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HIV: Make the Diagnosis and Take the Next Step

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Recommended Citation
Stewart, Julie G., Weinberg, Amy R. "HIV: Make the Diagnosis and Take the Next Step." Clinical Advisor: For Nurse Practitioners 13.7 (Jul 2010): 15-22.

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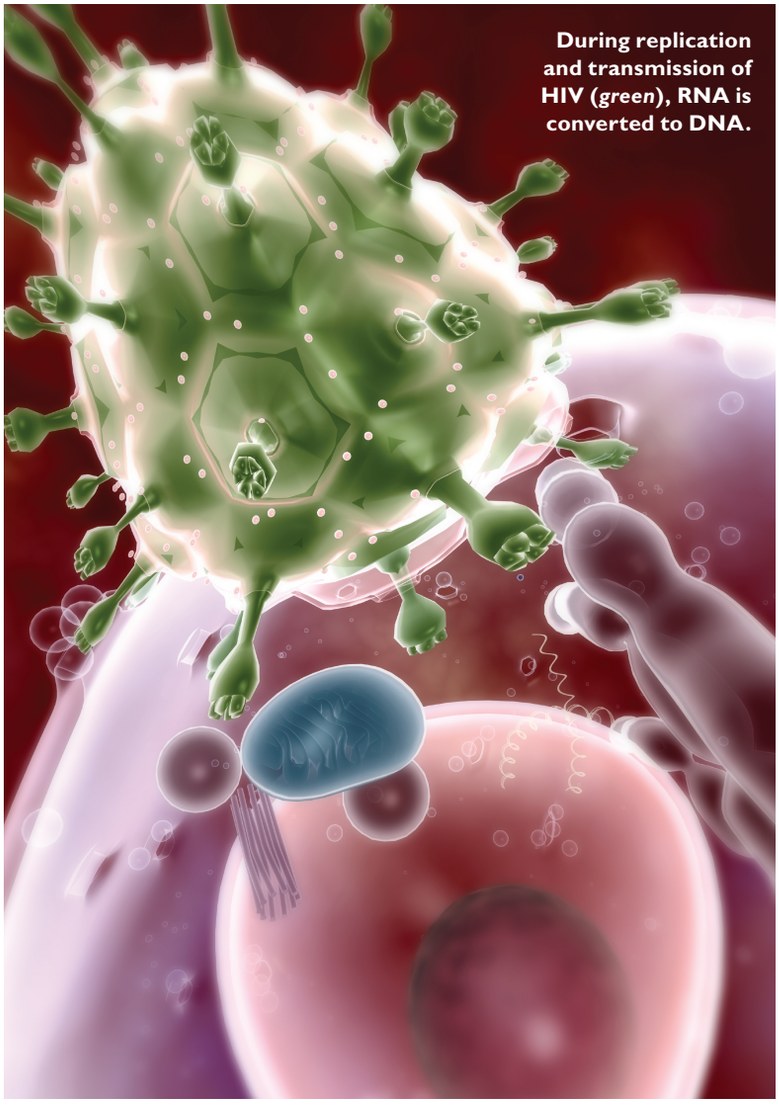
FEATURE: BY JULIE G STEWART, DNP, MSN, FNP-BC, AND AMY R. WEINBERG, DNP, MSN, FNP-BC

HIV: Make the diagnosis and take the next step

With the CDC urging screening for all willing patients, providers will be testing and managing a growing number of HIV-positive individuals.



During replication and transmission of HIV (*green*), RNA is converted to DNA.

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The CDC estimates that with more than 40,000 new infections annually, more than 1.2 million people in the United States are living with HIV—and 24% to 27% may not be aware of their infection status.[1] Studies have shown that HIV is often diagnosed late in the disease process, when the individual has already developed AIDS, which typically occurs 8 to 11 years after HIV infection.[2] Research also points to missed opportunities to offer HIV testing and diagnose the infection before AIDS develops, which would enable the newly diagnosed individuals to employ precautions to protect their partners from becoming infected.[3,4] Almost half of HIV transmissions studied by Brenner et al were attributed to transmission by newly infected persons.[5]

In response to these issues, the CDC put forth revised recommendations for HIV testing that encourage screening for patients in all healthcare settings after the person is notified that testing will be performed, unless he or she declines (opt-out screening).[4] Primary-care providers need a better understanding of trends in HIV infection and what to do when an HIV test is positive. In a recent survey of 1,165 primary-care providers, 54% of the respondents reported treating HIV-positive individuals, with 43% indicating an "increased" or a "dramatically increased" caseload over the past year.[6]

HIV viral dynamics

HIV is classified as a retrovirus that is completely dependent on CD4 T cells for copying

and surviving. The virus enters the CD4 T cell by binding onto receptors and fusing with the lipid outer layer. The virus then converts its ribonucleic acid (RNA) to deoxyribonucleic acid (DNA) through the enzyme reverse transcriptase. The enzyme integrase helps the virus to become part of the human DNA in the cell's nucleus. During transcription and translation, enzymes assist the HIV genes by converting them into messenger RNA, which then leaves the nucleus with the HIV codes within. The enzyme protease makes smaller pieces of the long strands of protein; these pieces become mature viral cores. The new virions bud from the CD4 T cell and go on to infect other cells and repeat the process. HIV can replicate itself billions of times each day.

Signs and symptoms of HIV infection

Acute retroviral syndrome (ARS) occurs early in the new infection. Approximately 50%–70 % of HIV-positive persons will experience an influenzalike illness that may consist of one symptom or a constellation of symptoms including fever, rash, pharyngitis, lymphadenopathy, and myalgias. Because these symptoms are nonspecific and frequently resolve on their own, without a high index of suspicion clinicians may not consider HIV infection in the differential diagnosis. An exposed individual usually becomes symptomatic two to four weeks after transmission and will have a markedly high HIV viral load (amount of virus in the serum).

The asymptomatic period of HIV infection can last from a few months to up to 15 years. This varies from person to person and is usually associated with the level of HIV viral load—typically, those with higher viral loads deteriorate faster than those with lower loads. During this time, the CD4 T cells usually decline at an average rate of approximately 50 cells/μL/year. The CDC defines AIDS as persons with both documented HIV infection and CD4 T cells <200/mm^3 whether other AIDS-defining conditions are present or not, or the presence of an AIDS-defining condition (*Table 1*).

Many patients will be asymptomatic during the clinical latency period, but various nonspecific findings on physical examination and in lab tests are associated with HIV. Generalized nontender lymphadenopathy involving the cervical, occipital, and/or axillary nodal chains is very common and can persist beyond primary infection. The presence of unexplained fevers, weight loss, night sweats, dementia, and neuropathy help rule in HIV infection. Skin lesions may be suggestive of HIV infection. Seborreahic dermatitis, psoriasis, molluscum contagiousum, and extensive

TABLE 1. CDC list of AIDS-defining conditions

Bacterial infections, multiple or recurrent*
Candidiasis of bronchi, trachea, or lungs
Candidiasis of esophagus†
Cervical cancer, invasive§
Coccidioidomycosis, disseminated or extrapulmonary
Cryptococcosis, extrapulmonary
Cryptosporidiosis, chronic intestinal (more than one month's duration)
Cytomegalovirus disease (other than liver, spleen, or nodes), onset at age >1 month
Cytomegalovirus retinitis (with loss of vision)†
Encephalopathy, HIV-related
Herpes simplex: chronic ulcers more than one month's duration) or bronchitis, pneumonitis, or esophagitis (onset at age >1 month)
Histoplasmosis, disseminated or extrapulmonary
Isosporiasis, chronic intestinal (more than one month's duration)
Kaposi sarcoma†
Lymphoid interstitial pneumonia or pulmonary lymphoid hyperplasia complex*†
Lymphoma, Burkitt (or equivalent term)
Lymphoma, immunoblastic (or equivalent term)
Lymphoma, primary, of brain
Mycobacterium avium complex or *Mycobacterium kansasii*, disseminated or extrapulmonary†
Mycobacterium tuberculosis of any site, pulmonary,†§ disseminated,† or extrapulmonary†
Mycobacterium, other species or unidentified species, disseminated† or extrapulmonary†
Pneumocystis jirovecii pneumonia†
Pneumonia, recurrent†§
Progressive multifocal leukoencephalopathy
Salmonella septicemia, recurrent
Toxoplasmosis of brain, onset at age >1 month†
Wasting syndrome attributed to HIV

* Only among children aged <13 years.

† Condition that might be diagnosed presumptively.

§ Only among adults and adolescents aged >13 years.

Source: Schneider E, Whitmore S, Glynn MK, et al. Revised surveillance case definitions for HIV infection among adults, adolescents, and children aged <18 months and for HIV infection and AIDS among children aged 18 months to <13 years — United States, 2008. *MMWR Recomm Rep.* 2008;57(RR-10):1-12. Available at www.cdc.gov/mmwr/preview/mmwrhtml/rr5710a1.htm; accessed June 10, 2010.

People with HIV are living longer and developing chronic diseases common to aging such as diabetes, cardiovascular disease, and osteoporosis.

condyloma are all diagnoses associated with HIV infection. Oral candidiasis (thrush) and oral hairy leukoplakia may be seen when CD4 T cells fall to less than 500/mm^3. Recurrent or severe herpetic lesions and chronic vaginal candidiasis should prompt consideration of HIV testing. Unexplained anemia, neutropenia, leukopenia, and an elevated protein level are all commonly seen laboratory abnormalities caused by HIV infection.

Diagnosis of HIV infection

During ARS, the viral load is very high—often >100,000 copies/mL. The standard test to detect ARS is the reverse transcriptase-polymerase chain reaction (RT-PCR). False-positive HIV viral loads do occur. If ARS is suspected, viral loads of <10,000 copies/mL should be repeated as this result may be a false positive or can indicate that the patient has had chronic HIV. Practitioners should note that the standard test for diagnosing HIV is the enzyme-linked immunosorbent assay (ELISA), which is confirmed with a Western blot. During ARS, the ELISA will likely be negative; the Western blot may be negative or indeterminate. These findings are consistent with the time needed for seroconversion—the development of antibodies to HIV. Seroconversion can take three to six months after infection.

After the diagnosis

Morbidity and mortality from HIV/AIDS has decreased significantly and people with HIV are living longer and developing chronic diseases common to aging such as diabetes, cardiovascular disease, and osteoporosis. This shift is attributable to the introduction of highly active antiretroviral therapy (HAART). Antiretroviral agents can be classified into six basic categories:

- nucleoside reverse transcriptase inhibitors
- non-nucleoside reverse transcriptase inhibitors
- protease inhibitors
- entry inhibitors
- fusion inhibitors
- integrase inhibitors.

Some of these drugs are manufactured in combination forms. Current recommendations suggest that if a patient is ready to start therapy, a three-drug regimen is preferable. (See aidsinfo.nih.gov/contentfiles/AdultandAdolescentGL.pdf [accessed June 10, 2010] for current guidelines on the use of antiretroviral agents in persons with HIV infection.)

Despite its benefits, HAART may be a lifelong regimen, and has short- and long-term implications that need to be considered when initiating therapy. Viruses can become resistant to certain antiretrovirals, and resistant virus can be transmitted to others in the same ways wild-type virus is transmitted (via blood or breast milk, sexually, or perinatally). Genotype resistance testing can be done to try to identify mutations that confer drug resistance.

Additionally, many of the HIV medications interact with commonly prescribed drugs. One study has estimated that HIV-positive individuals have an average life span 21 years shorter than their HIV-negative counterparts.[7] This is why after being diagnosed as HIV-positive, the patient should undergo a full history and physical examination to detect additional health issues that may be exacerbated by HIV and therapy. Initial labs must include an HIV viral load and CD4 T cell count, which will inform prognosis and determine the degree of urgency for initiating prophylaxis for opportunistic infections and HAART. Opportunistic infection can manifest at any CD4 T cell level; however, risk increases once CD4 T cell count drops below 200 cells/mm^3. Accepted thresholds of 200, 100, and 50 cells/mm^3 have been established, signifying risk of *Pneumocystis jiroveci*, *Mycobacterium avium*, and *Toxoplasma gondii* complex

TABLE 2. Recommended initial laboratory workup

CD4 panel
HIV viral load
HIV genotype (also consider tropism testing for CCR5, CX)
Complete blood count
Renal function tests
Liver enzymes
Hepatitis serologies (hepatitis A, B, C)
Toxoplasmosis antibody
Cytomegalovirus antibody
Urinalysis
Rapid plasma reagin/Veneral Disease Research Laboratory
Gonorrhea/Chlamydia
Fasting lipid profile
Herpes simplex virus

AT A GLANCE

- In one survey, 54% of primary-care providers reported treating HIV-positive individuals.
- The asymptomatic period of HIV infection can last from a few months to up to 15 years.
- Decreased morbidity and mortality from HIV/AIDS is attributable to higly active antiretroviral therapy.
- After diagnosis, HIV-positive patients should undergo a full history and physical examination.

infections, respectively; primary prophylaxis is recommend at these points.[8] Standard recommended initial laboratory workup is summarized in *Table 2*. Recommendations for prophylaxis of opportunistic infections can be found on the CDC Web site (www.cdc.gov/mmwr/preview/mmwrhtml/rr5804a1.htm; accessed June 10, 2010).

Referral to an HIV specialist is preferred, although initial laboratory workup can be done prior to the consultation to foster a more thorough discussion of the patient's options. Research has shown that quality of care for HIV patients is improved when the provider is an HIV specialist;[9] often the specialists are nurse practitioners or physician assistants.

In most cases, CD4 T cell levels and HIV viral load are checked every three months, with monitoring of CBC, metabolic panels, and lipid profiles every three to six months. Yearly tuberculosis testing (PPD), RPR testing, ophthalmologic and dental exams, gynecology exams (possibly necessary every six months if CD4 T cell count is low and/or dysplasia is present) should be done. Routine health maintenance screenings as per the general population include mammography, prostate-specific antigen screening, colonoscopy, electrocardiograms, and stress testing.

Conclusion

Compassionate, knowledgeable health-care providers can improve the likelihood that persons newly diagnosed with HIV infection will obtain the appropriate information to make good choices, prevent spread of the disease, and improve their own morbidity and mortality risks.

In summary, primary-care practitioners should:

- Verify presence of HIV infection with Western blot.
- Obtain baseline labs and perform a comprehensive physical assessment.
- Consult with an HIV specialist for plan of care.
- Reassure patient that with 100 % adherence to therapy, life expectancy is much longer than it was when HIV infection first came to the forefront when medication options were limited. ■

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