HIV TESTS

When researchers were seeking a way to identify HIV infection in the early 1980s, they found the most effective test to be one that detected the presence of antibodies to HIV. The enzyme-linked immunosorbent assay (ELISA) was approved for use in 1985. Based on its cost-effectiveness and high rate of accuracy, the use of the ELISA, combined with a supplemental test when a blood sample is reactive, has remained the standard in HIV testing. Other tests for HIV antibody and antigen have been developed as demand for testing has increased and as quicker and more cost-effective testing methods have been sought.

This issue of PERSPECTIVES offers an overview and an update of conventional testing methods, and presents research on new tests that detect HIV antibodies or antigen. The Implications for Counseling section explains how counselors can discuss the roles of current tests and prospects for other tests.

Research Update

When someone is infected with HIV, the body responds by developing antibodies to the virus, usually within six to eight weeks after infection. For a few people, it may take three to six months for the body to produce antibodies. Using conventional testing methods, a person is considered positive for HIV infection if blood samples are reactive in each of a series of tests that detect antibodies. When an initial ELISA test is reactive, it is repeated once or twice. If a repeat test is positive, it is followed with a supplemental test, either the Western blot test or immunofluorescence assay (IFA).

ELISA

The ELISA is considered the best available screening because of its low cost, standardization, high reliability, and relatively quick turnaround. Numerous versions of this test have been licensed by the Food and Drug Administration since 1985. The price of each ELISA test kit can be less than $2. Adding equipment, labor and other overhead needed to conduct an ELISA, the total cost of each test ranges from $12 to $20. Costs of performing an ELISA vary based on several factors, including locale and the number of tests conducted.

In recent years, refinements have been made to the ELISA to prevent cross-reactions to antibodies other than HIV and to prevent other false results. Currently, most versions of the ELISA use inactivated HIV viral proteins — or HIV antigen — isolated from cell cultures. Advanced technology is being used to make synthetic HIV antigens that are even more sensitive and specific. In a recent study of the ELISA's reliability and accu-
Estimated Costs of HIV Antibody Tests

<table>
<thead>
<tr>
<th></th>
<th>Manufacturer's price of each test</th>
<th>Total cost to perform test (includes price of test)</th>
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</thead>
<tbody>
<tr>
<td>Enzyme-linked Immunoabsorbent Assay (ELISA)</td>
<td>$2</td>
<td>$12-$20</td>
</tr>
<tr>
<td>Murex SUDS</td>
<td>$6-$9</td>
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<tr>
<td>Recombigen Latex Agglutination</td>
<td>$5</td>
<td>$15-$20</td>
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<tr>
<td>Immunofluorescence Assay (IFA)</td>
<td>$16</td>
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<td>Western Blot</td>
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racy, it was found to have a sensitivity of 99.7%. Sensitivity refers to the rate of false negative results: in the case of the ELISA, this means that 99.7% of test samples were correctly diagnosed as negative when antibodies were present, and that 0.3% of test samples — or 3 in 1,000 — were falsely diagnosed by the ELISA as negative when HIV antibodies were actually present. The test’s specificity was 98.5%. Specificity refers to the rate of false positive results: in the case of the ELISA, this means that 98.5% of negative test samples were correctly diagnosed as negative, and that 1.5% of the tests produced positive results when antibodies were not present.

Nonreactive results can occur in someone with HIV infection when testing is done before the body has produced antibodies to HIV — a time known as the “window period” — or when a person is late in the course of AIDS, at which time the body may stop producing antibodies. In addition, some ELISAs are specific only to antibodies to HIV-1, which is the primary strain of HIV infection found in the United States. Another virus, HIV-2, is found in some African countries, but very rarely in the United States.

False positive screening results, on the rare occasions they occur, may result from biological variations in the way a blood sample responds to a test, human laboratory errors, or health conditions such as hemophilia, autoimmune disorders, and alcohol-related hepatitis. Because false positive results can occur, a supplemental test is always necessary to conclude that HIV antibodies are present and to make a diagnosis of HIV infection.

Western Blot and IFA

The Western blot is the most commonly used supplemental test. Compared to the ELISA, it is more expensive, takes a longer time to perform, requires greater technical precision, and is more difficult to interpret. The total cost of performing a Western blot test is about $40, which includes about $24 for each test kit. As a supplemental test, the overall sensitivity and specificity of the Western blot are considered to be high, at 99.3% and 91.6%, respectively, as analyzed recently by the Centers for Disease Control and Prevention (CDC).

There has been some controversy regarding interpretation of the Western blot and what are considered inconclusive readings. The CDC has set specific guidelines regarding the interpretation of results. Interpretation of Western blot results involves reading several bands of reactivity that appear on a test strip. In order for a result to be considered positive, reactivity to certain bands must occur. For a result to be negative, it is necessary that no viral-specific bands show reactivity. In some cases, reactivity will occur, but not to the specific bands required for a positive reading. This result is called “indeterminate” and the overall result is called inconclusive. It is possible that this occurrence could signify early HIV infection or an early stage of seroconversion, or it could indicate infection with HIV-2. However, quite often when these bands appear, HIV is not present. When a result is inconclusive, a new blood sample is needed from the client. This step is required by California law.

While the Western blot has been the most commonly used supplemental test in most parts of the country, the IFA is generally considered to be at least as reliable as the Western blot, and it is more widely used in public health testing in California. A commercial version of the IFA received federal approval to be marketed in 1992. For several years prior to this, California officials distributed a “homemade” version of the IFA to local labs.

The IFA is less expensive and easier to perform than the Western blot. The total cost to perform each IFA is about $25, including $16 for testing reagents. With an IFA, HIV antigens are fixed on a slide and incubated with the test sample. Another antibody is added that reacts to the first complex. Fluorescent spots will appear on the slide if HIV antibodies are present, indicating a positive result.

Using conventional testing methods, results generally take from a week to as long as a month to be reported to clients. Waits are often greater in some rural areas, where test samples must often be sent to a second lab for supplemental testing.

Rapid Tests

There are other methods either
now available or being developed to detect HIV infection. Recently, there has been increased focus on these tests, particularly those that can be performed relatively quickly and easily outside a laboratory. In some cases, these tests are being considered as possible supplements or replacements to conventional testing methods.

With some rapid methods, test results could be available the same day blood is drawn, perhaps within an hour. However, because positive results need to be confirmed with a more complex test like the IFA or Western blot, both of which require a laboratory, clients could not receive positive results during the same visit. Currently, only two rapid tests have been licensed for use by the FDA. Other tests are being developed and may receive approval during the next several years. For the most part, all tests that have been approved or are awaiting approval claim sensitivity and specificity comparable to or greater than the ELISA.

The cost of most rapid tests is somewhat higher than for an ELISA. The price of some rapid tests that have been approved is around $5 each, and prices of future tests are expected to be similar. However, unlike the ELISA, little equipment is required for some rapid tests. Rapid tests are now being developed that do not require refrigeration or a reliable electrical power source.

The following rapid tests have been approved for use:

**Recombigen Latex Agglutination Test.** In 1988, the FDA approved the Recombigen HIV-1 latex agglutination test, which can produce a result within five minutes. This test is the first to use genetically engineered pieces of HIV antigen, which reduces cross-reactivity and nonreactivity that can cause false positive or false negative results. A large study found the sensitivity of the latex agglutination test to be

**Related Issue: Non-Blood Tests, Home Collection**

Rapid HIV blood tests are just one area of development for HIV diagnostic tests. Other research is exploring tests of urine, saliva and mucous membrane samples to detect HIV. These procedures are less invasive than blood tests, and some health care workers see these techniques as advantageous because they reduce the risk of infection from job-related needle sticks. These tests are also less costly, and they eliminate for clients the pain and inconvenience of providing blood samples.

A recent study of a saliva test found specificity above 99% and sensitivity at 96.2%, and a study of fluid from nasal and gum mucosa showed a 99.8% sensitivity rate and a 99.5% specificity rate. However, these techniques have not been studied as thoroughly as the ELISA test and therefore are considered relatively unproven. There are also storage and handling concerns, including temperature and humidity requirements, related to these testing techniques. It is unlikely that testing programs will switch to saliva, urine, or mucous membrane tests until they are conclusively proven to be as accurate as what is already available.

**Home-Collection Tests**

Testing methods by which someone can obtain a sample in his or her own home are also being investigated, but these have not been approved for use, and it is not clear when they may be approved. Protocols for home-collection testing vary. A commonly proposed method is that a person would take a blood sample with a finger stick, then send the sample to a lab for analysis. Notification of results would be done by telephone, which would involve some form of counseling, including referrals to local service providers.

Among the advantages of home-collection testing methods cited by supporters are that the client can test in private and maintain anonymity because the test sample is identified only by code number; the cost of the test is lower than it would be if testing were performed in a physician’s office or clinic; and there is no wait required before testing. Home-collection tests may be useful for people with little or no history of HIV infection risks because these people may have less need for risk assessment and health education counseling. Nearly 64% of people who received services at Alternative Test Site (ATS) programs in California during 1992 had little or no HIV risk behaviors. The seroprevalence rate for this group was 0.3%. It is argued that home-collection tests for these clients would preserve scarce public testing funds for people at higher risk.

Despite these advantages, ethical and counseling concerns are perhaps the biggest obstacles to the approval of home-collection tests. Opponents are concerned that phone counseling may not offer the support people need to deal with a positive result, and that clients may receive little if any individualized risk assessment or risk-reduction education.
99.4%, and the specificity, 99.6%. However, a recent study of this test found its sensitivity to be as low as 92%. The latex agglutination test is not widely used because many believe it is not as simple to use or interpret as the ELISA.

Murex Suds. The Murex SUDS test, approved in 1992, has received wide attention. This test is manually performed and relatively easy to interpret. While it takes as little as 10 minutes to perform the test, this can occur only after an extended period, perhaps up to one hour, to prepare test samples. Like the rapid latex agglutination test, the Murex SUDS test uses a mixture of latex particles coated with recombinant protein antigens. If antibodies are present in the blood, plasma, or serum being tested, a blue dot appears on a hand-held, disposable testing unit. If a result is negative, no color will appear on the test unit.

If a blue dot appears, the test is repeated in duplicate. If repeatedly positive, a supplemental test is performed to verify the result. The Murex test includes several safeguards, such as a negative control area that remains white when chemicals used to perform the test are properly administered. In addition, control samples are used. Murex company researchers claim the test has a 99.9% sensitivity rate and a 99.9% specificity rate. If antibodies are present, a blue dot appears on a hand-held, disposable testing unit. If a result is negative, no color will appear on the test unit.

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Detecting HIV Directly

While tests discussed above detect infection based on the presence of antibodies — an indirect method — other tests detect the virus directly. These methods may be helpful at very early stages of infection in some situations when a Western Blot result is indeterminate. For instance, there are some ELISA-based tests that use HIV antibodies to detect HIV antigens, such as p24. This method produces very few false positive results. However, the incidence of false negative results tends to be high, especially in HIV-infected people who are asymptomatic.

Related Issue: AIDS-Like Symptoms without HIV

In 1992, a variety of reports within the medical community and media suggested that scientists had detected an AIDS-like condition that occurred in the absence of HIV infection. These reports raised concern about the usefulness of HIV testing.

The issue first gained broad attention when a researcher at the University of California at Irvine released a report suggesting that a virus known as the "human intracisternal virus" had caused an AIDS-like disease in an older woman. The release of this report coincided with last year's International Conference on AIDS. In an emergency session at this conference, researchers discussed cases from around the world of severe immunosuppression without HIV. These cases included five people in New York and others identified by the Centers for Disease Control and Prevention (CDC). The CDC called for a more formal meeting in 1992 that resulted in the CDC's formal characterization of this form of immunosuppression in the absence of HIV infection as idiopathic CD4+ T-lymphocytopenia, or ICL.

Based on the CDC's characterization, a diagnosis of ICL is made when a person has repeated T-helper cell counts below 300, or fewer than 20% of all T-cells; tests negative for HIV infection; and has no other apparent cause for immune deficiency.

Reports of a non-HIV, AIDS-like condition — some type of acquired immunodeficiency — have appeared in medical literature at least since 1983. Characteristics of people with ICL are varied: they range from age 18 to 70, they are heterosexual and homosexual, and they are of various ethnic origins. People with ICL most often have been white and female. More than half have reported no risk factors for HIV infection.

The CDC has found about 60 possible cases of ICL in the United States. The number of deaths in the group as a whole is low; only one of 30 investigated cases had died, and this death was not attributed to ICL. In a report following the CDC's meeting, researchers found no common pattern of behavioral risk among these cases, and no convincing evidence of a transmissible virus as the cause of ICL.

Once research established ICL as distinct from AIDS, less attention has been paid to it. This is likely because so few people are afflicted with ICL and those with ICL, despite T-helper cell depletion, show relatively stable T-helper cell counts over time. Furthermore, unlike HIV, it does not appear that ICL can be transmitted through the blood supply.
In addition, the polymerase chain reaction (PCR) can detect tiny amounts of specific HIV DNA. This test produces high rates of false positive results and is used mainly for research. [For more information on the PCR test, refer to the "Silent Infection" issue of PERSPECTIVES, Vol. 1, No. 2; June 1991.]

**Future Testing Protocols**

Some researchers speculate that with continued development of rapid tests and continued improvements in ELISA tests, the Western blot or IFA may be replaced in the testing protocol by a three-test series consisting of multiple ELISA tests, along with rapid and "simple" tests. Simple tests are similar to rapid tests in that they do not need sophisticated equipment, yet they take longer than rapid tests to perform. The World Health Organization (WHO) cites research that has found combinations of ELISA, rapid and simple tests provide results at least as reliable as the ELISA and Western blot combination and at a much lower cost.

**Implications for Counseling**

It has always been necessary for counselors to assure clients about the accuracy of HIV testing. The development of improved versions of existing tests, such as the ELISA, as well as entirely new tests and testing methods, has allowed counselors to provide even greater assurance and detail about the scientific merit of testing procedures.

**Reliability**

Make sure clients understand that HIV testing is accurate. On rare occasions when asked for greater detail, it may be useful to explain the sensitivity and specificity of the test, and the meaning of these terms. Even after hearing this, some clients may still question the reliability of common testing methods. Assist these clients in two ways: explain the testing options that are available, and explore the reasons — and the feelings surrounding these — that the client may have for distrusting the test.

If asked about options, explain that other tests, for instance the polymerase chain reaction (PCR) or p24 antigen tests, can detect either virus or viral particles, but that these tests have significant limitations. If the PCR test is discussed, explain that this test has little use as an HIV test except at very early stages of infection. If appropriate and available, offer referrals to clients who ask for them.

Clients who raise questions about the accuracy of existing testing methods, and are not satisfied with answers they receive, may not be satisfied with any test. There may be a variety of reasons for this attitude. For instance, these people may have recently engaged in unsafe sex with an HIV-infected partner and may be convinced they too are infected; they may have peers with HIV and cannot imagine how they could escape infection; or they may be unable to accept any information unless it is absolute. Less commonly, a client may also suffer from a chronic mental illness and hold the delusion that he or she is infected with HIV or has AIDS despite laboratory evidence to the contrary.

Explore the client's reasons for testing and his or her reasons for distrust. Continue to explore the client's discomfort as long as progress is being made. If it appears the client is unable to progress in this discussion, it may be appropriate to review with the client the exchange that has taken place and the client's response, and then refer the client for additional counseling.

**Waiting for Results**

In most settings, clients receive test results two weeks after testing. Waits such as this are often viewed as a useful time that allows clients to understand the consequences of the test, respond to information presented in pre-test counseling, and prepare for a result. The period may also allow a person time to consider the seriousness of his or her risk behaviors and make behavioral changes.

Some counselors see the waiting period as too long and as harmful to the client. They argue that the prolonged period of uncertainty makes the testing process appear mystical, leads to
undue anxiety, and gives the client little control while awaiting these momentous results. Some clients report experiencing the wait as agonizing.

Be familiar with the protocol of the testing process from the time blood is drawn until results are disclosed, and explain this to the client. Explain that results cannot be reported immediately because a series of tests must be conducted, and acknowledge that the length of the process may be difficult for clients. Acknowledge and empathize with clients' frustrations. For clients who display anxiety about managing their lives while awaiting their results, discuss techniques to reduce stress and gain support during this period. [See the Case Study on page 7 to learn more about these techniques.]

When clients express an urgent need to obtain test results, learn more about the source of the urgency. It may be that the client recently engaged in unsafe behavior. If this is the case, explain the possible need to return for a follow-up test because he or she may be in the infection “window period,” the time during which HIV antibodies have not yet developed in someone who is infected.

Clients may express a need to receive a result quickly based on the belief that it is necessary to immediately begin drug treatment. If the client has not had symptoms of disease, explain that it is highly unlikely a two-week wait will have a detrimental effect on health. If the client has symptoms of disease, discuss these and recommend medical care.

When clients clearly express that they are unwilling to wait for results and wish to test elsewhere to avoid the conventional waiting period, provide referrals for testing options. In most parts of California, physicians provide test results in as few as two or three days. In some places, turnaround can be as short as one day. Explain that when clients test through a physician or elsewhere they may compromise confidentiality or anonymity, and they will most likely pay a fee. Explain the significance of these effects, and advise clients that some providers offer testing with little, if any, counseling.

Rapid Tests

While some people hope that rapid tests, such as the Murex SUDS, can be used in mainstream clinical settings to save money and therefore allow for more intensive counseling, there are several drawbacks to these tests. For instance, state law requires supplemental testing — which is not rapid — before a positive result is disclosed. In addition, the Murex test requires refrigeration and equipment not commonly found at most test sites. Rapid tests also require training for those performing the tests.

The likely discrepancy between disclosure procedures for negative results and positive results has prompted resistance to the use of rapid tests. One concern is related to fears that the method of delivering rapid test results inadvertently identifies those who are infected. Because a person who tests negative to a rapid test would need to visit the test site only once, it could be inferred that those who are not immediately given results are inconclusive or positive. Because of this, it is not advisable to establish post-test negative counseling in a distinguishably different context from post-test positive counseling.

Despite these limitations, some areas — for instance where few people are being tested and HIV seroprevalence is low — could benefit from a rapid test. It is useful for counselors to consider the possibilities for rapid tests because future development of a rapid supplemental test or the use of a series of rapid or ELISA tests in place of Western blot or IFA testing may make these alternatives more viable.

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A Counselor’s Perspective

“Some clients don’t want to believe they are uninfected. No test and nothing that I say will convince them. Discussions with these clients can be frustrating and anxiety-provoking for me, and I know to avoid power struggles. Instead, I explore, as I’m able, the source of the client’s concern, and then make the best follow-up referral that I can.”
Case Study

Mark, who is 35, says during pre-test counseling that waiting two weeks for results will cause him too much anxiety. He wants the test counselor to either produce a result in a shorter period or refer him to someone who can. Mark tested once before in 1988. His history of risk is unclear, but it appears he has had unsafe sex several times in the past two years.

Acknowledge Mark’s request for a test setting with a more rapid turnaround of results, and validate the difficulty some people have in waiting. If Mark states that he cannot tolerate waiting and is clear he wants to test elsewhere, refer him to physicians or others who can provide results in a shorter period. If the current setting provides an option for quicker turnaround of results, offer this. Explain the value of the anonymity or confidentiality offered in the current setting as well as dangers of a test result appearing on a person’s medical record.

If Mark chooses to test in the current setting, learn more about how he perceives the wait period and why this period is particularly difficult. Explore strategies that could help him alleviate his anxiety and make the wait more acceptable.

Explain telephone support services, such as AIDS hotlines and crisis support lines, and offer referrals. Discuss the social support available in Mark’s life, to determine if this is a resource for him. Learn how Mark has dealt with stressful events before. If these coping skills have been healthy, explore how he might use them now. Explain and offer written information about stress-management techniques and dealing with the waiting period. Emphasize how Mark may benefit from avoiding stressful situations. Recommend that he avoid alcohol and other drugs during the period because they may elevate anxiety.

Perform a more thorough assessment of risk behaviors Mark has engaged in over the last two years, especially those of recent months. His anxiety about the wait may be directly related to his perceived risk for being infected. If Mark is able to understand the relationship of his anxiety to his unsafe sex, he may be more motivated to avoid unsafe sex in the future. To help him avoid unsafe sex and anxiety, Mark may benefit from risk-reduction counseling or group support sessions. While he may not be able to receive this support before learning his result, taking steps to seek it may relieve some anxiety.

References

Test Yourself on HIV Tests

Test Yourself on HIV Tests:
1. True or False: The ELISA test used in 1993 is no different from the ELISA first approved in 1985.
2. True or False: A positive ELISA test alone is sufficient to determine HIV infection.
3. True or False: The occurrence of a condition known as IeL, which depletes T-helper cell counts in the absence of HIV and symptoms of illness, has proven to be very rare, to have no link to HIV, and not to be a new, transmissible virus.
4. True or False: A test’s sensitivity refers to the rate of test samples correctly diagnosed as positive when antibodies are present, and it indicates the rate of false negative results that are produced.
5. What is the sensitivity of the ELISA test? a) 50%, b) 100%, c) 99.7%, d) 20%.
6. True or False: It is widely believed that rapid tests will soon make all other tests obsolete.
7. True or False: There are few, if any, drawbacks to home HIV testing.
8. Rapid tests may have restricted usefulness for which of the following reasons? a) they require a non-rapid confirmatory test when a result is positive, b) test sites may not have appropriate facilities to perform a test, c) their results are highly suspect, d) a and b are correct.

Discussion Questions
1. How can counselors discuss the reliability and accuracy of tests such as the ELISA in simple terms and in ways that do not confuse the client?
2. How can counselors validate the effectiveness of the ELISA and other tests with clients who state that tests are imperfect and therefore their results invalid?
3. How can counselors deal with their personal frustrations related to the delay between the time a test is performed until results are reported?
4. What implications, if any, do rapid tests have on the counseling and testing process currently, and what implications might such tests have in the future?

Answers to Test Yourself
1. False. Versions of the ELISA have been improved continually since 1985.
2. False. A positive ELISA test must be validated by a Western Blot or other supplemental test.
3. True.
4. True.
5. C. The ELISA has a sensitivity of 99.7%.
6. False. It is generally believed that rapid tests may be useful in some settings, but for the foreseeable future, their usefulness is limited.
7. False. There are significant drawbacks to home HIV testing, including their reliability and accuracy, and concerns related to counseling.
8. D. Both a and b are correct.

Reader Response
PERSPECTIVES encourages counselors to respond to discussion questions presented in each issue. Replies may help in planning future issues. Share your thoughts related to the questions by writing: Editor, HIV Counselor PERSPECTIVES, UCSF AIDS Health Project, Box 0884, San Francisco, CA 94143.