Perspective

HIV Testing: Rationale for Changing Recommendations

HIV testing is an important and effective strategy for preventing HIV infection. Infected individuals who know their HIV serostatus are less likely to engage in high-risk sexual behavior, and it is estimated that knowledge of HIV serostatus in unaware persons could reduce new infections by more than 30%. The availability of rapid testing for HIV expands testing opportunities. Expanded routine, voluntary, and opt-out screening in health care settings is needed to reduce the number of persons who are unaware of their HIV-infected status, get newly diagnosed patients into care, and reduce transmission of HIV infection. This article summarizes a presentation on revisions to Centers for Disease Control and Prevention HIV screening recommendations made by Robert S. Janssen, MD, at the 9th Annual Ryan White CARE Act Clinical Update in Washington, DC, in August 2006. The original presentation is available as a Webcast at www.iasusa.org.

HIV testing is an important and effective HIV prevention strategy, and the availability of rapid testing expands testing opportunities. Expanded routine, voluntary, and opt-out screening in health care settings is needed to reduce the number of persons who are unaware of their HIV-infected status, get newly diagnosed patients into care, and reduce transmission of HIV infection. The Centers for Disease Control and Prevention (CDC) has issued revised recommendations for HIV testing of adults, adolescents, and pregnant women in health care settings.

Epidemiology and Risk

The number of persons living with HIV/AIDS has increased over the past decade with the continued occurrence of new infections and the reduction in AIDS mortality due to potent antiretroviral therapy and improved medical care. It is estimated that 1,039,000 to 1,185,000 persons in the United States are living with HIV infection, with some 252,000 to 312,000 (24%-27%) being unaware of their infection (Glynn et al, Nat HIV Prev Conf 2005). Data from 33 states with name-based reporting indicate that there were approximately 112,000 diagnoses in men and 45,000 in women from 2001 to 2004. Among men, transmission occurred via sex among men who have sex with men (MSM) in 61% of cases, heterosexual sex in 17%, injection drug use (IDU) in 16%, and IDU and MSM in 5%. In women, transmission occurred via heterosexual sex in 76% of cases and via IDU in 21%. As shown in Figure 1, the highest rates of HIV/AIDS diagnosis for 2004 in these 33 states were among black men, black women, and Hispanic men. Prevention of perinatal HIV infection in the United States has been very successful, with the number of cases in 2004 representing a reduction of approximately 95% since the peak number of cases in 1992 (CDC, *Surveillance Report*, 2005).

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CDC Prevention Strategies—2003: Focus on Testing as a Preventive Measure

In 2003, the CDC launched the "Advancing HIV Prevention" initiative, which included 4 strategies, 2 of which focused on increased efforts in HIV testing as a preventive measure. The 4 strategies were: (1) make HIV testing a routine part of medical care; (2) implement new models for diagnosing HIV infections outside of routine medical settings; (3) prevent new infections by working with persons diagnosed with HIV and their partners; and (4) further decrease perinatal HIV transmissions (CDC, *MMWR Morb Mortal Wkly Rep,* 2003).

HIV testing is an effective prevention intervention. A recent meta-analysis estimated that unprotected anal or vaginal intercourse with HIV-seronegative partners was reduced by 68% among HIV-infected persons who knew of their positive serostatus compared with those who were unaware (Marks et al, *J Acquir Immune Defic Syndr,* 2005). The CDC has estimated that the approximately 25% of persons unaware of their HIV infection account for 54% (upper bound of estimate, 70%) of new infection transmissions (Marks et al, *AIDS,* 2006). It is estimated that knowledge of HIV serostatus in unaware persons could reduce new infections by

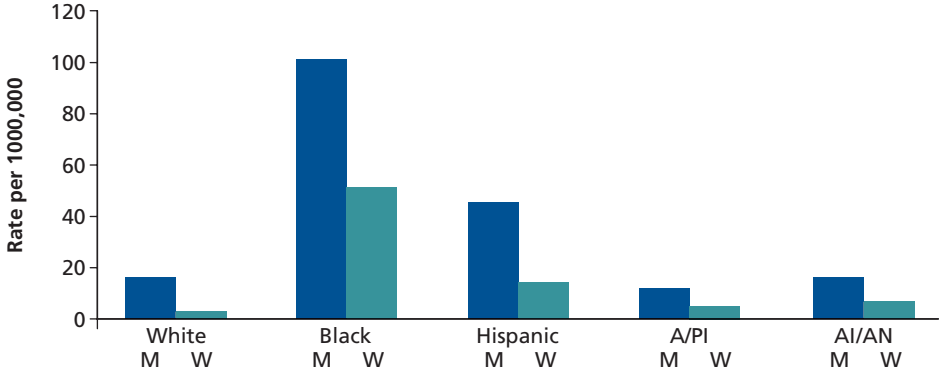

Figure 1. Estimated annual rate of HIV/AIDS diagnoses in 33 states in 2004. A/PI indicates Asian/Pacific Islander; AI/AN, American Indian/Alaska Native; W, women; M, men. Adapted from the Centers for Disease Control and Prevention: *HIV/AIDS Surveillance Report*, 2005.

greater than 30%.

Unawareness of HIV serostatus is common in high-risk and high-prevalence populations. Data from 1767 MSM in Baltimore, Los Angeles, Miami, New York, and San Francisco in the National HIV Behavioral Surveillance System showed HIV prevalence of 25%, with 48% of infected individuals being unaware of their infection. Unawareness rates were 79% in those aged 18 to 24 years and 70% in those aged 25 to 29 years. The highest prevalence was among black MSM (46%), who also had the highest rate of being unaware of infection (67%) (CDC, *MMWR Morb Mortal Wkly Rep,* 2005).

The need for increased testing is also emphasized by the high proportion of infected individuals who are diagnosed later in their disease course. Data from 2000 to 2003 in 16 sites indicate that among 4127 persons with AIDS, 45% were diagnosed with HIV infection within 12 months of their AIDS diagnosis ("late testers"). Compared with those tested early (more than 5 years before AIDS diagnosis), late testers were more likely to be younger (18-29 years old), heterosexual, less educated, and black or Hispanic. The need for HIV testing outside of routine medical settings is emphasized by the fact that only approximately 5% of late testers and 10% of early testers had infection diagnosed by testing during a routine medical checkup. The most common reason for testing among late testers was illness (~65%) and that among early testers was "self/partner at risk" (~30%; CDC *MMWR Morb Mortal Wkly Rep,* 2003).

Rapid HIV Tests

The availability of rapid HIV tests promises to make a major contribution to testing as a preventive measure. One important use of these tests will be as a remedy to the high rates of nonreturn for results of conventional HIV testing. For example, data from 2000 indicate that 31% of individuals with positive conventional test results at publicly funded sites did not return to the sites to receive test results. In addition, rapid testing technology can answer the need for immediate information or referral for treatment choices in perinatal settings and postexposure treatment settings. Further, it is highly suitable for screening in high-volume, high-prevalence settings.

US Food and Drug Administration (FDA)-approved rapid tests include the 4 clinically available tests—2 of which have Clinical Laboratory Improvements (CLIA) waivers, meaning that clinical laboratories can apply for certification—as well as 2 more recently approved tests. Sensitivity and specificity (and the lower limit of the 95% confidence intervals) of the 4 tests available for clinical use are generally above 99.0% and exceed the 98.0% required by the FDA. Only 1 of the rapid tests is approved for use with oral fluid. Use of rapid tests requires confirmatory testing with Western blot or indirect fluorescent antibody testing; enzyme immunoassay (EIA) cannot be used as a confirmatory test. Western blot testing can be performed with venipuncture for whole blood or using an oral fluid specimen. Patients with positive rapid test results and negative or indeterminate Western blot tests should have follow-up confirmatory testing after 4 weeks.

Data from postmarketing surveillance of the first FDA-approved rapid test in 2004 and 2005 involving 14 project areas and 347 testing sites (Wesolowski et al, *AIDS,* 2006) are shown in Table 1. Specificity of the test was high for both whole blood and oral fluid, with the positive predictive value using oral fluid being lower than that with whole blood. Use of the rapid test was associated with a higher proportion of patients being notified of both negative and positive results. Among patients receiving the rapid test, the project area-specific median (range) percentages were 99.5% (93.7%-100%) for receipt of negative results, 100% (89.8%-100%) for receipt of preliminary positive results, and 89.7% (49.4%-100%) for receipt of confirmed positive results. By comparison, among patients having conventional EIA testing, 77.3% (30.4%-98.5%) received negative results and 81% (33.3%-100%) received confirmed positive results.

Table **1**. Specificity and Positive Predictive Value of Rapid HIV Testing and Conventional Testing in Postmarketing Surveillance in 2004 and 2005

	Number of tests	Project-specific Median (Range) Percentages		
		HIV seropositive	Estimated specificity	PPV
Rapid Test				
Whole blood	135,724	0.8 (0.1-2.6)	99.98 (99.7-100)	99.2 (66.7-100)
Oral fluid	26,066	1.0 (0-4.0)	99.89 (99.4-100)	90.0 (50.0-100)
Conventional Test	31,811	1.5 (0.5-5.1)	--	--

Data are using the first rapid HIV test approved by the US Food and Drug Administration. Adapted from Wesolowski et al, *AIDS*, 2006.
PPV indicates positive predictive value.

The first approved rapid test was also used in the Mother Infant Rapid Intervention at Delivery (MIRIAD) study, for testing of women in labor for whom HIV serostatus was unknown (Bulterys et al, *JAMA*, 2004). Among 7680 women screened in 12 hospitals in 5 cities, 54 (0.7%) new HIV infections were identified. Rapid testing yielded 6 false-positive results and no false-negatives; EIA yielded 15 false-positive results. Specificity was 99.92% with rapid testing and 99.80% with EIA; positive predictive values were 90% and 76%, respectively.

Improving Scope and Yield of Testing

Data from 2000 to 2003 indicate that some 38% to 44% of adults aged 18 to 64 years have been tested for HIV in the United States, and that 16 to 22 million persons aged 18 to 64 years are tested annually. Most testing is done through private doctors or health maintenance organizations (Table 2). However, testing in hospitals, emergency departments (EDs), outpatient clinics, and in public community clinics accounts for greater proportions of positive test results. For example, testing in public clinics accounts for 9% of tests but 21% of positive test results.

The former CDC recommendations for HIV testing in adults and adolescents included routine screening in settings with high HIV prevalence (≥1%), targeted testing based on risk assessment, and annual testing for sexually active MSM. However, these recommendations do not appear to have increased testing in many settings, including the acute care setting. For example, in 108 million ED visits in 2000, including 68.3 million by patients aged 18 to 64 years, HIV serology was performed in 215,000; in 2002, there were 110 million ED visits, including 69.6 million by patients aged 18 to 64 years, and HIV serology was performed in 163,000.

HIV screening is feasible in acute care settings and can be facilitated by use of rapid tests and opt-out testing, in which testing is routine but can be refused by the client. A program of rapid test ED screening showed that an estimated 3.2% of tests were positive at Johns Hopkins ED in Baltimore, 2.7% at Grady ED in Atlanta, 2.3% at Cook County ED in Chicago, 1.3% at King-Drew Medical Center in Los Angeles, and 1.2% at Alameda County Medical Center in Oakland, compared with 1.1% of tests at CDC-funded counseling and testing sites. In an examination of the feasibility of voluntary, opt-out testing in sexually transmitted disease (STD) clinics in Texas in 1996 and 1997, the strategy increased the proportion of eligible clients receiving testing to 97% (23,020 of 23,686) compared with 78% (14,927 of 19,184) with voluntary, opt-in testing. The number of positive tests increased from 168 to 268. Since that time, opt-out testing has been routine, with proportions of eligible clients receiving HIV testing being 90% or more since the second half of 1998, and 95% or more since 2003.

An early examination of opt-out screening in pregnant women showed that whereas only 35% accepted testing with opt-in consent, with some feeling that agreeing to testing implied high-risk behavior, 88% accepted testing offered as routine opt-out testing, with clients exhibiting markedly less anxiety regarding testing. Previous CDC recommendations for pregnant women included: routine, voluntary testing as early as possible as a part of prenatal care; simplified pre-test counseling; flexible consent process; HIV rapid testing and treatment during labor and delivery for women without prenatal testing; and re-screening in the third trimester for select, high-risk women.

Table 2. Sources of HIV Tests and Positive Tests

Source	HIV tests* (%)	Positive tests† (%)
Private doctor or health maintenance organization	44	17
Hospital, emergency department, outpatient clinic	22	27
Public community clinic	9	21
HIV counseling/testing facility	5	9
Correctional facility clinic	0.6	5
Sexually transmitted disease clinic	0.1	6
Drug treatment clinic	0.7	2

*Adapted from Centers for Disease Control and Prevention, *MMWR Morb Mortal Wkly Rep*, 2004.
†Adapted from the supplement to HIV/AIDS Surveillance 2000-2003 (Centers for Disease Control and Prevention, unpublished data)

Revisions of Recommendations for Screening

Recent revisions of CDC recommendations for HIV testing include universal screening in health care settings (CDC, *MMWR Morb Mortal Wkly Rep*, 2006). The rationale for revising the previous recommendations included the facts that many HIV-infected persons access health care but are not tested for HIV until they are symptomatic and that awareness of HIV infection leads to substantial reductions in high-risk sexual behavior. The adoption of a universal screening strategy is facilitated by the reduced need for pre-test counseling associated with the high levels of knowledge about HIV in the general population. Further, there is inconclusive evidence about prevention benefits from typical counseling for persons who test negative. Screening in the antiretroviral therapy era is cost-effective as well.

A recent report concluded that even in relatively low-prevalence areas, cost effectiveness of routine HIV screening is similar to that of commonly accepted interventions (Sanders et al, *N Engl J Med,* 2005), estimates were $15,078 and less than $50,000 per quality-adjusted life year for HIV prevalence rates of 1% and greater than .05%, respectively. Another analysis concluded that routine, voluntary screening for HIV once every 3 to 5 years is justified on both clinical and cost-effectiveness grounds in all but the lowest-risk populations, and that one-time screening in the general population may also be cost-effective (Paltiel et al, *N Engl J Med,* 2005).

Revised recommendations for HIV screening are shown in Table 3. The new recommendations include routine, voluntary screening for all persons aged 13 to 64 years in health care settings, with screening not to be based on prevalence or risk. Opt-out screening is recommended, with the patient having

Table **3**. Revised HIV Screening Recommendations

Non-pregnant Adults and Adolescents

Intended for all health care settings, including inpatient services, emergency departments, and urgent care, sexually transmitted disease, tuberculosis, public health, community, substance abuse, and correctional facility clinics.

- Routine, voluntary HIV screening for all persons aged 13 to 64 years in health care settings, not based on prevalence or risk
- Repeat HIV screening of persons with known risk at least annually
- Opt-out HIV screening with the opportunity to ask questions and the option to decline; include HIV consent with general consent for care
- Prevention counseling in conjunction with HIV screening in health care settings not required
- Provision of clinical HIV care or establishment of reliable referral to qualified providers
- Review and revision of state and local regulations as needed
- Consideration of "sunset" provision in low-prevalence settings:
  - Initiate screening
  - If HIV prevalence shown to be less than 1 per 1000, continued screening no longer warranted

Pregnant Women

- Universal opt-out HIV screening
  - Include HIV in panel of prenatal screening tests
  - Consent for prenatal care includes HIV testing
  - Notification and option to decline
- Second test in third trimester for pregnant women:
  - Known to be at risk for HIV
  - In key jurisdictions
  - In high-prevalence health care facilities
- Opt-out rapid testing for women with undocumented HIV serostatus in labor or delivery
  - Initiate antiretroviral prophylaxis on basis of rapid test result
- Newborn testing if mother's serostatus unknown

Adapted from Centers for Disease Control and Prevention, *MMWR Morb Mortal Wkly Rep*, 2006.

the opportunity to ask questions and the option to decline testing.

These recommendations are intended to apply to all health care settings, including inpatient services, EDs, and urgent care, STD, tuberculosis (TB), public health, community, substance abuse, and corrections facility clinics. For low-prevalence settings, "sunset" provisions may be considered, in which screening can be discontinued if HIV prevalence is found to be below 1 per 1000 population.

Revisions for pregnant women (Table 3) include universal opt-out screening, a second test in at-risk women during the third trimester of pregnancy, opt-out rapid testing for women without documented HIV serostatus during labor or delivery, and testing of newborns of mothers with unknown infection status.

Expanded HIV screening raises a number of issues, including the question of who will pay for the testing. It is hoped that the recommendation for universal screening will stimulate payors to reimburse for testing as they do for other types of screening. There will still be a need for publicly funded testing. Expanded testing will also require renewed attention to ensuring that access to care is available for newly diagnosed patients. Although routine testing helps to remove the stigma of testing, there is still work to be done in reducing the stigma of diagnosis.

An increased number of diagnoses also entails increased demands in terms of partner notification. In this regard, important steps for clinicians and case managers include: communicating with health department partner services staff to become familiar with the services and how to access them; asking at the patient's initial visit about sex and drug injection partners and whether they have been informed of risk; screening patients for behavioral risks and STDs that may indicate a need for further discussion about partners; and referring patients to the health department for assistance with partner notification.

Presented by Dr Janssen in August 2006. First draft prepared from transcripts by Matthew Stenger. Reviewed and edited by Dr Janssen in February 2007.

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Suggested Readings

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