FOCUS A GUIDE TO AIDS RESEARCH

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The HIV Testing Debate

Peter Goldblum, PhD, MPH and Robert Marks

Since HIV antibody testing began three years ago, it has been the subject of a heated debate having medical, political, psychological and ethical ramifications. As researchers develop new tests to detect HIV infection and as medical professionals bolster arguments that early detection may lead to more effective treatment, people at risk for HIV infection may be overwhelmed by the debate and their options. Many will seek counsel from mental health practitioners.

This article will define the issues of the debate, discuss how these have changed over the past three years, and will suggest approaches for counseling clients about testing.

After infection by HIV, the body's immune system responds by producing antibodies that recognize and attach to specific proteins on the virus. These foreign proteins are referred to as antigens, and because antibodies are tailor-made for particular antigens, tests can be designed to detect specific antibodies.

Other detection tests, used for research and to supplement antibody test results, include those for HIV antigen, for the virus itself, for the virus' DNA, and for T-cells and beta$_2$ microglobulin, the levels of which may indicate whether a person's immune system has been compromised. (Virologist Judith Wilber discusses the mechanics of these tests on page 3.)

At the time antibody testing was introduced, most AIDS experts argued against using the test for more than screening blood donations. It was only after the anonymity of test results was guaranteed in some states and the accuracy of the test was confirmed, that testing was endorsed more widely. As it has become clear that knowledge of infection can lead to earlier treatment, advocacy of testing has become more common.

Advantages of Testing

Several factors have fueled arguments for the early detection of HIV infection. Most dramatic is recent epidemiological research that suggests that after seven to eight years of infection, 65 to 75 percent of those infected with HIV develop AIDS. This is a change from the situation as recent as a year ago, when people who were infected did not know if they would remain asymptomatic, develop ARC or go on to develop full-blown AIDS.

During the past two years, there has been growing interest in new treatments, ranging from FDA-approved drugs such as AZT and aerosolized pentamidine to experimental drugs, that may be effective in fighting HIV and in treating opportunistic conditions. Confirmation of HIV infection leads to the initiation of these interventions at an early stage in the infection, even prior to the occurrence of symptoms. Grassroots AIDS organizations throughout the United States have taken the lead in encouraging early detection and treatment, and many physicians speculate that such early intervention, while yet unproven, may be crucial to successful treatment. This strategy of taking the initiative in dealing with potential HIV infection has also given many people at risk for AIDS a sense of control over their destinies.

Testing may reveal vital information for sexual partners who have reason to believe one or both may be infected and who must make informed decisions about having children. In addition, it is important for those women with a history of risk who must make decisions about breastfeeding and infant inoculation. A negative test result may also reduce anxiety among people concerned that they have been infected, and a positive test result has been shown to motivate some individuals engaging in high-risk behaviors to adopt safer practices.

> *The key to transcending the debate about testing is to view the test as one of several approaches to cope with the epidemic rather than as a goal in and of itself.*

Finally, the knowledge of infection status may influence the situations into which a person places him or herself. Since employers, insurance companies, the military and the government, for example, may be able to force a person to be tested and may use test results in discriminatory ways, it may be wise for a person to submit to anonymous or even confidential testing to maintain control over that information.

Complications of Testing

At the same time that the rationale to take the antibody test has become more compelling, the reasons to avoid it have remained. There is a growing concern that the use of non-anonymous testing, which is important for tracking and controlling HIV infection, may foster further discrimination against those who are seropositive. People at high risk for AIDS, among others, advocate anonymous testing as well as the passage of laws to prohibit discrimination in employment, housing, insurance coverage and medical care for those who are HIV infected or even suspected of being HIV infected. Some suggest that people avoid testing unless it is anonymous or until such anti-discrimination protections have been adopted.

A second problem with HIV testing is the psychological danger to the individual tested. As there is anxiety for some people about not knowing their serostatus, for others, a positive test result may bring on a host of psychological reactions: nightmares, sleep disturbance, depression, suicidal behavior, anger, self-imposed withdrawal and social ostracism, relationship problems, and a preoccupation with unrelated or minor bodily symptoms.

continued on page 2

THE AIDS HEALTH PROJECT

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HIV Testing Debate. . .

continued from cover

Negative test results, on the other hand, may offer an individual a false sense of security and be perceived as permission to engage in unsafe behaviors. It is also important to note that while there is optimism among researchers about treatments such as AZT, there is also evidence that such treatments have long-term negative side effects and may not be as effective as they are presumed to be.

Finally, although researchers are confident that a positive antibody test result accurately detects HIV infection, recent studies have shown that a negative result does not necessarily mean that a person is uninfected. This is not caused by a problem with the test, but by a twist in the way the body responds to HIV.

One study, presented in June at the Fourth International AIDS Conference in Stockholm and supported by other research,[1] showed that in rare cases, antibodies to HIV may not form for up to 42 months after infection by the virus. Another study found that people who test positive for antibodies may revert to seronegativity over 2.5 years.[2] These studies used the polymerase chain reaction test (PCR) to detect the presence of HIV DNA at a time when antibodies were not being produced. (See Wilber article below for a further discussion of PCR.)

Experts have emphasized that most people will develop antibodies within six months of infection, or at least within one year, and will remain seropositive. Still, some who test negative may, in fact, be infected and it is unclear how many people fall into this category.

Reconciling Issues of Test Accuracy

The challenges to the accuracy of antibody testing, provoked by experiments using PCR, raise a number of questions about HIV testing. Is it safe for people who test antibody negative to have unsafe sex with others who test negative? How often should a person be tested? Should negative antibody test results be confirmed using PCR? Can other tests supplement the antibody test?

Since a negative result on any of the tests may be inaccurate, it may be wisest to begin to answer these questions by defining what information, in addition to test results, will add to a person's understanding of whether he or she is infected. To do this, individuals should evaluate the risk of exposure to HIV for themselves and their partners, and also the amount of risk they are willing to tolerate in their lives.

Two partners who are seronegative and whose histories indicate a low risk of exposure to HIV might consider unsafe sex practices to be relatively risk-free. If, however, their histories seem to contradict their negative test results, then they should consider what it might mean if these results are inaccurate. It continues to be true that "monogamous" relationships do not always remain as such and that safe sex among two people, no matter what their serostatus, may be the most reasonable course of action.

Researchers recommend that a person who has decided to be antibody tested be retested at least six months subsequent to any possible exposure to HIV. While experts may question the accuracy of the PCR study results, some may suggest that an individual who tests negative be retested every six months for at least 42 months, and perhaps longer. As time passes, however, the likelihood diminishes that a person is infected but not producing detectable antibodies. Again, understanding an individual's risk of exposure, as well as motivations for being tested, may help to decide about retesting. Relying upon retesting to justify unsafe sex may be foolhardy; relying upon it to permit early detection may be wise.

PCR, although it is offered commercially, is experimental and may be risky to use as a supplement to antibody test results. It is being studied and improved, and new tests are being developed, so there should be reliable back-up tests for antibody results in the future. Other tests currently used, however, such as antigen tests and T-cell counts, are not reliable for detecting early HIV infection among asymptomatic individuals.

The Counseling Process

In preparation for counseling, mental health professionals must first become familiar with testing options, what the tests measure, their levels of accuracy, and the potential benefits and risks involved in knowing one is infected. It is helpful to have ready access to community resources that can provide updated information about testing.

Some counselors may find themselves acting in conflicting roles, as counselor and as community activist, in response to the debate about testing and treatment strategies. It is important for counselors to limit their input regarding their own beliefs about whether to test in order to allow clients to come to their own decisions. While misinformation about the tests must be corrected, clients' choices must be understood in terms of their values and problem-solving styles. The decision about whether to be tested for HIV infection should be seen as an integral part of an overall medical and health promotion plan, and should include knowledge of community groups who work with seropositives.

The first step in counseling is to determine a person's level of risk for HIV infection. This requires evaluating his or her history, over the prior 15 years, of unprotected sexual activity, I.V. drug use, and blood transfusion or the use of blood products. Next, the counselor should assess the client's knowledge of HIV and its transmission and, if necessary, precede a discussion of testing with basic AIDS education. Finally, the counselor should discuss testing and how it fits into an overall strategy for AIDS prevention and HIV infection management. After a decision to test is made, counselors should help their clients prepare for emotional reactions to both positive and negative results, for disclosing the results, and for using the results to motivate behavior change.

Clinicians should take responsibility for providing a structure for facilitating the decision-making process. One process that has been used successfully is based on a "Benefit-Risk" analysis. The client is asked to list the potential benefits and risks of being tested. Each benefit is scrutinized to determine whether it can be accomplished in a way, other than antibody testing, that does not have a concomitant risk. For example, if an individual wants to be tested to lower the risk of contracting HIV through sexual contact, an understanding that safe sex guidelines hold true for those who test negative as well as those who test positive may obviate the person's need to take the test.

If a greater overall benefit has been established to proceed with the test, a careful review of risks must be undertaken. In some cases perceived risks are in fact groundless, such as the fear that someone could obtain one's name from an anonymous test site. Other risks can be reduced somewhat by careful planning. For example, a couple's concern about how they will handle test results may be answered by discussions with both partners prior to testing.

After a careful examination of the benefits and risks, the final choice—an educated decision—is the client's alone to make.

Conclusion

The key to transcending the debate about testing is to view the test as one of several approaches to cope with the epidemic rather than as a goal in and of itself. This is true both on a political and a personal level.

Most public health officials agree that mandatory governmental testing would do more harm than good: it would encourage people at highest risk, those for whom the test is likely to mean the most, to avoid testing for fear of discrimination. On the other hand, the argument put forth by some AIDS activists that testing and early intervention is crucial for those who are most likely to be infected assumes that there is a consensus that early intervention and experimental treatment is the appropriate course for everyone.

Practitioners must go beyond the testing debate, and even AIDS itself, to help clients see testing in the context of broader

issues such as their beliefs about medicine, death, quality of life, religion and spirituality, and politics. This global view may make the decision to test no easier, but it can reframe the debate and help define testing as one of many tools that may help clients make other life decisions.

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Diagnosis/Treatment/Prevention

Research Methods for Studying HIV Infection

Judith Wilber, PhD

As the reasons for HIV detection become more numerous and as the available types of testing increase, scientific knowledge of the tests is important both in the decision to be tested and in the interpretation of results.

In addition to the familiar HIV antibody tests, there is a growing array of other tests available for detecting HIV infection, including those that measure the virus, the antigen, viral DNA and indicators of immune dysfunction. These tests vary not only in terms of what they measure, but also in terms of their methods and reliability. This article outlines the different tests and discusses their technical aspects.

All of the tests, except for the antibody tests used at alternative test sites and blood banks, are designated "research" tests because the significance of each is not yet fully understood. When research tests are used on individuals, their results must be interpreted with caution, in the context of continuing medical evaluation, using other tests to substantiate them.

Antibody Screening Tests

The body's immune system produces antibodies in response to antigens, specific foreign substances such as bacteria or viruses, like HIV, or parts of these substances. Since antibodies are so specific, test results demonstrating the presence of particular antibodies indicate that the immune system has come into contact with the corresponding foreign substance.

Until recently, most of the interest in HIV testing has been focused on antibody assays because they are best suited for testing large numbers of people and have been used widely since 1985 in blood bank screening programs. The enzyme-linked immunosorbent assay (ELISA), the most common antibody test, is considered accurate, but should be supplemented by the Western blot test or the immunofluorescence assay (IFA) in order to validate positive test results.

The use of antibody tests to determine whether a person is infected with HIV is based on two reliable assumptions: (1) people who have been infected with HIV will produce detectable antibody, and (2) those who have detectable antibody are infected with HIV. How long it takes for the body to produce antibodies to the HIV is a troubling question. It usually takes four to 12 weeks after infection and, in some cases, the process may take as long as a year. Recent studies, however, have uncovered rare exceptions to this, where, for instance, antibodies were not produced for as long as 42 months after HIV DNA was detected in blood cells.

Unlike common antibody tests, which use antigen from human cells, genetically engineered tests use antigen synthesized in bacteria or yeasts. An example of these is the latex agglutination test, a simple and rapid test to perform that is similar to over-the-counter pregnancy tests. It was developed for screening HIV antibody in areas such as Africa where the facilities may not be available to handle the technology involved in ELISA, Western blot or IFA. Since strict quality control, confirmatory testing, and counseling are essential to HIV testing, given the impact of test results, latex agglutination is not recommended for use at home or in other non-laboratory settings.

Viral Culture

The classic method for detecting viral infection is to grow the virus from the tissues of a person suspected of being infected. Culturing HIV is a time-consuming, labor intensive, and expensive procedure usually reserved for studying the effects of anti-viral agents and vaccines on HIV.

At least 90 percent of people who test positive for HIV antibody will have positive viral cultures. On the other hand, there is some concern that people with no detectable antibody may have the virus hidden in macrophages, a white blood cell, or other cells. A hidden virus like this could be detected by culturing white blood cells. It is extremely rare, however, to find individuals with a positive HIV culture and negative antibody results.

Antigen Tests

Testing for antigen is a means of looking for the proteins of the virus itself in blood specimens. The most common assay for HIV antigen detects the p24 core protein. This antigen is present in the blood a few weeks before an individual tests positive for antibodies and then decreases as antibody levels increase and antigens are neutralized by antibodies. HIV p24 antigen is seldom found in the blood of asymptomatic antibody positive individuals and therefore should not be used to determine whether someone is infected. Detection of antigen in the blood later in the course of infection may indicate that the virus has become active. This has been interpreted to mean that the person will soon develop symptoms of HIV disease.

Antigen testing can then be useful in monitoring therapy with AZT and other drugs. Testing should be repeated over time and antigen neutralization should be performed if the test is positive. Results should be followed and combined with other findings, such as T-cell counts and beta$_2$ microglobulin levels, to form a complete clinical picture.

Tests for HIV DNA

Tests to measure viral DNA incorporated into human genes have been developed and will detect HIV infection even though the virus is inactive and has not produced antigen, which would evoke the body's antibody response.

Polymerase chain reaction (PCR), also know as gene amplification, is a new test that is the most sensitive of all HIV detection tests developed so far. This method makes multiple copies (a million-fold or more) of the part of the HIV DNA being sought. Some studies have found evidence of HIV DNA long

continued on page 4

HIV Detectability

This graph shows the relative time after infection by HIV that these tests will detect the presence of the virus. Since people vary in their responses to HIV, no exact amount of time can be attached to these periods.

HIV Test Method	Relative Time after Infection
PCR	^---++
Virus Culture	^-------++
p24 Antigen	^----------++----------++++++++++++++
Antibody Tests	^----------++
Beta$_2$ Microglobulin	^==========> > > > > > > > >
T-cell Count	^==========< < < < < < < < <

^ point of infection; -- undetectable; + detectable; = normal level; > high level; < low level

continued from page 3
before antibody is formed and even before cultures are positive. The implication of a positive PCR in the absence of any other positive assays is not clearly understood at this time, but may indicate inactive or hidden HIV.

Results of PCR, which is being offered on a limited commercial basis to individuals, should be interpreted with caution. In this test especially, there is a chance of false positive results if the proper care is not taken in the laboratory.

Indicators of Immune Dysfunction

T-cells are lymphocytes, members of the body's immune system, whose numbers are depleted by HIV infection. $Beta_2$ microglobulin is a molecule found on most human cells that is released into the blood stream when a cell dies. Lowered T-cell and increased $beta_2$ microglobulin levels have been shown to correlate with the compromised immune status of people who are infected with HIV and may indicate disease progression.

Neither of these assays, however, is specific to HIV infection and other common conditions, including infection by other viruses, can cause these levels to fluctuate. Therefore, these tests should be used only for periodic monitoring of progression of HIV disease or for monitoring the efficacy of treatment.

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BRIEFS

Recent Reports

Anonymous Versus Confidential Antibody Testing. The availability of anonymous, versus confidential, testing increased the numbers of clients tested at Oregon HIV-antibody test sites by 50 percent for the total sample, and by 125 percent for gay men alone, according to *The Lancet* (August 13, 1988).

In December 1986, 25 Oregon counties began offering a choice of anonymous antibody testing, where clients were identified by number only, or confidential testing, where clients gave name, birthdate, address and telephone number. Prior to this, only confidential testing had been available.

Researchers from Oregon state and county health departments and from the Centers for Disease Control divided clients into three groups according to questionnaire responses: those who would have avoided testing had they not been assured of anonymity, those who would have been tested in either case, and those who were undecided.

Twenty-nine percent of all 1198 subjects who responded to the questionnaire said they would not have been tested had they not been offered anonymity. For members of groups identified with risk factors, these numbers were higher: 49 percent of gay men and 30 percent of female prostitutes. The researchers also found that demand for testing among gay men increased from a median of 42 per month in the four months prior to the institution of anonymous testing to 108 in the four months after.

The study results show that anonymity in antibody testing preferentially drew gay men, currently the group in Oregon at highest risk for HIV infection. Anonymity also shortened the period gay men said they waited before being tested.

(Editor's note: These findings confirm the earlier results of an AIDS Health Project survey (1987) of 417 clients visiting alternative HIV antibody test sites in San Francisco. The survey found that 47 percent of the sample said that they would have foregone testing if anonymity had not been guaranteed. Among gay men, this figure was 82 percent.)

AZT-Associated Muscular Disease. Researchers from St. Mary's Hospital and Medical School in London reported in a letter to *The Lancet* (September 17, 1988) that eight of 113 AIDS and ARC patients receiving zidovudine (AZT) developed, within a year, clinical and biochemical evidence of myopathy (muscular disease). The condition could be attributed only to treatment with AZT.

Five of the patients were on full-dose treatment (1200 mg. daily) and three were on reduced doses (600 to 800 mg. daily). The myopathy was predominantly in the upper leg and, for half the patients, pain accompanied the condition. All the patients experienced pronounced wasting and loss of power in the affected muscles and three patients had muscle tenderness.

AZT treatment was stopped in six of the cases and all of these showed biochemical evidence of resolving the myopathy. For four of these patients, the myopathy was also clinically resolved. For two of the eight patients whose AZT treatment was continued at reduced dosages, there was no improvement in the myopathy. The change in the myopathy for two of the patients for whom treatment was stopped could not be evaluated because of medical complications.

Of the array of other drugs that patients were also given, none, other than AZT, could be implicated as causing the myopathy. In addition, the presence of muscle pain and tenderness distinguished the AZT-associated myopathy from HIV-associated myopathy. The results emphasize the need for monitoring AZT use in severely ill patients and for caution in treating with AZT patients in the early stages of HIV infection.

Next Month

Black gay and bisexual men are often overlooked in general discussions about AIDS. Part of this problem is related to the lack of data on the effects of HIV disease on this population. **Vickie M. Mays, PhD,** Associate Professor of Psychology at UCLA, and **Susan D. Cochran, PhD,** Associate Professor of Psychology at California State University, Northridge, are conducting a national study on the subject. They will report in the December issue of **FOCUS** on the epidemiology of HIV disease in the black community and the clinical context for HIV counseling of black gay and bisexual men.

Society has also failed to target gay and bisexual youth in its AIDS prevention efforts, according to **Paul Gibson, LCSW,** a therapist in private practice, an AIDS consultant and the former director of a shelter for runaway youth. In the December issue, Gibson discusses AIDS prevention strategies for young gay and bisexual males.

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