are made on the basis of the absolute CD4+ cell count and CD4 percent alone.

Plasma HIV-1 RNA (viral load): These results can be used both to confirm HIV-1 infection and to assess the current extent of viral replication. Higher viral loads generally predict a more rapid decline in CD4+ cell count, and there is some evidence supporting the benefits of antiretroviral therapy in patients with high viral loads, regardless of CD4+ cell count. When choosing an RT-PCR assay, untreated patients should be tested using the standard (first-generation) assay, which can quantify HIV-1 RNA at higher levels. Ultrasensitive assays should be reserved for patients on therapy or for untreated patients with undetectable viral load results with the standard assay.

HIV serology: This should be repeated in patients whose HIV diagnosis has not been firmly established. Such a case would be a patient with a single positive serology who has a normal CD4+ cell count and a low or undetectable viral load.

HIV resistance test: Infection with drug-resistant virus is increasing in many communities. Baseline resistance testing was initially recommended only for patients with acute or recent infection. However, recent evidence suggests that transmitted resistant mutants can persist for many years after initial infection, providing support for broader use of baseline testing. Testing should be performed as early as possible, regardless of whether the patient requires immediate antiretroviral therapy. Genotype testing is preferred for this indication, since it is less expensive and more likely than phenotype testing to detect resistant mutants present at low levels (eg, minority viral populations).

Complete blood count (CBC) with differential: This is a baseline and routine test performed to determine whether a patient has anemia, leukopenia, or thrombocytopenia--common conditions in HIV-infected patients. The presence of anemia or leukopenia generally requires further evaluation, and may affect the choice of antiretroviral agents.

## **Baseline Laboratory Testing: Chemistry and Metabolic Tests**

*View the “Baseline Laboratory Test Checklist, Part 2: Chemistry and Metabolic Tests” at the end of this document >>*

Chemistry panel: A chemistry panel should be obtained at baseline and routinely thereafter and should include assessment of both renal function (blood urea nitrogen [BUN] and creatinine) and liver “function” (aspartate aminotransferase [AST], alanine aminotransferase [ALT], bilirubin, and alkaline phosphatase). Patients with abnormal renal function require further evaluation, including assessment of possible HIV-associated nephropathy (HIVAN) in black patients. Abnormal transaminases may be an indication of alcohol abuse or underlying viral hepatitis, even in patients with negative serologies. The chemistry panel typically includes a total protein and albumin. Physicians should note that an elevated total protein is common among HIV-infected patients due to HIV-related polyclonal gammopathy, and generally requires no further work-up unless it is severe. However, a low albumin result suggests more advanced disease with malnutrition or protein-losing enteropathy.

Urinalysis: Consider baseline testing, especially in black patients who are at risk of HIVAN, which may also present as proteinuria.

Glucose-6-phosphate dehydrogenase (G6PD): Physicians should consider baseline testing in patients at risk for G6PD deficiency (eg, persons of African or Mediterranean descent), in order to identify those at risk of hemolysis with receipt of oxidant drugs, such as dapson, primaquine, or sulfonamides. G6PD testing is much less accurate when performed during episodes of hemolysis.

Fasting lipid panel: It is becoming increasingly important in the HAART era to establish the patient's baseline lipid profile prior to starting antiretroviral agents, many of which may increase cholesterol and triglyceride levels. The presence of hyperlipidemia at baseline may affect the choice of initial antiretroviral regimens. If hyperlipidemia is recognized only after initiation of therapy, it cannot be determined whether it was caused by therapy or was present at baseline. The lipid test should be performed after a 9- to 12-hour fast, and should be deferred if the patient is acutely ill.

Testosterone level: Although not a routine test, evaluation of testosterone levels should be considered in men who report fatigue, weight loss, depression, or change in libido or sexual function. Physicians should note that the test is most accurate when performed in the morning. A total testosterone level that is low or in the lower end of the normal range is usually sufficient to establish a diagnosis of hypogonadism; however, a free testosterone level assessment should also be ordered in symptomatic patients with a normal total testosterone level. Alternatively, total and free testosterone levels can be ordered at the same time.

### **Baseline Laboratory Testing: Serologic Tests**

*View the "Baseline Laboratory Test Checklist, Part 3: Serologic Tests" at the end of this document >>*

Nontreponemal syphilis serology (VDRL, RPR, STS): This is an important baseline test that should be repeated yearly, or more frequently in patients at high risk. Positive serologies should be confirmed with a treponemal serologic test, such as an FTA-ABS or MHA-TP (which are usually performed as reflex tests by the clinical laboratory), since biologically false-positive results are not uncommon, especially among injection drug users. Patients with evidence of syphilis in both tests should be asked about prior diagnosis and treatment of syphilis. Lumbar puncture should be performed in patients with abnormal neurologic examination and should also be considered in patients with late latent syphilis or syphilis of unknown duration, in those experiencing treatment failure, or in patients who cannot use benzathine penicillin.

## Hepatitis serologies:

**Hepatitis B.** HBsAg should be performed in all HIV-infected patients to rule out chronic hepatitis B, since the risk factors for HIV and HBV are identical. HBsAb and possibly anti-HBc should also be ordered to determine whether the patient is a candidate for vaccination against HBV. Patients who have a positive anti-HBc with a negative HBsAg and HBsAb should be screened for chronic HBV infection by evaluating the patient's HBV viral load using an HBV DNA PCR assay.

**Hepatitis C.** Anti-HCV antibody is indicated in all HIV-infected patients; however, physicians should note that false-negative test results can occur. A negative serology should therefore be confirmed with a quantitative HCV RNA assay in seronegative patients with abnormal hepatic transaminases or those at high risk due to injection drug use. Patients found to be coinfecting with hepatitis C require further evaluation, especially if they are candidates for treatment. Further evaluation should include assessment of HCV RNA, HCV genotype, and alpha-fetoprotein level, as well as radiographic imaging of the liver and liver biopsy.

**Hepatitis A.** Vaccination against hepatitis A is indicated in many nonimmune, HIV-infected patients. Total HAV antibody can be used to determine whether the patient is already immune to HAV. Determination of HAV antibody status is felt to be more cost-effective when compared with routine vaccination without screening in areas with an HAV seroprevalence over 30%.

Anti-Toxoplasma IgG: This serology is used to determine whether the patient is latently infected with *Toxoplasma gondii*, a protozoan pathogen that can cause encephalitis when the CD4+ cell count falls below 100 cells/mm<sup>3</sup>. Seronegative patients should receive prevention counseling that emphasizes avoidance of contact with cat feces and undercooked meat. Those who are seropositive should receive *Toxoplasma* prophylaxis if their CD4+ cell count is below 100 cells/mm<sup>3</sup>.

Anti-CMV IgG: This test is sometimes recommended in HIV-infected patients to determine whether the patient is latently infected with CMV. The primary reason for screening for CMV in the HIV-infected patient population is to identify those who are seronegative, in order to provide appropriate counseling about avoidance of CMV infection through safer sexual practices and receipt of CMV-negative or leukocyte-reduced blood products when transfusion is necessary. However, the vast majority of HIV-positive individuals, especially men who have sex with men (MSM) and drug users, are already seropositive at the time of HIV diagnosis, and test results have no specific implications for seropositive patients since primary prophylaxis of CMV disease is not currently indicated. Therefore, some groups recommend serologic testing only in patients who are believed to be at lower risk for CMV infection.

Anti-varicella IgG: This test should be considered in patients who do not give a reliable history of chickenpox or shingles, primarily to identify those nonimmune patients who would require varicella zoster immune globulin (VZIG) in the event of exposure. Most HIV-infected adults either have a history of chickenpox or are found to be seropositive with testing.

## **Baseline Laboratory Testing: Other Infections and Cancers**

*View the “Baseline Laboratory Test Checklist, Part 4: Other Infections and Cancers” at the end of this document >>*

Screening for other sexually transmitted diseases: Now that gonorrhea and *Chlamydia* can be diagnosed by urine tests in symptomatic or asymptomatic patients using nucleic acid amplification or hybridization tests, baseline and routine screening is recommended for at-risk patients, and appropriate treatment should be provided to those who test positive. It is important to note that women are especially likely to harbor such infections without symptoms. A pelvic examination should be performed and should include a wet mount to look for evidence of *Trichomonas* vaginitis.

Cervical and/or anal Pap smear: A baseline cervical Pap smear using liquid-based cytology is a standard test in HIV-infected women to screen for the presence of HPV-related dysplasia. This test should be repeated once during the first year and annually thereafter if results are normal. Abnormal Pap smears should be further evaluated by colposcopy. There is also growing support for the use of anal pap smears, especially in women and MSM, to screen for the presence of HPV-related anal dysplasia. Patients with abnormal results should be further evaluated by high-resolution anoscopy, with biopsy of suspicious lesions.

Tuberculin skin testing: The tuberculin skin test (TST) is a standard baseline test for all HIV-infected patients. Induration of at least 5 mm at 48 hours is considered positive. Patients who test positive should be treated for latent infection after active tuberculosis has been ruled out. Repeat testing should be considered in patients considered to be at high risk for tuberculosis and in cases where the initial test was performed in a patient with a low CD4+ cell count prior to initiation of HAART. “Anergy testing” is no longer recommended.

Chest radiograph: This test is NOT usually considered a standard test in an asymptomatic patient, although some clinicians order it to establish a baseline image for future comparison and to rule out subclinical tuberculosis. Injection drug users, in particular, may have increased interstitial markings that could be confused with *Pneumocystis carinii* pneumonia (PCP) or other pneumonias.

Dilated funduscopic examination: Referral to an ophthalmologist for dilated funduscopic examination should be considered in patients with advanced HIV disease (eg, CD4+ cell count < 50-100 cells/mm<sup>3</sup>) to screen for CMV retinitis.

Other healthcare maintenance issues: With improvements in antiretroviral therapy, HIV-infected patients are living longer and are beginning to develop health problems associated with aging. Routine healthcare maintenance interventions that were typically ignored in the pre-highly active antiretroviral therapy (HAART) era are now just as important in HIV-positive patients as they are among HIV-negative individuals. Clinicians caring for HIV-infected patients need to be aware of standard prevention guidelines, such as recommendations regarding screening for colorectal, prostate, breast, and gynecologic cancers.

## Unnecessary Tests

### Blood tests *NOT* indicated for Asymptomatic Patients

Physicians should be aware that a number of frequently ordered blood tests are not routinely indicated in asymptomatic patients at baseline (Table 2).

**Anti-HSV antibodies** have no diagnostic or therapeutic implications and are likely to be positive in most patients. Some groups recommend type-specific serology for HSV-2, although the decision about whether to offer treatment and/or prophylaxis is made on clinical grounds alone.

**Serum cryptococcal antigen** testing is a useful screening tool for patients with CD4+ cell counts below 100 cells/mm<sup>3</sup> who present with fever and/or headache. However, this test has no utility in screening asymptomatic patients.

**Acid-fast bacillus (AFB) blood cultures** are used to make the diagnosis of disseminated *Mycobacterium avium* complex (MAC), but they should not be drawn in asymptomatic patients with CD4+ cell counts higher than 50 cells/mm<sup>3</sup>.

## Blood Tests That Are *NOT* Indicated for Asymptomatic Patients

### Anti-HSV antibodies

- Likely to be positive in most patients
- Result has no diagnostic or therapeutic implications

### Serum cryptococcal antigen

- Useful screening tool for patients with CD4+ cell counts < 100 cells/mm<sup>3</sup> who present with fever and/or headache
- NOT useful for screening asymptomatic patients.

### AFB blood cultures

- NOT necessary in asymptomatic patients with CD4+ cell counts > 50 cells/mm<sup>3</sup>

## Vaccinations

Before giving routine vaccinations to newly diagnosed HIV-infected patients, the clinician should first consider the immune status of the patient since the efficacy of vaccination is dependent upon the patient's CD4+ cell count. Vaccination should be deferred in patients with low CD4+ cell counts who will soon be starting antiretroviral therapy, since vaccination is more likely to be effective after immune reconstitution has taken place. In patients with low CD4+ cell counts (eg, < 200 cells/mm<sup>3</sup>) despite antiretroviral therapy, vaccination should be considered optional. The following is a list of routine vaccinations and how they should be administered in HIV-infected patients (Table 3):

Pneumococcal polysaccharide vaccine: Generally recommended at baseline and every 5-6 years in HIV-infected patients because of the increased risk of pneumococcal disease, though data on the efficacy of vaccination are conflicting.

Influenza vaccine: Generally recommended each fall in HIV-infected patients, not because of increased risk or severity of influenza in HIV-infected patients, but because influenza can mimic HIV-associated complications (eg, PCP, abacavir hypersensitivity reactions).

Tetanus toxoid: Follow standard guidelines for HIV-negative adults, with dT boosters every 10 years.

Hepatitis B vaccine: Indicated in all nonimmune HIV-infected patients, especially if at ongoing risk.

Hepatitis A vaccine: Indicated for nonimmune patients at risk (eg, MSM and international travelers) and for patients coinfecting with HCV because of risk of fulminant hepatitis. Consider in all nonimmune HIV-infected patients.

Haemophilus influenzae type b vaccine: Not indicated for HIV-infected adults, since most cases of *H influenzae*-related disease in this population are due to non-type b strains.

### Recommendations Regarding Administration of Routine Vaccinations in HIV-Infected Patients

Vaccinations	Recommendations
All vaccinations	<ul style="list-style-type: none"> <li>▪ Defer in patients with low CD4+ cell counts starting antiretroviral therapy</li> <li>▪ Optional in patients with low CD4+ cell counts (&lt; 200 cells/mm<sup>3</sup>) while on anti-retroviral therapy</li> </ul>
Pneumococcal polysaccharide vaccine	<ul style="list-style-type: none"> <li>▪ Generally recommended at baseline and every 5-6 years thereafter</li> </ul>
Influenza vaccine	<ul style="list-style-type: none"> <li>▪ Generally recommended each fall</li> </ul>
Tetanus toxoid	<ul style="list-style-type: none"> <li>▪ dT boosters every 10 years</li> </ul>
Hepatitis B vaccine	<ul style="list-style-type: none"> <li>▪ Indicated in all nonimmune HIV-infected patients</li> </ul>
Hepatitis A vaccine	<ul style="list-style-type: none"> <li>▪ Indicated for               <ul style="list-style-type: none"> <li>◦ Nonimmune patients at risk (eg, MSM and international travelers)</li> <li>◦ Patients coinfecting with HCV</li> </ul> </li> <li>▪ Consider in               <ul style="list-style-type: none"> <li>◦ All nonimmune HIV-infected patients</li> </ul> </li> </ul>
<i>Haemophilus influenzae</i> type b vaccine	<ul style="list-style-type: none"> <li>▪ NOT indicated for HIV-infected adults               <ul style="list-style-type: none"> <li>◦ Most cases due to non-type b strains</li> </ul> </li> </ul>

## **Special Considerations: Education and Counseling**

The initial encounter with the patient provides an important opportunity for patient education and counseling. At the time of diagnosis, many patients harbor outdated notions about their prognosis, the effectiveness of therapy, and the natural history of HIV infection. These misconceptions often fuel the significant coping difficulties faced by most patients who learn that they are infected. Education about current prospects for therapy and for prolonged survival are critical in helping patients accept their diagnosis, and can also be used to introduce the subject of adherence, which is worth discussing even if antiretroviral therapy is not immediately indicated. Patients also need to be educated about the logistics of HIV care. How do they make appointments? What do they do in the event of acute medical problems or emergencies? How do they get refills on medications? Who are the other clinicians who might be involved in their care? Can they call or send emails if they have questions between appointments?

Counseling should also address risk reduction and prevention of HIV transmission to others. HIV-infected patients should be asked about sexual behavior, especially with respect to disclosure of HIV status to sexual partners and use of condoms, to determine whether there is an ongoing risk of transmission. Injection drug users should also be asked about needle-sharing behavior and offered referral to drug treatment programs and/or needle exchange programs, if available. Many HIV-infected patients, particularly those who are having sex only with people whom they assume to be HIV-positive, are unaware of the potential for superinfection, including reinfection with a drug-resistant strain of HIV. Counseling regarding this risk is increasingly supported in the medical literature, and may provide an additional motivation for safer sexual behavior.

For a detailed discussion of HIV prevention in the treatment setting, see the accompanying module by Myron S. Cohen, MD.

## **Special considerations: Initiation of Antiretroviral Therapy**

Virtually all initial encounters with treatment-naïve patients will include a discussion of indications for antiretroviral therapy. Current guidelines from the United States Department of Health and Human Services recommend therapy for symptomatic patients or those with an AIDS-defining illness, including those with CD4+ cell counts < 200 cells/mm<sup>3</sup>. Patients with CD4+ cell counts between 200 and 350 cells/mm<sup>3</sup> are also considered candidates for therapy, as are those with viral loads above 100,000 copies/mL.

These guidelines are somewhat less aggressive than those in place during the early years of the HAART era. The move toward deferral of therapy came about for a variety of reasons, including the recognition that HIV could not be eradicated using antiretroviral therapy, that therapy was complex, toxic, and adversely affected quality of life, and that resistance was inevitable unless adherence was near perfect. However, we may soon see a return toward earlier therapy. Today's initial regimens are dramatically simpler than those commonly used in the early years of the HAART era. For example, it is now

possible to prescribe highly potent regimens that consist of just 2 pills per day. Long-term toxicity may no longer be inevitable, as there are now a number of drugs available that seem to be relatively free of the mitochondrial and metabolic side effects that plagued early regimens. Finally, earlier initiation of therapy may preserve options for intermittent therapy. CD4-guided treatment interruption strategies, while still controversial, appear to be safe in patients with relatively high CD4+ cell count nadirs. Deferral of therapy, on the other hand, may commit patients to lifelong treatment without the possibility of safe interruption.

The decision of whether to treat patients with acute or recent infection is especially complex, primarily because of the paucity of clinical data. Intermittent therapy initiated during primary infection has been shown to improve HIV-specific cellular immunity; however, this response did not result in prolonged virologic control. Current guidelines recommend consideration of therapy for acutely- or recently infected patients, although these recommendations are based on somewhat hypothetical considerations. It is possible that immediate initiation of a short or intermittent course of antiretroviral therapy during primary infection might be beneficial, but no randomized trials of immediate vs deferred therapy in this setting have been conducted. Patients diagnosed at this stage should be counseled about the potential risks and benefits of treatment, and those who are motivated and likely to be adherent should be considered for therapy, preferably as part of a clinical trial or research study.

### **Special Considerations: Prophylaxis**

Unfortunately, some patients with HIV infection present with advanced HIV disease and may be at risk for opportunistic infections (OIs). In such cases, prophylaxis should be instituted immediately, often before antiretroviral therapy (Table 4). The consequences of nonadherence with OI prophylaxis are less serious than with HAART, and a trial of OI prophylaxis can help the patient and clinician to assess potential barriers to adherence with antiretroviral therapy. Patients presenting with CD4+ cell counts below 200 cells/mm<sup>3</sup> require prophylaxis against PCP, preferably with trimethoprim-sulfamethoxazole (TMP-SMX). Alternatives include dapsone, aerosolized pentamidine, and atovaquone. Those with CD4+ cell counts below 100 cells/mm<sup>3</sup> and who are seropositive for *Toxoplasma gondii* (positive anti-*Toxoplasma* IgG) are at risk for toxoplasmosis and should receive prophylaxis with TMP-SMX (1 double-strength tablet daily), or with dapsone plus pyrimethamine. Patients with CD4+ cell counts below 50 cells/mm<sup>3</sup> require prophylaxis for MAC with either weekly azithromycin or daily clarithromycin. Primary prophylaxis against fungal or viral infections is not routinely recommended.

## Prophylaxes to Prevent First Episode of Opportunistic Disease in HIV-Infected Patients With Low CD4+ Cell Counts

Pathogen	Preventive Regimens	
	CD4+ Cell Count Indication (cells/mm <sup>3</sup> )	First Choice
<b>Strongly Recommended</b>		
Pneumocystis carinii	< 200	TMP-SMX QD
Toxoplasma gondii	< 100*	TMP-SMX QD
Mycobacterium avium complex	< 50	Azithromycin (1200 mg QW) or clarithromycin (500 mg BID)
<b>Evidence for Efficacy but Not Routinely Indicated</b>		
Cryptococcus neoformans	< 50	Fluconazole (100-200 mg QD)
Histoplasma capsulatum	< 100 <sup>†</sup>	Itraconazole capsule (200 mg QD)
Cytomegalovirus (CMV)	< 50 <sup>‡</sup>	Oral ganciclovir (1 g TID)

TMP-SMX, trimethoprim-sulfamethoxazole

\*Patient should also have IgG antibody to Toxoplasma

<sup>†</sup>Endemic geographic area

<sup>‡</sup>Patient should also be positive for CMV antibody

Source: US Public Health Service (USPHS); Infectious Diseases Society of America (IDSA); USPHS/IDSA Prevention of Opportunistic Infections Working Group. 2001 USPHS/IDSA guidelines for the prevention of opportunistic infections in persons infected with human immunodeficiency virus. November 28, 2001. Available at <http://aidsinfo.nih.gov>. Accessed October 24, 2004.

### Other Special Considerations for the First Encounter

**Mental health assessment:** Many patients benefit from more in-depth psychological counseling to help them accept and understand the implications of their diagnosis. Referrals to appropriate mental health professionals or support groups should be offered as indicated, and if clinical depression is suspected, the clinician should consider use of antidepressant therapy and/or referral to a psychiatrist. Both depression and bipolar disorder are more common among HIV-infected patients, and the incidence of mania increases with advancing HIV disease. Before prescribing antidepressants to patients with clinical depression, the clinician should ask the patient about a history of significant mood swings or manic behavior, since the use of antidepressants without a mood stabilizer can precipitate manic behavior.

Substance abuse: A disproportionate number of HIV-infected patients have significant drug or alcohol abuse problems at the time of diagnosis, since substance abuse is a risk factor for HIV infection. In addition to its direct adverse health effects, active substance abuse markedly increases the risk of nonadherence to medical care. These issues are best addressed long before antiretroviral therapy is required, and usually require referral to the appropriate treatment programs.

Case management: Referral to an HIV case manager can also be helpful for many patients, especially for those who are uninsured or underinsured, disabled, or who have inadequate housing. Many such patients may qualify for Medicaid, AIDS Drug Assistance Programs (ADAP), or other forms of pharmacy support, as well as a variety of other entitlement programs. Case management can be particularly helpful for supporting adherence to medical, mental health, and substance abuse visits.

Reporting and partner notification: Throughout the United States, cases of AIDS must be reported to public health authorities, although laws regarding reporting of HIV infection vary from state to state. Clinicians should be aware of the reporting regulations in their state and should take care to report appropriately, since such reports directly influence the level of federal funding (eg, Ryan White CARE Act) received by their state or community. Patients should be encouraged to notify sexual and drug-using partners of their HIV status. Laws vary from state to state regarding the physicians' ability or duty to notify partners when the patient refuses; in some cases, the health department can be enlisted to notify exposed partners without revealing the name of the patient. Physicians can also offer direct assistance, such as inviting the patient to bring the partner to a visit where the diagnosis can be discussed together and the partner can be offered testing.

Primary vs specialty care: It has been repeatedly demonstrated that HIV-infected patients do better when treated by HIV experts. Expert care has been associated with longer survival, decreased hospital time, and lower cost than care by generalists. There is no well-established definition of an "HIV expert." While some have received subspecialty training in infectious diseases, others have no subspecialty training but have become experts as a result of clinical experience and continuing medical education. Moreover, not all infectious disease specialists can be viewed as HIV experts. Expertise in HIV care is usually defined on the basis of clinical experience (the number of HIV-infected patients managed) and ongoing continuing medical education, including attendance at HIV-related medical conferences.

All patients with HIV infection should be cared for by HIV experts and should ideally begin seeing such a physician before initiation of the first antiretroviral regimen. This can be achieved in one of several ways. In some cases, the HIV expert, who is usually an internist or family practitioner, also provides primary medical care for the patient. In other cases, the HIV expert provides ongoing care only for HIV infection, while the primary care clinician coordinates care and manages other medical problems. A third model, which is especially well suited for patients living in rural areas or communities with minimal access to HIV experts, involves periodic use of an HIV expert in a consultative role, sometimes via telephone or email contact. The initial encounter is an

appropriate time to determine and discuss the healthcare model to be employed, which is sometimes dictated by external factors such as the patient's insurance status.

Advance directives: Now that antiretroviral therapy has become so effective, the emphasis of HIV care has shifted away from end-of-life issues. Nevertheless, everyone should have advance directives (eg, living wills and durable powers of attorney for health-related decisions), and this is no less true for HIV-infected patients. The initial encounter may not always be the best time to bring this up. On the other hand, when this information is presented in a routine fashion to asymptomatic patients, it is often less threatening than when the discussion is initiated at the time of declining health status.

## **Conclusions**

Given the growing time constraints facing clinicians today, it may not be possible to cover all of the issues discussed in this article in a single, initial visit. In some cases, for example, the medical evaluation may need to be deferred in order to deal with more immediate issues, such as patient counseling and education. The components of the "initial evaluation" may in fact need to be spread out over a series of early clinic visits, especially in healthy asymptomatic patients who do not require immediate antiretroviral therapy or treatment of opportunistic infections.

The initial encounter with the newly diagnosed patient with HIV infection is an invaluable opportunity for the clinician to gather information from the patient, while at the same time providing the patient with information he or she needs to deal with this new diagnosis. Early encounters should ideally lead to the formation of a long-lasting partnership between the clinician and patient, which is essential for successful therapy of HIV infection.

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### Post-Test

1. Which of the following should be assessed during the initial encounter?

Approximate time and source of infection

- A. Family medical history
- B. Risk of coinfection or latent infection
- C. Sexual and/or drug-using contacts
- D. All of the above should be assessed

2. Which of the following immune function parameters should be assessed at the initial encounter to guide treatment decisions?

- A. CD4+ cell count
- B. CD8+ cell count
- C. CD4+/CD8+ ratio
- D. All of the above should be assessed

3. After performing the test at the first encounter, how often should nontreponemal syphilis serology be assessed in HIV-infected patients?

- A. At least once a year
- B. Every 2 years
- C. Every 5 years
- D. It is not necessary after the first encounter

4. Which of the following vaccinations is NOT indicated for HIV-infected adults?

- A. *Haemophilus influenzae* type b vaccine
- B. Hepatitis A vaccine
- C. Hepatitis B vaccine
- D. Pneumococcal polysaccharide vaccine

5. Which of the following prophylaxes is routinely indicated for an HIV-infected patient with a CD4+ cell count of 150 cells/mm<sup>3</sup>?

- A. Azithromycin
- B. Fluconazole
- C. Ganciclovir
- D. Trimethoprim-sulfamethoxazole

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## Physical Examination Checklist

Patient Name \_\_\_\_\_ Provider/Attending \_\_\_\_\_

Code \_\_\_\_\_ Risk Level \_\_\_\_\_ Race \_\_\_\_\_

D.O.B \_\_\_\_\_ Phone Number \_\_\_\_\_

Additional Comments \_\_\_\_\_

Fundoscopic examination

Screen for cytomegalovirus retinitis and other HIV-related ocular complications.

• Results: \_\_\_\_\_

• Consider dilated fundoscopic examination by ophthalmologist in patients with advanced HIV disease (eg, CD4+ cell count < 50-100 cells/mm<sup>3</sup>)

Oropharynx examination

Screen for candidiasis, oral hairy leukoplakia, and other oral lesions

Assess dentition and look for gingivitis

• Results: \_\_\_\_\_

Lymph node examination

• Generalized lymphadenopathy common

Screen for asymmetric or rapidly enlarging lymph nodes - may reflect underlying infection or malignancy

• Results: \_\_\_\_\_

Genital and anal examination

Screen for internal and external lesions

Herpes Result: \_\_\_\_\_

Condylomata Result: \_\_\_\_\_

## Physical Examination Checklist

Patient Name \_\_\_\_\_ Provider/Attending \_\_\_\_\_

Neurologic examination

- Assess overall neurologic status                      Result: \_\_\_\_\_
- Assess lower-extremity peripheral nerve function
  - Measure vibratory sensation in the toes              Result: \_\_\_\_\_
  - Check ankle reflexes                                      Result: \_\_\_\_\_

Skin examination

- Screen for
  - Seborrheic dermatitis                                      Result: \_\_\_\_\_
  - Psoriasis    Result: \_\_\_\_\_
  - Folliculitis    Result: \_\_\_\_\_
  - Kaposi's sarcoma    Result: \_\_\_\_\_
  - Common warts    Result: \_\_\_\_\_
  - Molluscum contagiosum                                      Result: \_\_\_\_\_
  - Cutaneous manifestations of opportunistic infections      Result: \_\_\_\_\_

## Baseline Laboratory Test Checklist

### Part 1: HIV-Related and Hematologic Tests

---

Patient Name \_\_\_\_\_ Provider/Attending \_\_\_\_\_

Code \_\_\_\_\_ Risk Level \_\_\_\_\_ Race \_\_\_\_\_

D.O.B \_\_\_\_\_ Phone Number \_\_\_\_\_

Additional Comments \_\_\_\_\_

CD4+ cell count

Perform at baseline

• Result: \_\_\_\_\_

Perform every 3-6 months (depending on rate of CD4+ cell count decline)

• Result: \_\_\_\_\_

Plasma HIV-1 RNA (viral load) Result: \_\_\_\_\_

- Confirm HIV-1 infection
- Assess extent of viral replication
- Use standard (rather than ultrasensitive) assays in untreated patients

HIV serology Result: \_\_\_\_\_

- Repeat if HIV diagnosis has not been firmly established

HIV resistance test Result: \_\_\_\_\_

- Perform as soon as possible after HIV diagnosis
- Genotype testing is preferred

Complete blood count (CBC) with differential

- Perform at baseline and routinely thereafter
- Assess for

Anemia Result: \_\_\_\_\_

Leukopenia Result: \_\_\_\_\_

Thrombocytopenia Result: \_\_\_\_\_

## Baseline Laboratory Test Checklist

### Part 2: Chemistry and Metabolic Tests

---

Patient Name \_\_\_\_\_ Provider/Attending \_\_\_\_\_

Code \_\_\_\_\_ Risk Level \_\_\_\_\_ Race \_\_\_\_\_

D.O.B \_\_\_\_\_ Phone Number \_\_\_\_\_

Additional Comments \_\_\_\_\_

Chemistry panel

- Perform at baseline and routinely thereafter

Assess renal function

BUN Result: \_\_\_\_\_

Creatinine Result: \_\_\_\_\_

Assess liver "function"

AST Result: \_\_\_\_\_

ALT Result: \_\_\_\_\_

Bilirubin Result: \_\_\_\_\_

Alkaline phosphatase Result: \_\_\_\_\_

• If abnormal renal function identified:

- Evaluate further
- Assess possible HIV-associated nephropathy in black patients

• If abnormal transaminases identified:

- May indicate alcohol abuse or underlying viral hepatitis

• If elevated total protein identified:

- No further work-up required, unless severe

• If low albumin identified:

- May suggest advanced disease, malnutrition, or protein-losing enteropathy

Urinalysis Result: \_\_\_\_\_

- Consider baseline testing, especially in black patients

**Baseline Laboratory Test Checklist****Part 2: Chemistry and Metabolic Tests**

---

Patient Name \_\_\_\_\_ Provider/Attending \_\_\_\_\_

 Glucose-6-phosphate dehydrogenase (G6PD) Result: \_\_\_\_\_

- Use to identify patients at risk of hemolysis with receipt of oxidant drugs (ie, dapsone, primaquine, or sulfonamides)
- Consider baseline testing in patients at risk for G6PD deficiency
  - Persons of African descent
  - Persons of Mediterranean descent
- Testing less accurate when performed during episodes of hemolysis

 Fasting lipid panel Results: \_\_\_\_\_

- Perform after a 9- to 12-hour fast
- Defer if patient is acutely ill

 Testosterone level

- Consider in men who report
  - Fatigue
  - Weight loss
  - Depression
  - Change in libido or sexual function
- Testing is most accurate when performed in the morning

 Total testosterone levels Result: \_\_\_\_\_

- Low levels suggest a diagnosis of hypogonadism

 Free testosterone levels Result: \_\_\_\_\_

- Order in symptomatic patients with normal total testosterone levels
- Can also be ordered concurrently with total testosterone test

## Baseline Laboratory Test Checklist

### Part 3: Serologic Tests

---

Patient Name \_\_\_\_\_ Provider/Attending \_\_\_\_\_

Code \_\_\_\_\_ Risk Level \_\_\_\_\_ Race \_\_\_\_\_

D.O.B \_\_\_\_\_ Phone Number \_\_\_\_\_

Additional Comments \_\_\_\_\_

Nontreponemal syphilis serology ( VDRL,  RPR,  STS)

• Perform at baseline Result: \_\_\_\_\_

• Repeat yearly Result: \_\_\_\_\_

- Repeat more frequently in high-risk patients

• Confirm positive serologies with a treponemal serologic test

○ FTA-ABS Result: \_\_\_\_\_

○ MHA-TP Result: \_\_\_\_\_

○ Lumbar puncture Result: \_\_\_\_\_

• Recommended for patients with abnormal neurologic examination

• Consider for

- Patients with late latent syphilis
- Patients with syphilis of unknown duration
- Patients experiencing treatment failure

## Baseline Laboratory Test Checklist

### Part 3: Serologic Tests

---

Patient Name \_\_\_\_\_ Provider/Attending \_\_\_\_\_

Hepatitis testing

- HBsAg Result: \_\_\_\_\_
- HBsAb and possibly anti-HBc Result: \_\_\_\_\_
  - Order to assess candidacy for HBV vaccination
- HBV DNA PCR assay Result: \_\_\_\_\_
  - Perform in patients with positive HBsAg or positive anti-HBc with negative HBsAg and HBsAb
- Anti-HCV antibody Result: \_\_\_\_\_
- Quantitative HCV RNA assay Result: \_\_\_\_\_
  - Perform in
    - Seronegative patients with abnormal hepatic transaminases
    - Seronegative injection drug users
    - Seropositive patients
  - HIV/HCV coinfection requires further evaluation to include:
    - HCV RNA Result: \_\_\_\_\_
    - HCV genotype Result: \_\_\_\_\_
    - Alpha-fetoprotein levels Result: \_\_\_\_\_
    - Radiographic liver imaging Result: \_\_\_\_\_
    - Liver biopsy if patient believed to be a candidate for therapy
      - Result: \_\_\_\_\_
- Total HAV antibody Result: \_\_\_\_\_
  - Use to assess candidacy for HAV vaccination

## Baseline Laboratory Test Checklist

### Part 3: Serologic Tests

---

Patient Name \_\_\_\_\_ Provider/Attending \_\_\_\_\_

*Toxoplasma gondii* serology (anti-*Toxoplasma* IgG)      Result: \_\_\_\_\_

- Use to screen for latent infection
- Seronegative patients
  - Counsel to avoid contact with cat feces and undercooked meat
- Seropositive patients
  - Provide *Toxoplasma* prophylaxis when CD4+ cell count < 100 cells/mm<sup>3</sup>

CMV serology (anti-CMV IgG)      Result: \_\_\_\_\_

- Sometimes recommended to identify latent CMV infection
  - Men who have sex with men and drug users at higher risk, presumed positive
  - Consider in lower-risk patients
- Seronegative patients
  - Provide prevention counseling
    - Safer sexual practices
    - Receipt of CMV-negative or leukocyte-reduced blood products during transfusion
- Seropositive patients
  - Primary prophylaxis NOT currently indicated

Anti-varicella IgG      Result: \_\_\_\_\_

- Consider in patients who do not give a reliable history of chickenpox or shingles
- Seronegative patients
  - Provide varicella zoster immune globulin (VZIG) in event of exposure

## Baseline Laboratory Test Checklist

### Part 4: Other Infections and Cancers

---

Patient Name \_\_\_\_\_ Provider/Attending \_\_\_\_\_  
Code \_\_\_\_\_ Risk Level \_\_\_\_\_ Race \_\_\_\_\_  
D.O.B \_\_\_\_\_ Phone Number \_\_\_\_\_  
Additional Comments \_\_\_\_\_

Screen for sexually transmitted diseases in addition to syphilis

Urine test (for both symptomatic and asymptomatic patients)

- Screens for Chlamydia Result: \_\_\_\_\_
- Screens for Gonorrhea Result: \_\_\_\_\_
- Perform at baseline
- Perform routinely thereafter for at-risk patients
  - Women are at higher risk for asymptomatic infection

Pelvic examination Result: \_\_\_\_\_

- A wet mount should be performed to screen for *Trichomonas vaginitis*

Cervical and/or anal Pap smear

Cervical Pap smear using liquid-based cytology

- Use to screen for human papillomavirus (HPV)-related dysplasia
- Perform at baseline Result: \_\_\_\_\_
- Perform a second time during the first year Result: \_\_\_\_\_
- Normal results -repeat test annually
- Abnormal results
  - Evaluate by colposcopy Result: \_\_\_\_\_

Anal Pap smears Result: \_\_\_\_\_

- Especially recommended in women and men who have sex with men
- Use to screen for HPV-related anal dysplasia
- Abnormal results
  - Evaluate by high-resolution anoscopy Result: \_\_\_\_\_
  - Biopsy suspicious lesions Result: \_\_\_\_\_

## Baseline Laboratory Test Checklist

### Part 4: Other Infections and Cancers

---

Patient Name \_\_\_\_\_ Provider/Attending \_\_\_\_\_

Tuberculin skin testing Result: \_\_\_\_\_

- Perform at baseline in all HIV-infected patients
- Positive result
  - Induration  $\geq$  5 mm at 48 hours
- Treat latent infection once active tuberculosis is ruled out
- Consider repeat testing in
  - Patients at high risk for tuberculosis
  - Cases where initial test performed in a patient with a low CD4+ cell count prior to HAART
- “Anergy testing” is NOT recommended

Chest radiograph Result: \_\_\_\_\_

- NOT a standard test for asymptomatic patients
- Consider to establish baseline image for future comparison
- Consider to rule out subclinical tuberculosis

Cancer screening

- Follow recommendations for screening for

- Colorectal cancer Result: \_\_\_\_\_
- Prostate cancer Result: \_\_\_\_\_
- Breast cancer Result: \_\_\_\_\_
- Gynecologic cancers Result: \_\_\_\_\_