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HIV screening for all: The new standard of care

ABSTRACT

The US Centers for Disease Control and Prevention has revised its recommendations for screening for human immunodeficiency virus (HIV) (*MMWR Recomm Rep* 2006; 55(RR14):1–17) and now recommends HIV screening for all patients age 13 to 64 years in all health care settings, including hospital emergency departments, urgent care clinics, inpatient services, sexually transmitted disease clinics, tuberculosis clinics, and primary care offices.

KEY POINTS

Before being tested, patients should first be notified that testing will be performed unless they decline ("opt out" of screening). Separate written consent is not required, nor is prevention counseling.

People at high risk for HIV infection should be screened annually. This includes injection-drug users and their partners, people who exchange sex for money or drugs, people with an HIV-positive sex partner, and people who themselves or whose sex partners have had more than one sex partner since their most recent test.

HIV screening should be included in the routine panel of prenatal screening tests for all pregnant women. Repeat screening in the third trimester is recommended in communities with elevated rates of HIV infection among pregnant women.

FOR THE FIRST TIME in 13 years, the US Centers for Disease Control and Prevention (CDC) has revised its recommendations for testing for human immunodeficiency virus (HIV) in adults, adolescents, and pregnant women in health-care settings.[1] The report makes sweeping recommendations to enhance testing for HIV.

In short, the CDC now recommends that all patients between the ages of 13 and 64 be tested for HIV infection at least once when they are in any health care setting, including urgent care and emergency room visits and primary care appointments. Patients at higher risk (which includes heterosexuals who themselves or whose sex partners have had more than one sex partner since their last HIV test) should be tested once a year.

To ease the burden on the health care system, written consent and preventive counseling are not required. However, testing must be voluntary, and patients must be informed that they will be tested. An innovation is that permission for testing should be obtained in an "opt-out" manner: ie, health care providers inform patients that they will be tested for HIV unless they decline, rather than asking them if they would like to be tested for HIV (the "opt-in" approach).

WHY THESE CHANGES ARE NEEDED

These recommendations were formulated in response to data suggesting that the current strategy of testing on the basis of risk has failed to identify a substantial segment of HIV-infected Americans. In fact, more than 250,000 people—one fourth of all people infected with HIV in the United States—do

not know they are infected. This failure has triggered a reassessment of who should be tested and how consent for testing should be obtained.

The HIV epidemic is not over; in fact, it is expanding and evolving. After an initial decline in new infections, rates are again increasing. Of these new infections, 54% are estimated to be acquired from the 25% of infected people who are unaware of their serostatus.[2]

The increase in incidence of new infections is particularly alarming in persons of color, in women, and in people who acquire HIV through heterosexual contact. For example, 29% of those diagnosed with HIV infection between 2001 and 2004 were women. Of these, 76% were infected via heterosexual contact, and 68% were African American.[3] Infections are also increasing in rural communities, in adolescents (age 13 to 19 years), and in young adults (age 20 to 24).[1,4]

Traditionally, people who have had multiple sexual partners and men who have sex with men have been considered at increased risk. Now, high-risk sexual behavior has been clarified: gay or straight, you are at increased risk if you have had more than one sex partner since your last HIV test or if you have a partner who has had more than one partner since your last HIV test. Other risk groups are intravenous drug users, those who exchange sex for money, and those who have received unscreened blood products.

1/4 of people with HIV in the United States do not know they have it

In sum, the epidemiology of the disease has shifted strikingly, with many newly infected people coming from populations that do not consider themselves at risk.

Despite this reality, after the intense publicity of the 1980s and 1990s, the disease has moved out of the national conscience. Although HIV is now part of the fabric of America, many people are less aware of the virus than in the early days of the US epidemic, when fewer people were living with HIV.

The need to diagnose those unaware of their HIV infection has led to the recommendation to test all patients between the ages of 13 and 64 at least once, and to offer testing more frequently to those at higher risk as defined above.

HOW TO TEST MORE PEOPLE

The CDC recommendations also attempt to define the optimal strategies to maximize the number of people who undergo HIV testing.

Make patients opt out, not in

The CDC recommendations suggest that providers use the opt-out testing strategy, much like the one used for other tests such as blood cultures or screening tests for diabetes. In this scenario, patients are informed that they will be tested unless they decline.

Experience has shown that opt-out testing yields higher testing rates than opt-in testing, in which patients are asked if they are willing to be tested for a certain condition. For example, in a study in women receiving prenatal care, only 35% accepted HIV testing when it was offered using an opt-in approach, while 88% accepted it when an opt-out strategy was used.[5] Among the reasons cited by those who declined in the opt-in scenario was the fear that the provider would perceive them as engaging in high-risk behaviors.

Test everywhere

Many people in populations at risk, such as young adults, do not have an established primary care provider, but instead receive much of their care in acute care settings. Therefore, testing should be offered in all health care settings, including hospital emergency departments, urgent care clinics, labor and delivery suites, and primary care offices. The availability of highly accurate rapid testing kits increases the feasibility of this approach and eliminates the need to require patients to return for a follow-up visit to learn the results.

WHY SCREEN EVERYBODY?

Benefit to the patient

To be routinely recommended, a screening test must meet two major criteria. First, the test must be able to detect the condition earlier than without screening, with sufficient accuracy. Second, treating the disease early in its course should improve the likelihood of favorable health outcomes compared with later treatment.[6]

HIV screening easily meets these criteria. The sensitivity and specificity of the combination of the screening enzyme-linked immunosorbent assay (ELISA) and the confirmatory Western blot test exceed 99%, and rapid tests have sensitivities and specificities exceeding 98%.[7] Furthermore, currently infected patients can live at least 13 or 14 years longer with antiretroviral therapy than without, and several studies confirm that they live longer if they begin treatment earlier rather than later.[8–11]

Benefit to those not infected

Unlike many screening tests such as those for cancer, which benefit only the person tested, HIV screening has additional public health ramifications that must be considered.

For example, studies have shown that people who know they are infected are more likely to follow safe sexual practices and are therefore less likely to transmit the virus to others.[2,12] In addition, patients who then receive treatment have a reduced viral burden, which reduces the risk of transmission to a partner as well.

A clear example of this lower risk of transmission of the virus is in pregnant women. Untreated, approximately 25% of pregnant HIV-positive mothers transmit the virus to their babies. But if pregnant women undergo rapid testing in the labor and delivery suite and if those who test positive are given intrapartum therapy and the infant receives therapy postpartum, the rate of transmission can be reduced by more than 50%. And mothers who are diagnosed earlier (ie, during prenatal visits) and who achieve a viral load of less than 1,000 copies per mL with antiretroviral therapy before delivery transmit the virus to their newborn children in less than 1% of cases.[13]

Screening is cost-effective

Many have questioned whether universal testing is an appropriate expenditure of health care dollars. Some argue that the prevalence of HIV in many communities does not justify the costs of screening.

Several recent studies have analyzed the cost-effectiveness of universal screening for HIV.[9–11] HIV testing in a population with a 1% prevalence of HIV infection costs approximately $40,000 per quality-adjusted life year (QALY) saved, based on improved outcomes with antiretroviral therapy. When one incorporates the effects of decreased transmission into the model as well, the cost declines to $15,078 per QALY saved. Although the general US population has a prevalence of HIV infection of only 0.1%, when the transmission benefit is included, the cost remains less than $45,000 per QALY saved.

Screening procedures are generally considered to be cost-effective if they cost $50,000 or less per QALY saved. HIV testing of the general population meets this target and is comparable in cost to other widely accepted procedures such as colonoscopy and mammography.

RAPID TESTS ARE AVAILABLE

HIV screening can be performed using the standard test or rapid tests. In the standard testing procedure, a sample is initially tested using an ELISA. If the ELISA result is positive in duplicate, a confirmatory test (ie, a Western blot) is performed. If both tests are positive, the risk of a false-positive test is remote—about 1 in 6 to 7 million tests.[7]

HIV screening can now be performed using rapid tests that give results in minutes. These are ideal in settings in which patients may not return for follow-up, such as emergency departments or urgent care clinics. The rapid tests incorporate only the initial screening test (the ELISA).

Although the sensitivity and specificity of the ELISA by itself exceed 98%, its positive predictive value is lower in populations at lower risk. A confirmatory test is always required and helps clarify which ELISA results are false-positive. If a patient tests positive on an ELISA, the physician should wait for the result of the Western blot to confirm the diagnosis before definitively informing the patient that he or she is HIV-infected.

Patients with "indeterminate" Western blots should be evaluated by an infectious disease physician to differentiate between evolving HIV seroconversion and an indeterminate

Wait for the Western blot before telling the patient that he or she is HIV-positive

test triggered by other factors such as autoantibodies. This can be accomplished using clinical criteria, other laboratory studies, or both.

WHO WILL PAY FOR HIV CARE?

Identifying the quarter of a million HIV cases that remain undiagnosed will stress the HIV care network in the United States, and we must be sure that the resources are allocated to provide care to this group.

At present, a large proportion of HIV care is financed through the Ryan White Care Act. Established in 1990, this act is the largest federally funded program (excluding Medicare and Medicaid) for the care of those living with HIV and acquired immunodeficiency syndrome (AIDS) and includes both medical and psychosocial services. Universal testing will require a commitment in Washington to increase not only the medication budget in the Ryan White Care Act, but also the budget for providers and clinic operations, so that care for the uninsured and underinsured is secure. Otherwise, we risk informing patients that they have a treatable but otherwise terminal disease without giving them access to care.

Many HIV patients from small towns keep their diagnosis a secret for fear of discrimination

Patients with undiagnosed HIV infection will inevitably present to the health care system when their disease becomes symptomatic. Spending health care dollars early in disease in this population leads to downstream cost savings. Early diagnosis limits the costs of more complex care, lengthy hospitalizations, and loss of productivity as well as the costs associated with those to whom the individual may have transmitted the disease.

In addition to providing money for treatment, payers will need to commit to paying for the screening tests as well. Some agencies have made this commitment. For example, New Jersey Medicaid has consented to cover widespread HIV screening. Others have not yet indicated support. The adoption of this CDC recommendation by the US Preventive Services Task Force, to whom many managed care companies look to establish a standard of care, will help lead to broad acceptance of and reimbursement for universal HIV screening.

AN APPEAL TO PHYSICIANS

We urge physicians and health care systems to embrace these new recommendations. Although the opt-out approach will increase the number of patients who agree to be tested, the success of universal screening still requires acceptance by physicians in many health care settings. If physicians are not actively interested, tests will not be ordered and widespread screening will not occur.

Physicians are concerned about the burden of finding and notifying patients who may test positive. Yet we order diagnostic studies regularly and must inform patients of diagnoses of cancer or other life-changing illnesses that may require immediate intervention.

Physicians in smaller metropolitan areas and rural regions routinely comment that HIV is not a problem in their community. But in our practice we see many patients from these communities who keep their diagnosis a secret even from the local health care system for fear of discrimination.

Many have commented that children 13 years old are too young to test. Yet the influx of adolescents in high school who are newly diagnosed is frightening, and whether gay or straight, they report that they did not think they were at risk for HIV infection. More married or committed patients who assumed they were in a long-term monogamous relationship have had to learn that they were not. In sum, physicians cannot predict an individual's risk of infection as well as they could in the past.

A few patients may face increased anxiety with testing, but universal testing is already performed in large segments of the population. For many years, blood donors, military personnel, and many of those obtaining insurance policies have been screened for HIV infection.

The AIDS epidemic has now passed the 25-year mark, and our approach to it must mature as the epidemic evolves. The CDC recommendation that universal HIV screening become part of standard health care is a step in the right direction. We hope to again decrease the number of annual new infections and to initiate treatment for those infected before the late stages of disease, when therapy may be less effective. ■

REFERENCES

1. **Branson BM, Handsfield HH, Lampe MA, et al; Centers for Disease Control and Prevention (CDC).** Revised recommendations for HIV testing of adults, adolescents, and pregnant women in health-care settings. MMWR Recomm Rep 2006; 55(RR-14):1–17.
2. **Marks G, Crepaz N, Janssen RS.** Estimating sexual transmission of HIV from persons aware and unaware that they are infected with virus in the USA. AIDS 2006; 20:1447–1450.
3. **Centers for Disease Control and Prevention (CDC).** Trends in HIV/AIDS diagnoses—33 states, 2001–2004. MMWR Morb Mortal Wkly Rep 2005; 54(45):1149–1153.
4. **Centers for Disease Control and Prevention.** HIV/AIDS Surveillance Report, 2004. Vol. 16. Atlanta: US Department of Health and Human Services, Centers for Disease Control and Prevention; 2005. **www.cdc.gov/hiv/stats/hasrlink.htm.** Accessed 3/12/2007.
5. **Simpson WM, Johnstone FD, Goldberg DJ, Gormley SM, Hart GJ.** Antenatal HIV testing: assessment of a routine voluntary approach. BMJ 1999; 318:1660–1661.
6. **US Preventive Services Task Force.** Methodology. In: Guide to Clinical Preventive Services, 2nd ed. Report of the U.S. Preventive Services Task Force. Baltimore: Williams and Wilkins, 1995:xxxix–lv. **odphp.osophs.dhhs.gov/pubs/guidecps/PDF/Frontmtr.PDF.** Accessed 3/12/2007.
7. **Mylonakis E, Paliou M, Lally M, Flanigan TP, Rich JD.** Laboratory testing for infection with the human immunodeficiency virus: established and novel approaches. Am J Med 2000; 109:568–576.
8. **Walensky RP, Paltiel AD, Losina E, et al.** The survival benefits of AIDS treatment in the United States. J Infect Dis 2006; 194:11–19.
9. **Sanders GD, Bayoumi AM, Sundaram V, et al.** Cost-effectiveness of screening for HIV in the era of highly active antiretroviral therapy. N Engl J Med 2005; 352:570–585.
10. **Bozzette SA.** Routine screening for HIV infection—timely and cost-effective. N Engl J Med 2005; 352:620–621.
11. **Paltiel AD, Weinstein MC, Kimmel AD, et al.** Expanded screening for HIV in the United States—an analysis of cost-effectiveness. N Engl J Med 2005; 352:586–595.
12. **Marks G, Crepaz N, Senterfitt JW, Janssen RS.** Meta-analysis of high-risk sexual behavior in persons aware and unaware they are infected with HIV in the United States: implications for HIV prevention programs. J Acquir Immune Defic Syndr 2005; 39:446–453.
13. **Public Health Service Task Force.** Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV-1 Transmission in the United States. October 12, 2006. **www.aidsinfo.nih.gov/ContentFiles/PerinatalGL.pdf.** Accessed 3/12/2007

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Neuropathic pain

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TO THE EDITOR: Dr. Mark Stillman's article about neuropathic pain in the August 2006 issue (*Cleve Clin J Med* 2006; 73:726–739) was excellent. However, when discussing drug treatment, he did not mention the cost of drugs. Although pregabalin (Lyrica) is quicker in action than gabapentin (Neurontin), it seems to be equal in effectiveness, and it costs considerably more.

Costco.com lists a month's supply of gabapentin 40 mg three times a day for $32, while Drugstore.com lists pregabalin 75 mg three times a day for $158. Amitriptyline 25 mg daily costs $11 for a month's supply.

Since many patients have either no drug benefit or pay a premium when brand names (eg, Lyrica) are used, it is appropriate for physicians to know the costs of medications and to be able to advise patients appropriately.

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