

HIV screening: We can do better

The CDC and USPSTF recommend routine HIV screening of adults. This review of the tests at your disposal, and a new diagnostic algorithm from the CDC, provide guidance.

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PRACTICE RECOMMENDATIONS

› *Screen all adolescents and adults ages 15 to 65 years for human immunodeficiency virus (HIV) infection. (A)*

› *Screen younger adolescents and older adults who are at increased risk for HIV infection on an annual basis. (A)*

› *Screen all pregnant women for HIV, including those who present in labor who are untested and whose HIV status is unknown. (A)*

Strength of recommendation (SOR)

- (A)** Good-quality patient-oriented evidence
- (B)** Inconsistent or limited-quality patient-oriented evidence
- (C)** Consensus, usual practice, opinion, disease-oriented evidence, case series

For the first 15 years of the epidemic, human immunodeficiency virus and acquired immunodeficiency syndrome (HIV/AIDS) was uniformly fatal. Between 1981 and 1996, approximately 362,000 people in the United States succumbed to the disease.¹ That began to change in the mid 1990s, though, when highly active antiretroviral therapy (HAART) came into routine use. From that point forward, HIV became a chronic, manageable disease for most patients; an estimated 1.2 million people in the United States are now living with HIV infection.²

Unfortunately, the number of new infections continues to grow. There are more than 50,000 new infections in the United States each year,² and an estimated 180,900 people have it but are undiagnosed, leading to further spread of the disease.³ The Office of National AIDS Policy has issued a National HIV/AIDS Strategy that seeks to reduce new infections by 25% in 2015, in part by identifying people with the disease who do not know their HIV status.⁴

But screening hasn't quite gotten the traction that health officials would have liked.

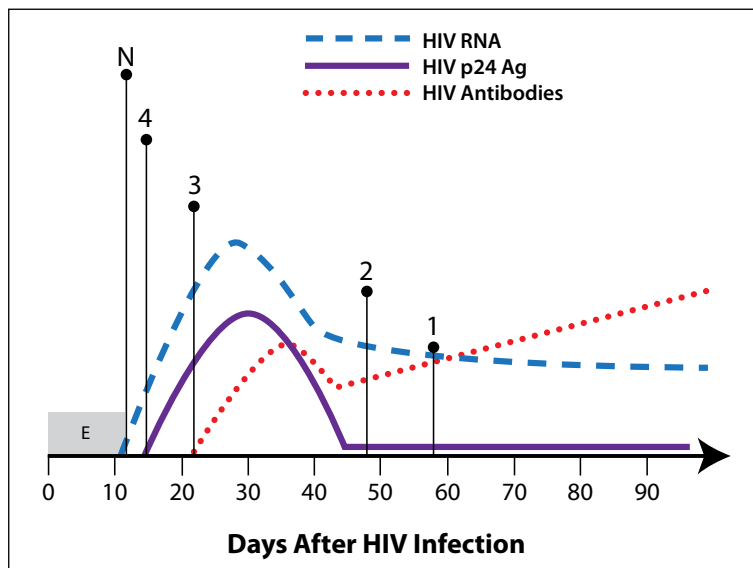
Lack of awareness by physicians? Or an unwillingness of patients?

In 2006, the Centers for Disease Control and Prevention (CDC) began recommending routine HIV screening for individuals between the ages of 13 and 64, with patients given the ability to opt out of such testing.⁵ That same year, the CDC also removed some prior barriers to testing, such as requiring written consent and pretest counseling. But as of 2009, fewer than 50% of US adults had ever been tested for HIV⁶—possibly the result of physicians being unaware of the guidelines, patients being unwilling to be tested, and/or reimbursement issues.

FIGURE 1

Screening for HIV infection: Which tests can detect which markers, and when?¹⁰

Vertical lines indicate the earliest time at which HIV can be reliably detected by the first- (1), second- (2), third- (3), and fourth-generation (4) enzyme immunoassays and nucleic acid amplification test (N), which measures HIV RNA. These are superimposed on a graphical depiction of the kinetics of circulating HIV RNA, p24 antigen, and HIV antibodies. The eclipse period (noted below as an "E") is the time when infection is occurring but HIV RNA is not yet detectable.



Ag, antigen; E, eclipse period; HIV, human immunodeficiency virus; RNA, ribonucleic acid.

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■ Conflicting recommendations may have played a role. When the CDC released its 2006 recommendations, the United States Preventive Services Task Force (USPSTF) felt there was insufficient evidence to support routine HIV screening and issued a grade C recommendation. At that time, the USPSTF recommended that only high-risk individuals and pregnant women be tested (A recommendation, meaning there was high certainty that the net benefit was substantial).

However, in April 2013, based on new evidence regarding the clinical and public health benefits of early identification of HIV infection and subsequent treatment, the USPSTF updated its recommendations. The USPSTF now encourages clinicians to screen all adolescents and adults age 15 to 65 years for HIV (A recommendation).⁷ Shortly thereafter, the American Academy of Family Phy-

sicians (AAFP) also endorsed routine HIV screening, although the AAFP calls for such screening to begin at age 18.⁸

■ Insurance now covers it... A USPSTF A recommendation carries significant health policy implications because the Affordable Care Act requires private and public health insurance plans to cover preventive services recommended by USPSTF.⁹

Integrating screening into your practice

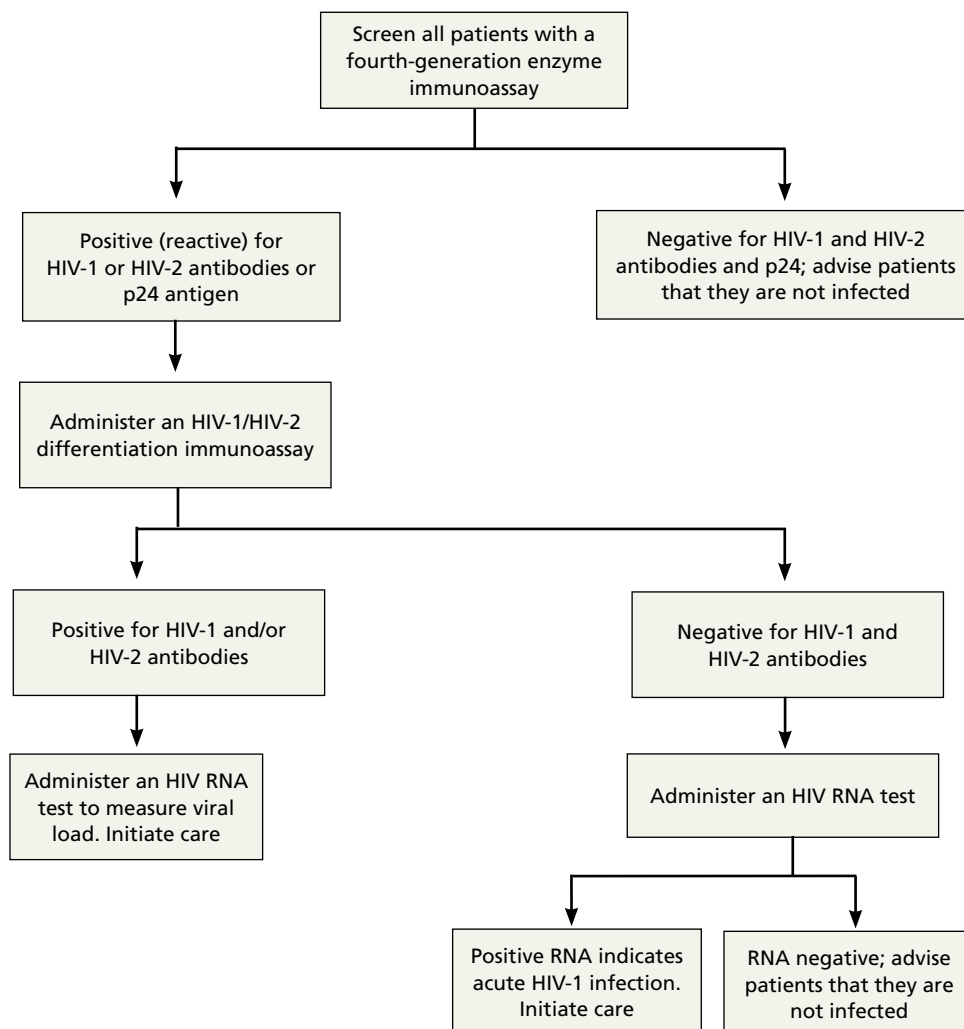
Serologic tests have come a long way. The first HIV antibody test was an enzyme immunoassay (EIA) that was introduced in 1985 and used mainly to screen the blood supply. This first-generation EIA identified only immunoglobulin G (IgG) antibodies to HIV type 1 (HIV-1). More sensitive and specific second- and third-generation EIAs have since been developed to detect both IgG and IgM antibodies, as well as antibodies to HIV-2. The third-generation assays also can detect antibodies as soon as 3 weeks after infection.

The fourth-generation EIAs were approved by the US Food and Drug Administration (FDA) in 2010¹⁰ and are the first step in the CDC's current HIV diagnostic testing algorithm. These tests can detect HIV-1/HIV-2 IgG and IgM antibodies and also p24 antigen, which is present within 7 days of the appearance of HIV RNA.¹¹ The fourth-generation assay allows for reliable detection within about 2 weeks of infection (FIGURE 1).¹⁰

■ Rapid HIV tests are also an option.¹² These tests can detect IgG and IgM antibodies in samples of saliva, whole blood, serum, and plasma. Results of rapid tests usually are available in 20 to 30 minutes and allow physicians to give patients the results while they are still in the office. In 2013 the FDA approved a combination p24 antigen/antibody rapid HIV assay that according to the manufacturer can detect infection earlier than other currently available rapid tests.¹³

■ When rapid tests are most useful. Rapid tests can be particularly useful for testing women presenting in labor who have not been screened for HIV as part of prena-

FIGURE 2

Alternative HIV diagnostic algorithm from the CDC*¹⁷

➤ Fourth-generation assays allow for reliable detection of HIV infection within about 2 weeks of infection.

HIV, human immunodeficiency virus; RNA, ribonucleic acid.

* The Centers for Disease Control and Prevention has made this proposed algorithm, which replaces the Western blot with a HIV-1/HIV-2 differentiation immunoassay, available for public comment. Studies suggest it performs better than the existing algorithm.

Adapted from: Centers for Disease Control and Prevention, *MMWR Morb Mortal Wkly Rep*, 2013.¹⁷

tal care. They also can be used to determine the need for postexposure prophylaxis in the event of a needlestick injury. According to manufacturer's data, the sensitivity of rapid tests ranges from 99.3% to 100% and specificity from 99.7% to 99.9%.¹² However, in real-world experience these numbers have been slightly lower.¹² By comparison, the sensitivity

and specificity of the fourth-generation EIAs are 99.4% and 99.5%, respectively.¹⁴

■ **The downside...** A disadvantage of rapid HIV testing is that under current FDA-approval status and CDC guidance, tests performed on oral fluid must have serologic confirmation. In addition, patients tested during the "window period" of seroconversion

➤
 When speaking with a patient who tests positive on a rapid test, consider using the phrase "preliminary positive" results.

(after infection occurs but before antibodies are detectable) will test negative with rapid HIV tests and must be reminded that repeat testing should be done within 4 to 6 weeks of their last potential exposure to the virus. In high-prevalence settings such as urban emergency departments (EDs), rapid HIV tests have detected a significant number of new infections.¹⁵ However, ED physicians and urgent care providers have been reluctant to perform HIV tests due to the lack of follow-up for most patients treated in these settings.

■ **Over-the-counter (OTC) tests.** Approved by the FDA in 2012, the OraQuick In-Home HIV Test is the only available OTC test for use at home. Patients can go to the company's Web site at www.oraquick.com to learn more about HIV and testing, and the company offers 24-hour phone support. It's not clear how many patients are taking advantage of this home testing option. The test costs approximately \$40 and several studies suggest that this price may deter patients from using it.¹⁶ In addition, it's not clear how patients who test positive using an OTC test will get appropriate medical follow-up.

New testing algorithm eliminates Western blot

Historically, a patient with a reactive (positive) EIA result would undergo the Western blot assay as a confirmatory test. Although the Western blot for HIV is highly specific (99.7%), it tests only for the IgG antibody. This could lead to a false negative test in a patient in whom IgG seroconversion has not yet occurred. Additionally, the time for HIV con-

firmation with the Western blot often is one week or longer.

Recently, the CDC has made available for public comment a diagnostic algorithm that removes the Western blot as a recommended test (**FIGURE 2**),^{17,18} This algorithm replaces the Western blot with an assay to differentiate HIV-1 and HIV-2 antibodies. Patients for whom this test is negative should undergo additional testing for HIV RNA to determine if HIV-1 is present. Positive HIV RNA would indicate acute or more recent infection. Studies suggest that this new algorithm is better than the existing algorithm at detecting HIV infections, and many reference labs have already adapted it.^{17,18}

Choosing your words carefully when giving patients their results

Patients can be given the results of a rapid HIV test during their visit, but a positive result on a rapid test should be confirmed by serologic testing. When speaking with a patient who tests positive on a rapid test, consider using the phrase "preliminary positive" results. This allows the patient to more easily process the results, knowing that a confirmatory blood draw will be done. State laws vary regarding how patients can receive HIV test results. Most states allow negative serologic test results to be given over the telephone (or electronically). For positive tests, it is preferable to give these results at a face-to-face consultation so that you can ensure the patient will have access to medical care. For more on HIV testing and lab reporting laws by state, see <http://www.cdc.gov/hiv/policies/law/states/index.html>. **JFP**

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