

# HUMAN IMMUNODEFICIENCY VIRUS (HIV) DISEASE PRIMARY CARE OF HIV-INFECTED ADULTS

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**ABSTRACT : HIV infection is increasingly becoming a chronic illness as effective treatment allows patients to live longer and stay healthier. HIV-infected patients often benefit from having both a generalist familiar with primary care medicine and a HIV expert involved in their care. This article is geared at the generalist who is involved with the care of HIV-infected patients and presents a series of cases to address topics important in the primary care of patients with HIV infection.**

Patients with human immunodeficiency virus (HIV) infection are living longer and often staying healthier, thus increasing the need for physicians to be familiar with their primary care needs. This article will present a series of illustrative cases to help address issues important in the primary care of patients with HIV infection.

## DIAGNOSING HIV INFECTION

*CASE 1 : Ms. Li is a 28-year-old woman who presents to her primary care physician because of new skin problems. She otherwise feels well. She is engaged to be married later this year. She is on an oral contraceptive and does not use condoms. She reports being only sexually active with her fiancé and believes they are in a mutually monogamous relationship. She has been in four previous sexual relationships and believes one partner may have used intravenous (IV) drugs in the past. She denies ever having a sexually transmitted illness ; however, she was seen in the emergency room five years ago and diagnosed with pelvic inflammatory disease. Her physical exam is normal except for a severe case of seborrheic dermatitis.*

### Recognizing and screening for chronic HIV infection

The primary care of patients with HIV infection starts by recognizing which patients are at risk for HIV infection and offering appropriate screening. Ms. Li has many

clues that should lead her primary care physician to consider screening her for HIV. She has new severe seborrheic dermatitis, a history of sexual activity with a partner who was potentially at risk of having HIV, serial monogamy with several sexual partners, and a history of a possible sexually transmitted disease (STD). She also does not use condoms. All of these factors should alert her physician to discuss with her the pros and cons of obtaining an HIV test. Table I outlines the classic risk factors for HIV and other conditions that should alert one to consider testing for chronic HIV infection [1]. Any patient who asks for an HIV test should be screened.

The Center for Disease Control and Prevention in the US now recommends that screening for HIV infection be incorporated into routine primary care visits [2]. Two recent *New England Journal of Medicine* articles found routine voluntary screening even in relatively low-prevalence populations to be as cost-effective as many commonly accepted screening interventions [3-4]. All HIV testing should be voluntary and confidential. Mandatory testing may inhibit patients from seeking out appropriate care.

Ms. Li should be counseled regarding the concern that HIV is a possibility and consent for HIV testing should be obtained. Screening for chronic HIV infection is usually accomplished by obtaining an enzyme linked immunoassay (ELISA) antibody test. Ms. Li needs to understand that it can take up to six months for detectable antibodies to develop following infection and if she may have been recently exposed the test should be repeated in six months. If the ELISA is positive a more specific test, generally the Western Blot (WB) antibody test, is performed before the patient is diagnosed with HIV infection.

Ms. Li should be counseled regarding safe sexual practices and one should ensure she understands how to use a condom at the time HIV screening is offered. If there is any concern regarding intravenous drug use (IVDU), patients also need to be counseled regarding the importance of sterile needle and syringes and not sharing any injection paraphernalia.

Rapid HIV testing is increasingly being performed and is encouraged by the CDC in situations where patients are likely not to return for the results of their HIV test. A rapid test using blood, oral fluid or urine can be done even in settings with limited resources and the results can be available in 10-60 minutes. Positive results should be confirmed with a very specific test such as the WB and requires a return visit [5].

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**TABLE I**  
INDICATIONS FOR HIV SCREENING

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**HIGH-RISK BEHAVIORS**

- Multiple sexual partners including serial monogamous relationships
- History of giving or obtaining sex for drugs or money
- History of anal intercourse
- History of sex with an intravenous drug user, person at risk for HIV, or person with known HIV infection
- History of a sexually transmitted disease
- History of intravenous drug use
- History of having received blood or blood products before 1985

**CLINICAL SIGNS/CLUES**

- Desires HIV screening
  - Active tuberculosis
  - Herpes zoster in a healthy person < 50 years
  - New severe psoriasis or other new unexplained severe skin disorder
  - History of hepatitis B or C
  - Cervical cancer or HPV infection
  - Thrush not related to recent antibiotic use
  - Unexplained cachexia or weight loss
  - Diffuse lymphadenopathy
  - Unexplained thrombocytopenia, leukopenia, or anemia
  - History of an opportunistic or unusual infection in an otherwise healthy individual
  - Prolonged unexplained illness despite evaluation
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*Adapted with permission from Mayo Clinic Proc 2002 ; 77 : 957-63. [1]*

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*CASE 2 : Ms. Jones is a 47-year-old woman who presented to her primary physician six years ago with complaints of fever, fatigue, swollen glands, rash and sores in her mouth. She reported being sexually active only with her husband. Her physical exam was remarkable for posterior cervical lymphadenopathy and aphthous ulcers. Her physician diagnosed probable rubella. Six years later she presented to her local emergency room complaining of persistent fatigue following a course of antibiotics for "bronchitis." Her physical exam was remarkable for oral thrush. Her CBC revealed pancytopenia. After an extensive evaluation she is found to be HIV positive with a CD4 count of 17.*

**Recognizing and testing for acute HIV infection**

This case illustrates an unfortunately not uncommon scenario. Mrs. Jones most likely was symptomatic with acute or a primary HIV infection when she saw her physician with complaints suggestive of a viral syndrome six years ago. Most patients infected with HIV are not diagnosed until many years after infection, despite the fact that most patients with primary HIV infection are symptomatic. The most common symptoms of primary HIV infection are fever, sore throat, rash, fatigue, weight loss and myalgias, often mimicking a mononucleosis syndrome. About one quarter of symptomatic patients have symptoms and signs suggestive of aseptic meningitis. Primary HIV infection presents in many varied ways : patients occasionally have

illnesses associated with severe immunodeficiency related to sudden declines in the CD4 count, gastrointestinal symptoms such as abdominal pain and diarrhea may be prominent or patients may have only mild or no symptoms [6].

When primary HIV is suspected, an ELISA antibody test should be obtained and either a viral load test that measures the number of HIV particles in plasma or a p24 antigen test should be done. Viral load testing is more sensitive for HIV infection ; however, the p24 antigen is more specific. The specificity of the viral load is greatly increased if a cut off of 10,000 copies/ml is used. Patients with the acute retroviral syndrome have very high viral loads, and this allows one to separate true positives from false positives. The ELISA test is usually negative but if the ELISA is positive the WB should be negative or indeterminate in primary HIV infection [7].

**INITIAL EVALUATION  
FOR HIV-INFECTED PATIENTS**

*CASE 3 : Mr. Best was referred to you after testing positive for HIV during a STD screen at a local STD clinic. He reported having unprotected sex with multiple male partners. One of his partners was recently diagnosed with AIDS, which prompted him to get tested. He has not been seen by a physician for several years and now is very anxious about the diagnosis.*

### **How does one counsel a patient with a new diagnosis of HIV infection ?**

Delivering the diagnosis of HIV infection is often difficult. The best approach is to prepare the patient with pre- and post-HIV test counseling. All patients who are to be tested should receive information regarding how acquiring and transmitting HIV can be prevented, the importance of obtaining test results, and the meaning of test results in understandable language. This preventive counseling is useful in patients with either positive or negative test results [8]. Once the test comes back positive, the physician has to be prepared to provide emotional support and must be knowledgeable regarding available HIV resources. Appropriate referral to social workers or nurses with expertise in HIV counseling and who are able to assist with other needs of the patient (e.g. housing, food, medical care coverage, and emotional support) is often critical.

The patient's knowledge regarding HIV needs to be assessed. Physicians should explicitly discuss and clarify any misconceptions regarding HIV transmission risk to partners associated with specific sexual activities or needle sharing. Patients should be counseled regarding the most effective methods for preventing transmission (e.g. sexual abstinence, consistent and correct use of condoms regardless of the serostatus of partners). Patients who inject illicit drugs should be strongly encouraged to cease injecting and enter substance abuse treatment programs. Persons who continue to inject drugs should be advised to always use sterile injection equipment and to never reuse or share needles, syringes, or other injection equipment [8].

The emotional impact of hearing an HIV-positive test result may prevent patients from clearly understanding the information and additional counseling sessions are often necessary.

*You meet Mr. Best for the first time and calmly counsel him regarding to the meaning of his positive HIV test, the need for further care, and the importance of preventing transmission. You discuss the necessity of always using condoms within every sexual encounter, including oral sex, regardless of the HIV status of his partner.*

### **What history is important to obtain from an HIV-infected patient at the initial encounter ?**

The baseline medical history is similar to the standard general medical history obtained for non-HIV infected patients. This should include a detailed past medical history particularly with respect to unusual illnesses in the past that in retrospect may now be thought to be HIV related, a detailed social history, medication use, allergy information, family history and a complete review of systems. History of previous sexually transmitted diseases, hepatitis, tuberculosis or exposure to tuberculosis and results of previous tuberculin skin tests (TST) should be obtained. Immunization history should be documented, especially the last tetanus booster, pneumococcal vaccine, and hepatitis A and B vaccines. Family

history, especially of coronary artery disease, has become important, as HIV patients are living longer and developing treatment related hyperlipidemia and diabetes. Travel history to areas of endemic infection, occupational history, and information regarding pets and other animal contact can all provide clues to future potential infection risk [9-10]. The review of systems should be thorough and comprehensive, with an emphasis on symptoms potentially related to HIV (e.g. fever, night sweats, weight loss, oral thrush, swallowing difficulties, respiratory symptoms, depressed mood, neurological symptoms such as visual changes, memory impairment and neuropathy).

The date of the diagnosis of HIV infection, dates of prior negative HIV test results, timing of high risk behaviors and possible exposure to HIV and symptoms suggestive of acute retroviral infection are all important pieces of history. This information can be used to estimate the approximate date of infection and give one an idea of the speed of progression of the disease. Patients who were diagnosed or treated for HIV infection elsewhere should have the diagnosis confirmed and a thorough antiretroviral medication history taken. The antiretroviral medication history is generally more helpful than the results of resistant testing in estimating resistance that has developed during treatment with prior regimens and is critical for future treatment success.

Patients should be asked whether they can recall their lowest CD4 cell count and their highest viral load. Patients should be asked about prior HIV-associated complications including opportunistic infections, malignancies, and HIV-related symptoms [9].

### **What physical examination findings are especially important in patients with newly diagnosed HIV ?**

A complete physical examination should be done in all newly diagnosed HIV patients. This is an opportunity to specifically look for signs of HIV-related conditions and opportunistic infections, as well as establishing a baseline for future visits. Many HIV-related conditions affect the skin and therefore the skin exam needs to be detailed and complete. One should look for lesions suggestive of Kaposi's sarcoma, disseminated infection and inflammatory skin conditions such as psoriasis. Patients should be examined for lymphadenopathy and hepatosplenomegaly. A detailed oropharyngeal examination looking for Kaposi's sarcoma, oral thrush, oral hairy leukoplakia, gingivitis, and aphthous ulcers is also indicated. A baseline neurological exam including a mini-mental status exam should be included, and if there is any evidence of HIV dementia, full neuropsychological testing should be obtained. Special attention should also be paid to external genitalia and the perirectal area. Ulcerative lesions, vesicles and crusted lesions should be cultured for herpes simplex virus, syphilis and chancroid. Men who have sex with men and HIV-infected women are at increased risk for anal high grade squamous intraepithelial lesion (HSIL). Some evidence supports anal Papanicolaou

nicolaou (pap) smears in these populations. Further studies on screening and treatment program of anal HSIL need to be completed before a general recommendation can be made. Some clinicians screen high-risk patients (e.g. any patients with perianal warts) with annual anal Pap smears [11-12].

The initial exam in HIV-infected women should include a bimanual pelvic examination, speculum exam and Pap smear to rule out cervical dysplasia and cancer. The exam in HIV-infected men should include a digital rectal and prostate exam. Rectal tone, discharge and tenderness should be specifically noted in all patients with a history of anal intercourse.

### **What laboratory tests should be ordered in newly diagnosed HIV-infected patients ?**

Patients who have no documentation of their HIV serological test result should have a repeat ELISA with confirmatory WB testing at the initial visit. CD4 cell count and plasma HIV viral load should be obtained to assess prognosis, determine the need for antiretroviral therapy, and to define a baseline for monitoring response to therapy. HIV resistance testing is very helpful in patients presenting during or shortly after acute HIV infection but over time, resistant virus is generally overgrown by wild-type virus, so in patients with chronic infection, resistance testing is helpful only if it yields positive results. Other reasonable baseline laboratory tests include a CBC, G6PD screening in patients at high risk (e.g. African American, Mediterranean, East Indian, and Southeast Asian patients), fasting glucose, lipid profile, liver function tests, creatinine and urinalysis. Baseline serologic testing for *Toxoplasma gondii*, Cytomegalovirus (CMV), and viral hepatitis A, B, and C should be obtained. Screening for syphilis, chlamydia and gonorrhea should be done in every HIV-infected patient regardless of risk behavior. Women's pelvic exam should include a wet mount examined for *Trichomonas* species [9]. TST and a chest X-ray to detect latent or active tuberculosis are recommended.

### **What immunizations are appropriate for a patient with newly diagnosed HIV ?**

All newly diagnosed HIV-infected patients should have their immunization history reviewed and updated. HIV-infected patients who are asymptomatic with a CD4 cell count  $> 200$  cells/mm<sup>3</sup> should respond well to immunization. Options for patients with low CD4 counts are to delay immunization (particularly if initiating treatment and an increase in CD4 is expected) or immunize and repeat vaccination when the CD4 cell count increases to  $> 200$  cells/mm<sup>3</sup>. A tetanus booster should be given every 10 years. The pneumococcal vaccine should be given and should be repeated once five years after the initial vaccine. The hepatitis B series should be given if the patient is seronegative. Hepatitis A immunization is recommended if the patient is a man who has sex with men, lives or has impending travel to endemic areas, has

chronic hepatitis C, a history of chronic liver disease, or a history of IVDU. An annual influenza vaccine should be considered.

Live vaccines, including oral polio vaccine, varicella zoster vaccine, BCG, oral typhoid vaccine, yellow fever vaccine, and inhaled influenza vaccine (Flumist) are generally contraindicated in HIV-infected patients. Measles-mumps-rubella vaccine is contraindicated in HIV-infected patients only if they are severely immunodeficient (CD4 cell counts  $< 200$  cells/mm<sup>3</sup>).

*You obtained a thorough history, performed a complete physical examination, and ordered the previously recommended tests. The results of Mr. Best's laboratory tests are significant for previous exposure to CMV and toxoplasmosis with positive IgG serologies. His CD4 cell count is 560 cells/mm<sup>3</sup> and his viral load is 55,000 copies/ml. Other serological tests and his TST results are negative. You offer him a tetanus booster, a Pneumovax and immunization against hepatitis B. You reassure Mr. Best that even though he is infected with HIV, the chance of him developing an illness associated with HIV is not of immediate concern.*

### **PROPHYLAXIS OF OPPORTUNISTIC INFECTIONS**

*CASE 4 : Mr. Cote is a 50-year-old homosexual man who was recently diagnosed with AIDS and central nervous system (CNS) toxoplasmosis. He presented with fever, altered mental status, and his CT brain revealed multiple ring enhancing lesions. His initial CD4 cell count was 45 cells/mm<sup>3</sup>, and HIV viral load 66,000 copies/ml. His TST was negative (0 mm). He recovered remarkably after the initiation of pyrimethamine and sulfadiazine which was continued for 6 weeks. Highly active antiretroviral therapy was started shortly after initiation of toxoplasmosis treatment with Emtricitabine, Tenofovir and Efavirenz. His follow-up CD4 cell count 3 months later is 86 cells/mm<sup>3</sup>. You are seeing Mr. Cote as his primary care physician at 3 months follow-up. He has clearly improved clinically and had finished his treatment for CNS toxoplasmosis. What medications are recommended for Mr. Cote to prevent opportunistic infections ?*

#### **Primary prophylaxis**

Prevention of opportunistic infections in HIV patients has evolved since AIDS was first recognized 20 years ago. During the first decade of the epidemic, emphasis was placed on improving the quality and duration of life for HIV-infected patients by better recognition of, better therapy for and introduction of chemoprophylaxis against important opportunistic infections. Even after highly active antiretroviral treatment (HAART) was introduced in the United States in 1995, prophylaxis against opportunistic infections continues to improve quality of life and improve survival among patients infected with HIV. USPHS and IDSA have created guidelines for primary prophylaxis of opportunistic dis-

**TABLE II**  
**PROPHYLAXIS TO PREVENT FIRST EPISODE OF OPPORTUNISTIC DISEASE**  
**IN ADULTS AND ADOLESCENTS INFECTED WITH HUMAN IMMUNODEFICIENCY VIRUS**  
(2002 USPHS/IDSAGUIDELINE)

PATHOGEN	PREVENTIVE REGIMENS		
	Indication	First Choice	Alternatives
<i>PNEUMOCYSTIS CARINII</i>	CD4 cell count < 200/mm <sup>3</sup> OR Oropharyngeal candidiasis	Trimethoprim-sulfamethoxazole (TMP-SMZ) 1 DS/d OR 1 SS/d	Dapsone 100 mg/d OR Dapsone 50 mg/d + pyrimethamine 50 mg/wk + leucovorin 25 mg/wk OR Dapsone 200 mg + pyrimethamine 75 mg + leucovorin 25 mg/ wk OR Aerosol pentamidine 300 mg/mo OR Atovaquone 1500 mg/d OR TMP-SMX 1 DS *3/wk
TUBERCULOSIS	TST 5 mm OR Prior positive TST without treatment OR Contact with case of active TB	Isoniazid 300 mg/d + pyridoxine 50 mg/d for 9 months OR Isoniazid 900 mg + pyridoxine 100 mg 2*/wk for 9 months	For MDR-TB exposure, expert consultation is recommended
TOXOPLASMOSIS	+ anti-Toxoplasma IgG and CD4 < 100 cells/mm <sup>3</sup>	TMP-SMX 1 DS/d	TMP- SMX 1 SS/d OR Dapsone 50 mg/d + pyrimethamine 50 mg/wk + leucovorin 25 mg/wk OR Dapsone 200 mg/wk + pyrimethamine 75 mg/ wk + leucovorin 25 mg/wk OR Atovaquone 1500 mg/d ± pyrimethamine 25 mg/d + leucovorin 10 mg/ d
<i>MYCOBACTERIUM AVIUM</i> COMPLEX	CD4 < 50 cells/mm <sup>3</sup>	Azithromycin 1200 mg/wk OR Clarithromycin 500 mg bid	Rifabutin 300 mg/d OR Azithromycin 1200 mg/ wk + rifabutin 300 mg/d
VARICELLA	Chickenpox OR Shingles exposure susceptible (no hx of disease and varicella seronegative)	VZIG 5 vials (6.25 ml) + IM < 96 hr post exposure ideally in 48 hr	

*Adapted from 2002 USPHS/IDSAGuidelines for Prevention of Opportunistic Infections in Persons Infected with Human Immunodeficiency Virus [13].*

ease as summarized in Table II [13].

Primary prophylaxis against *Pneumocystis carinii pneumonia* (PCP) is indicated when the CD4 cell count is < 200 cells/mm<sup>3</sup>, or there is a history of oropharyngeal candidiasis. Recommended first line treatment is trimethoprim-sulfamethoxazole (TMP-SMZ), one double strength (DS) or single strength (SS) tablet daily [13].

Primary prophylaxis against *Toxoplasma gondii* is indicated when the IgG antibody to *Toxoplasma* is positive and the CD4 cell count is less than 100 cells/mm<sup>3</sup>. The preferred regimen is TMP-SMZ DS one tablet daily [13].

Primary *Mycobacterium avium* complex (MAC) prophylaxis is indicated when CD4 cell count is less than 50 cells/mm<sup>3</sup>. Azithromycin 1,200 mg weekly or clarithromycin 500 mg twice daily are the recommended regimens [13].

Treatment for latent tuberculosis is warranted with a TST reaction 5 mm or if the patient has had a prior positive TST without treatment or contact with an active case of active tuberculosis. Recommended treatment for presumed latent tuberculosis in patients with HIV infection is isoniazid 300 mg and pyridoxine 50 mg daily for 9 months [13].

#### Prophylaxis discontinuation

The susceptibility to opportunistic infections continues to be accurately indicated by CD4 cell count. It has become increasingly clear that chemoprophylaxis is not needed indefinitely for most patients who are receiving HAART.

Primary and secondary prophylaxis for PCP can be discontinued in adult patients who respond to HAART with an increase in CD4 cell count to > 200 cells/mm<sup>3</sup> for at least 3 months.

Toxoplasmic encephalitis (TE) primary prophylaxis should be discontinued if the patient's CD4 cell count increases to  $> 200$  cells/mm<sup>3</sup> for at least 3 months. Although patients with CD4 cell counts of  $< 100$  cells/mm<sup>3</sup> are at greatest risk for developing TE, the risk of TE occurring with discontinuation of prophylaxis when the CD4 cell count has increased to 100-200 cells/mm<sup>3</sup> has not been studied as rigorously as discontinuation with a rise to  $> 200$  cells/mm<sup>3</sup>. Currently continued prophylaxis is recommended. Discontinuation of TE secondary prophylaxis can be done when the patient has successfully completed initial therapy for TE, remains asymptomatic with respect to signs and symptoms of TE, and has a sustained increase in CD4 cell count to  $> 200$  cells/mm<sup>3</sup> following HAART (e.g. 6 months) [13].

Primary prophylaxis for MAC can be discontinued with an increase in CD4 cell count to  $> 100$  cells/mm<sup>3</sup> for at least 3 months. Patients on treatment for disseminated MAC can discontinue chronic maintenance therapy or secondary prophylaxis when they have completed at least 12 months for treatment of MAC, remain asymptomatic and have an increase in their CD4 cell count to  $> 100$  cells/mm<sup>3</sup> for at least six months [13].

*Mr. Cote clearly needs to continue secondary prophylaxis for CNS toxoplasmosis since he is still at risk for recurrence with a CD4 cell count of 86 cells/mm<sup>3</sup>. Prophylaxis can be discontinued when he achieves a sustained response to HAART with a CD4 cell count  $> 200$  cells/mm<sup>3</sup> for  $\geq 6$  months. TMP-SMZ DS one tablet daily would also provide prophylaxis against Pneumocystis carinii pneumonia. Azithromycin 1,200 mg weekly is recommended until his CD4 cell count is  $> 100$  cells/mm<sup>3</sup> for at least 3 months to prevent disseminated MAC. Once his CD4 cell count has increased to greater than 200 cells/mm<sup>3</sup>, his TST should be repeated since the reliability of TST may diminish as the CD4 cell count declines.*

## ANTIRETROVIRAL TREATMENT

*CASE 5 : Ms. Kane is a 19-year-old woman who was found to be HIV positive during STD screening. She became sexually active at the age of 15 and reports that she has been involved in unprotected sex with multiple partners. She was diagnosed with Neisseria gonorrhoea recently and found at that time to be HIV positive. Her CD4 cell count is 560 cells/mm<sup>3</sup>, and HIV viral load 54,000 copies/ml. She is asymptomatic and her physical exam is unremarkable. She is accompanied by her mom who asks about treatment.*

*CASE 6 : Mr. Walter is a 50-year-old man who has a past history of homosexuality. He is currently married and has been in monogamous relationship for the past 15 years. He was diagnosed with shingles a year ago, and presented recently to his primary physician with difficulty swallowing. His review of system is significant for increasing forgetfulness. He is found to be HIV positive with a CD4 cell count of 12 cells/mm<sup>3</sup> and viral load of 460,000 copies/ml. His exam is remarkable for several molluscum contagiosum lesions on his nose and both cheek, oral thrush, and cervical lymphadenopathy. An upper endoscopy reveals esophageal candidiasis.*

### When should antiretroviral treatment be started ?

The "right" time to start antiretroviral therapy is a moving target. There is a strong evidence for improved survival and reduced disease progression with treatment of symptomatic patients and in patients with CD4 cell counts  $< 200$  cells/mm<sup>3</sup>. Mr. Walter would clearly benefit from treatment and has over a 50% chance of dying or developing a new AIDS defining illness in the next three years if he does not initiate antiretroviral treatment. The optimal time to initiate antiretroviral therapy for patients with CD4 cell counts  $> 200$  cells/mm<sup>3</sup> is uncer-

**TABLE III**  
INDICATIONS FOR INITIATING ANTIRETROVIRAL THERAPY  
FOR THE CHRONICALLY HIV-1-INFECTED PATIENT

CLINICAL CATEGORY	CD4 Cell Count	Plasma HIV RNA copies/cc	Recommendation
AIDS-DEFINING ILLNESS OR SEVERE SYMPTOMS	Any Value	Any Value	Treat
ASYMPTOMATIC	CD4 cell count $< 200$ /mm <sup>3</sup>	Any Value	Treat
ASYMPTOMATIC	CD4 cell count $> 200$ /mm <sup>3</sup> but $< 350$ /mm <sup>3</sup>	Any Value	Treatment should be offered after full discussion of pros and cons with each patient
ASYMPTOMATIC	CD4 cell count $> 350$ /mm <sup>3</sup>	100,000	Most clinician recommend deferring therapy but some clinicians will treat
ASYMPTOMATIC	CD4 cell count $> 350$ /mm <sup>3</sup>	$< 100,000$	Defer therapy

*Adapted from Guidelines for the use of antiretroviral agents in HIV-1-Infected adults and adolescents ; April 7, 2005. Panel on clinical practices for treatment of HIV infection convened by the Department of Health and Human Services (DHHS) [14].*

tain and likely dependent on many variables. Most HIV specialists believe that evidence supports initiating therapy in asymptomatic HIV-infected persons with CD4 cell counts of 200-350 cells/mm<sup>3</sup>. The strength of the recommendation for therapy must balance other considerations, such as the patient's readiness for treatment, stability of the patient's CD4 cell count and potential drug toxicities. For asymptomatic patients with CD4 cell counts of > 350 cells/mm<sup>3</sup> and plasma HIV RNA > 100,000 copies/ml most experienced clinicians generally defer therapy but some clinicians may consider initiating treatment. Current recommendations for patients with CD4 cell counts of > 350 cells/mm<sup>3</sup> and plasma HIV RNA < 100,000 copies/ml is to defer therapy. Current recommendations from US Department of Health and Human Services for initiation of antiretroviral therapy are summarized in Table III [14].

Ms. Kane is unlikely to benefit from starting antiretroviral medication at this point since her risk of progression to AIDS or death after 3 years is minimal and antiretroviral medication is not without significant drug-related toxicity. She should be followed with a CD4 cell count and HIV viral load every 3-4 months and treatment is indicated if she develops symptoms of an AIDS related illness or her CD4 cell count decreases to < 350 cells/mm<sup>3</sup>. The patient's willingness to start and commitment to compliance with treatment is always critical to review and understand before antiretroviral treatment is prescribed.

#### PREVENTIVE CARE

*CASE 7 : Mrs. Hand is a 33-year-old woman with chronic HIV infection who has had a stable CD4 count between 350 and 420 cells/mm<sup>3</sup> and a viral load of 6,000-12,000 copies/ml for the past three years. She is not on antiretroviral medication. She continues to feel well.*

*CASE 8 : Mr. Jones is a 55-year-old overweight man who was recently started on Lopinavir/Ritonavir, Zidovudine and Lamivudine. He has no personal history of coronary artery disease ; however, his father had a myocardial infarction at age 64. He smokes one pack of cigarettes daily. His CD4 count is 280 cells/mm<sup>3</sup> and his viral load is less than 50 copies/ml. He reports feeling generally well.*

#### **How often should patients with stable HIV infection be seen and what routine testing is indicated ?**

The frequency of evaluation depends on both the stage of disease and the rate at which it is progressing [9]. Asymptomatic patients such as Mrs. Hand who have a stable and adequate CD4 count with a low viral load can be monitored for their HIV disease every 3-4 months. Mr. Jones needs monitoring of not only his CD4 count but also of his CBC, lipids, liver function tests and glucose which can be adversely affected by his antiretroviral therapy.

*Mr. Jones' CBC is normal, his total cholesterol is 245 mg/dl, HDL 33 mg/dl, triglycerides 260 mg/dl and LDL 150 mg/dl. His fasting blood sugar is elevated at 145 mg/dl.*

#### **Coronary artery disease prevention**

Coronary artery disease (CAD) is the number one killer of adults in many developed countries and patients with HIV may be at increased risk. Blood pressure needs to be assessed regularly and treated according to standard guidelines [15]. Advanced HIV disease and antiretroviral treatment are associated with lipid abnormalities. Lipid levels should be monitored prior to and within 4-6 weeks of any change in antiretroviral therapy. Patients with abnormal lipid levels should be managed according to standard guidelines with consideration for their HIV infection [9, 16-17]. Insulin resistance and impaired glucose tolerance are extremely common in patients treated with protease inhibitors. Fasting glucose levels should also be measured prior to and following any change in antiretroviral therapy. Switching from protease inhibitors to other agents may lead to the resolution of hyperglycemia and diabetes, but is not always in the best interest of the patient. Lifestyle changes in the form of diet and exercise should be recommended for all patients [9].

Nicotine dependence is very common among HIV-infected patients and quitting smoking is often the intervention that will have the most benefit on a patient's overall health and risk for coronary artery disease. Patients should be offered support in moving toward the desire to quit and with plans toward smoking cessation.

#### **Osteoporosis screening and prevention**

Premature osteopenia and osteoporosis are common in HIV-infected patients, particularly those on antiretroviral therapy. Screening for osteoporosis with a bone densitometry test is recommended for all women over the age of 65 and for postmenopausal women under age 65 who have one or more additional risk factors for osteoporosis. Risk factors include immobility, excessive alcohol use, tobacco use, hyperthyroidism, steroid use, European heritage, low body mass index, and chronic renal failure. Appropriate calcium and vitamin D supplementation should be reviewed with all patients. Patients taking antiretroviral therapy who have additional risk factors for osteoporosis may want to consider screening for osteoporosis even when they fall out of standard guidelines [9].

#### **Cancer screening**

Since patients with HIV are living longer, those who are medically doing well on or off treatment need usual cancer surveillance. Standard guidelines should be followed for breast, colon and prostate cancer screening [18]. Women should have two pap smears repeated approximately six months apart (presuming the first is normal)

and then annually if both pap smears are normal [9]. This aggressive screening for cervical cancer is recommended because of the increased risk and aggressiveness of cervical cancer among HIV-infected women. HIV-infected patients are at an increased risk of developing anal cell carcinoma and digital rectal exams need to be performed annually, and more frequently in those with a history of anal warts or rectal complaints [19]. Anal pap smears have potential as a screening test for anal cell carcinoma and their usefulness is undergoing evaluation in clinical trials [20].

### **Sexually transmitted illness screening and prevention**

Patients need to be counseled regularly regarding the importance of condom use to both prevent transmission of their infection and to prevent superinfection with a second strain of HIV and infection with other sexually transmitted illnesses. They need to be asked at each visit about their sexual activity, and screened at least annually for syphilis, gonorrhea and chlamydia. Women should have a test for trichomonas at the time of annual pap testing. Patients who are engaging in frequent high risk sexual behavior need to be screened for sexually transmitted diseases more frequently.

### **Substance abuse**

Active substance abuse of alcohol or illicit drugs is strongly associated with missing clinic appointments and failing HAART due to poor adherence. Dying from liver failure is a major cause of death among persons infected with HIV and alcohol use significantly contributes to mortality [21]. Chemical dependence issues need to be addressed at the time the person first seeks care and constantly readdressed. Chemical dependency treatment can be life saving despite the fact that chemical dependency is a life-long problem and relapses are common.

### **Additional recommendations**

Women should be screened regularly for pregnancy and counseled to seek medical attention immediately if they have new irregular bleeding, a missed menses, or new pelvic pain. Pregnancy is common among HIV-infected women and they have an increased risk of ectopic pregnancy. The earlier pregnancy is detected the greater the chance of preventing transmission to the fetus. Therefore a high index of suspicion for pregnancy with early testing is important. Depression is prevalent among HIV-infected persons and twice as high among women as men. The presence of depression and domestic violence should be screened for on a regular basis [9]. Immunizations should be reviewed and administered as discussed earlier in this article.

## **SUMMARY**

In summary, patients with HIV although still frequently diagnosed with late stage disease, are living longer and

staying healthier, particularly when compliant with treatment. Good communication skills are one of the most important tools the primary care provider has in his or her "toolbox." Primary care is primarily about communication. Patients need to be screened and effectively counseled regularly regarding ways to decrease their risk of acquiring further sexual or blood borne infection and how to prevent transmission of their infection to others. They need to understand why prophylactic and anti-retroviral medications are important and why adherence is crucial. The primary care physician should be alert to verbal and nonverbal clues to treatment noncompliance or behavioral risks that may put patients at increased risk for treatment failure. Counseling regarding behaviors that will adversely or positively affect patients' long term health is vital to obtaining desired healthy outcomes. Physician counseling has been shown to be positively related to change in health behavior and should not be underestimated [22]. Primary care of HIV patients although complex, when undertaken with a positive attitude can be rewarding for both patients and physician.

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