Silent infection refers to a condition in which a person carries HIV for an extended period, perhaps as long as several years, without producing antibodies to the virus. An individual with silent HIV infection would not test positive to traditional antibody tests, such as an enzyme-linked immunosorbent assay (ELISA), Western blot or immunofluorescence assay (IFA).

RESEARCH UPDATE

Silent HIV infection has been the subject of research since the mid-1980s, and in 1987 it was reported that long periods of latency can exist between the time a person is infected with HIV and the time that person’s body produces antibodies to the virus.

In 1988, researchers at the Fourth International Conference on AIDS in Stockholm reported findings of a study in which HIV was detected before seroconversion in several individuals. The study showed that 14 of 16 HIV-infected individuals tested positive to a polymerase chain reaction (PCR) test at least six months before they tested positive on a Western blot test. PCR is a highly sensitive laboratory test that can identify the presence of HIV by detecting viral DNA in the body even before the body produces antibodies to the virus. (Please see “A Related Issue: Methods for Studying HIV Infection,” on page 3.)

Also in 1988, researchers detected HIV DNA in five of 16 antibody-negative sexual partners of seropositive individuals. Another study indicated that some individuals became antibody positive, then reverted to a negative status.

A 1989 University of California Los Angeles study raised perhaps the biggest concern that individuals may be infected with HIV, but test antibody negative for extended periods.

Studying viral cultures to detect HIV, researchers found HIV in several individuals who repeatedly engaged in high-risk behaviors, but had not produced antibodies to the virus up to 35 months later. HIV was found in viral cultures from 31 of 133 gay men who were seronegative at the start of the study. Four of the 31 men had seroconverted by the time the study was published. In three of these men, tests of earlier blood samples showed that HIV was present before seroconversion at 23 months in one man, and at 35 months in the other two.

In 1991, principal investigator David Imagawa stated that the 27 individuals whose viral cultures contained HIV, but who remained antibody negative when the study was published, had yet to develop antibodies. The researchers expect to publish a follow-up report in 1992.

Following the UCLA study, other researchers, including those with the federal government, have questioned the validity of these results and the reported prevalence of HIV infection among those who test antibody negative. A study conducted by the Centers for Disease Control (CDC) showed a significantly lower rate of silent infection. This study found that about 95% of a group of 39 individuals tested HIV antibody positive within 5.8 months of infection. The study, reported in 1989, estimated the median time from infection to first detection of antibody at 2.4 months.

In a study of 78 antibody-negative men in the San Francisco City Clinic cohort study, which is made up mostly of men at high risk for infection, 76 participants tested PCR negative. The two remaining men tested PCR positive in 1985, but later samples of...
Evidence for Silent HIV Infection

Participants were men in the San Francisco City Clinic Cohort Study.

Evidence against Silent HIV Infection

Participants were gay men in the Multicenter AIDS Cohort Study.

Questions About PCR

Researchers have disputed the prevalence of silent infection because of the reliance on PCR for reports of silent infection. PCR is an experimental and relatively new laboratory test and its reliability is still being studied. One study, in which two of 107 antibody negative homosexual men tested PCR positive, revealed that PCR tests can produce false-positive results. The two subjects who tested PCR positive in the study later tested PCR negative and antibody negative on follow-up testing of both the original sample and a sample taken eight to 10 months later. Another study found that a PCR test failed to detect the virus when antibody was present. Of 28 antibody positive subjects in this study, 25 tested positive by PCR.

Possible causes for false-positive PCR readings include contamination of a seronegative specimen with microscopic amounts of material from a seropositive specimen, or misinterpretation of the test in the laboratory.

With continued study of the reasons why silent infection occurs, some researchers expect to be able to more accurately assess its prevalence. In addition, methods of studying silent infection are expected to be greatly improved as PCR testing is performed more often and more widely.

In the meantime, most researchers believe that antibody testing by ELISA, with a supplemental test by Western blot, is the proven and most effective method to determine HIV infection. It is generally believed that most individuals develop HIV antibodies within two to 12 weeks after infection and almost all remaining individuals seroconvert within six months after being infected. CDC researchers have stated that individuals "who have engaged in high-risk activities in the past, who have stopped such activities, and who have been found to be negative for HIV antibodies at least six months later do not routinely need to be retested."
formation of antibodies. This means either that HIV can infect the body without triggering the immune system, or that the loss of antibodies may occur after infection and after production of antibodies.

**Conclusion**

While some researchers claim that silent infection occurs, others dispute its existence or state that if it does occur, it is extremely rare. This lack of agreement, and the existence of conflicting research reports makes it particularly difficult to understand the phenomenon. This is particularly frustrating for clients who have concerns about silent infection and counselors who attempt to discuss the issue with them.

**A Related Issue:**

**Methods of Studying HIV Infection**

Antibody tests by enzyme-linked immunosorbent assay (ELISA), with supplemental Western blot testing or immunofluorescence assay (IFA), are considered the most effective means to detect HIV infection and the best method to test large numbers of people. The ELISA is used widely because of its reliability, the definitiveness of a positive result, and the test’s low cost. Use of the test has been reinforced by several years of practical application, dating from 1985 when antibody tests were first used in blood bank screening programs.

Antibody detection, as performed on specimens at the state’s anonymous and confidential test sites, is effective because more than one test is performed for reactive samples. When a sample is positive or indeterminate by an ELISA, a supplemental Western blot or IFA test is performed. Western blot and IFA are highly sensitive and specific for detecting HIV antibody.

In addition to antibody tests, there are other tests that have application to measuring either for HIV infection or the general state of an individual’s immune system:

**HIV-Specific and General Immune Tests:**

**Polymerase Chain Reaction (PCR)**

Infection can be detected by PCR, which tests for viral DNA in genes and can be effective even when HIV is inactive and has not produced antibodies. PCR, which is also known as gene amplification and has applications outside of HIV, is the most sensitive of all HIV detection tests so far developed.

Results of PCR tests should be interpreted with caution because PCR is an experimental laboratory measurement that has not yet been refined, and its potential uses are not fully understood. In addition, the test’s high sensitivity may make it susceptible to incorrect results. Results also can be misinterpreted in the laboratory.

**P24 Antigen**

P24 antigen is a protein component of the core of HIV. Tests for p24 antigen measure the amount of this viral protein in the blood. A positive result suggests active HIV replication. P24 antigen is present in the blood a few weeks before an individual tests positive for antibodies and then decreases or goes away as antibody levels increase. Later in the course of disease, p24 antigen levels rise again. Detection of p24 antigen may indicate an individual will soon develop symptoms of HIV disease. Asymptomatic, antibody positive individuals are unlikely to have p24 antigen.

**T-helper cells**

T-helper cell counts, which are widely used to monitor an infected person’s health, can be used to determine impaired immune system functioning. T-helper cells are lymphocytes that are targeted and depleted by HIV. Typically, as HIV disease progresses, the T-helper cell count declines. However, declines in T-helper cell counts are not specific to HIV infection. Other conditions, including infection by other viruses or immune-suppressing illnesses, or treatment with chemotherapies can also lower T-helper cell counts.

**Beta_{2}-Microglobulin**

Beta_{2}-microglobulin is a protein found on most human cells and is released into the blood stream when a cell dies. It is typical for beta levels to rise as HIV disease progresses. Lowered T-helper cell and increased beta_{2}-microglobulin levels may be related to impaired immunity in people infected with HIV or other viruses.
References

IMPLICATIONS FOR COUNSELING

Silent infection is a complex phenomenon for which counselors can provide little definitive information. While a discussion of silent infection may be useful for some clients who raise the issue, there are many occasions when a discussion may be inappropriate and harmful and may cause anxiety or lead a client to unnecessarily believe he or she is infected.

Occasions to Discuss Silent Infection

For clients who believe they are at high risk for infection, but who have tested antibody negative, a counselor's first recommendation should be to take another antibody test in six months. This is especially useful if a client has recently engaged in high-risk activities and may be in the infection "window period," which is generally described as the time, usually no longer than six months, after an individual has been infected but before antibodies to the virus have been produced.

Many counselors believe it is appropriate to talk about silent infection only in cases where clients who are at risk of infection have tested antibody negative more than once and raise the issue that they believe people can be infected without testing antibody positive. When clients state this, counselors should try to learn the reasons for the client's belief to determine if a discussion of silent infection will be relevant in addressing their concerns.

The following are possible reasons clients may believe they are infected:

• An individual has symptoms of disease, and believes these symptoms are related to HIV. While a counselor can ask about such symptoms, it is necessary to remember that many symptoms associated with HIV are also associated with other illnesses and may not indicate HIV infection. And, in the few reported cases of silent infection, seronegative subjects have also been asymptomatic. Individuals experiencing symptoms of disease should be referred to a physician or other medical provider who has a thorough knowledge of HIV infection, and clients should be reminded that counselors are not medical care providers. In many cases, symptoms of disease may be related to other sexually transmitted diseases (STDs). Counselors can provide referrals and recommend that clients be screened for STDs.

Approaches to Discussion

A counselor may choose to address concerns of silent infection by first explaining the concept. Some clients may be aware of the phenomenon of silent infection, but may have misconceptions of it. At the outset, a counselor can reassure a client that most individuals produce antibodies within three months and that recent studies show that 95% of all people produce antibodies within six
A Related Issue: Why Antibodies May Develop Slowly in Some Individuals

Researchers are now attempting to learn why some people develop antibodies to HIV more slowly than others. It is widely believed that individuals seroconvert at different rates of time based on the route of HIV infection.

For instance, individuals who are infected by blood-based contact generally seroconvert more quickly than individuals infected by contact with semen or by vaginal fluids. In blood-borne transmission, the conversion period is generally six weeks to two months. The median conversion period for sexually transmitted infection can vary depending on virulence of the strain of virus contracted, the amount of virus contracted and the number of times a person is exposed.

Beyond these differences based on mode of infection, researchers suspect there may be other, yet unproven, reasons for a lag in antibody development in some individuals. For instance, individuals may seroconvert based on variations in the response of their immune systems.

Studies have suggested that in some individuals with high levels of T-suppressor cells, these cells may inhibit viral replication. If HIV is replicating slowly within an individual, the immune system may not detect the low level of virus present. In such cases, antibodies may not develop until the virus is detected.

It has also been suggested, though never proven, that individuals who seroconvert slowly may be infected with a different, and perhaps unknown, strain of HIV.
uncomfortable in even returning for a follow-up antibody test. As of mid-1991, at least two laboratories in California perform commercial PCR testing. They are Pathology Institute, which is based in Berkeley and operates several clinical labs in Northern California, and Specialty Laboratories, which has its laboratory in Santa Monica. A physician must order a PCR test, which costs about $150. The test is not likely to be available at public clinics.

When counselors recommend follow-up testing for an antibody negative or positive person, it is important to provide appropriate referrals. For instance, counselors should be assured that a provider of follow-up tests offers appropriate counseling in addition to giving results. Individuals may also need help finding appropriate health care providers, such as a physician who speaks the client's language or one who will order a test without charting it on a patient's medical record.

**Concern About Discussing Silent Infection**

It is important for counselors to understand the potential for anxiety, fear and confusion when discussing issues of silent infection with clients. For instance, the possibility of silent infection may lead clients to fear that they are infected even if they have tested antibody-negative. And, individuals may be confused about the reliability of a negative antibody result.

There are occasions when a client may believe he or she is infected but a counselor believes a discussion of silent infection is inappropriate. The following are two such occasions:

- **When a discussion of silent infection may not appropriately address the client's disbelief.** For instance, some individuals who do not accept an antibody-negative test result may actually be at very low risk, but still believe they are infected. For example, this might occur with individuals who have seen many friends die of AIDS and cannot understand why they themselves are not infected. Other individuals may associate each passing symptom or illness with HIV infection regardless of whether they have been at risk. And, for a variety of reasons, some individuals may simply not want to believe they are negative. These clients' concerns should be acknowledged empathically, and they may benefit from a support group for the "worried well" or other counseling.

  - **When the client is unlikely to understand the issue of silent infection and its implications.** For such clients, a counselor should recommend a follow-up antibody test in six months. If this has been done, and the result is negative, a counselor may suggest that a client seek a thorough medical examination from a physician or public clinic.

**A COUNSELOR'S PERSPECTIVE**

"I'm hesitant to send a client out for another kind of test for HIV because a lot of my clients don't have a regular physician, they aren't empowered enough to find one who is sensitive to HIV, or who speaks their language, and besides, they have no money. The antibody test is the best thing for this person."

With clients for whom silent infection is a concern, it is especially important to discuss the need to avoid behaviors that continue to put them at risk for infection. Individuals who may be infected but who have not produced antibodies may believe incorrectly that they cannot infect others. The counselor must correct this inaccuracy.

**Fear of Undermining the Antibody Test**

Counselors may be reluctant to discuss the possibility of silent infection or other tests that measure infection for fear that such discussion will undermine confidence in antibody test results. It is important to remember that the antibody test is highly accurate and is the most effective test for determining whether an individual is infected with HIV. Regardless of whether silent infection is discussed, it is important that the counseling session include a clear description of the HIV infection window period.

In addition, regardless of whether silent infection is discussed, it is especially important..."
A Case Study

Steven, a 32-year-old gay man, has for several years engaged in high-risk sexual behaviors. These include unprotected anal intercourse with several partners whom he now knows are infected with HIV. When Steven is told by his antibody test counselor that he has tested negative, he offers no noticeable reaction. He then tells the counselor that he believes he is infected because of the sexual activities he has engaged in. And, he says that for the last year or so he has had several minor infections that he had not previously experienced. He then states that he has heard that people can be infected without testing positive to antibody tests, and that he must be one of these people.

Counseling Intervention

The counselor can begin by trying to learn more about the specific reasons Steven believes he is infected. The counselor can ask Steven his feelings regarding his health and his past behaviors.

As part of this discussion, the counselor should try to learn to what extent Steven's feelings might be related to grief, loss, anger or fear. If Steven has had friends or acquaintances with HIV infection, the counselor can empathize with this, and explain that it is understandable he would believe he is infected because his friends have been.

The counselor must explain that Steven's sexual practices have put him at risk for infection, and that regardless of whether he is infected it is essential that in the future Steven engage only in safer sex.

The counselor may then state that while many people have become infected after engaging in unsafe behaviors similar to Steven's, many others have engaged in unsafe sex without being infected. It should be stated that "luck" may be the primary reason for this, and that such luck may end at any time. The counselor can also explain that Steven's symptoms of infection may be related to other sexually transmitted diseases (STDs) or infections for which he should be monitored by a physician. If appropriate, the counselor may then begin discussing about silent infection by reinforcing to Steven the reliability of the antibody test, and asking Steven for his knowledge of silent infection. The counselor can clarify any misconceptions, and state that silent infection, if it does occur, is very rare and that there is no clear understanding of how it happens. The counselor can explain that most people develop antibodies within two to 12 weeks, and almost all people develop antibodies within six months of infection, but it is possible that a very few individuals may be infected for some time beyond this period without developing antibodies. The counselor can tell Steven that for these few people, other tests may be helpful in determining infection.

The counselor can, if appropriate, explain other tests available, such as T-helper cell counts, beta2-microglobulin and perhaps PCR. These tests can be presented as valuable in determining an individual's overall health, but it must be stressed that they are not definitive methods for detecting HIV infection.

Steven should be told of the precautions to take in seeking any other tests, such as finding a physician who is knowledgeable and sensitive to HIV concerns, and finding a physician who is willing to keep the record of such tests off Steven’s permanent medical chart. The counselor can help Steven evaluate his current physician, and, if appropriate, provide a referral to an HIV-knowledgeable physician who can evaluate Steven’s health and determine the relevance of other tests.

The counselor may end the session by providing emotional support. The counselor can state that many individuals with feelings similar to Steven’s have benefited from support groups for the “worried well,” and that it might be helpful for Steven to consider such a group.

Finally, the counselor should make sure Steven adequately understands that regardless of whether he is infected, it is essential to eliminate any practices that might infect himself or others.
TEST YOURSELF

1. A 1989 study by researchers at the Centers for Disease Control (CDC) found that within six months of infection with HIV, what percentage of individuals produce antibodies to the virus? a) 95%, b) 50% c) 99.7%, d) 100%.

2. True or False: Silent infection refers to a situation in which an individual is infected without ever being at risk for infection.

3. CDC researchers report that silent infection a) is reaching epidemic proportions, b) is a phenomenon that occurs, but is rare, c) has been proven not to exist, d) occurs only among injection drug users.

4. Individuals who are believed to be at risk for infection, but who test antibody negative, can definitively learn their HIV status by taking which of the following tests? a) T-helper cell counts, b) beta-2 microglobulin, c) either a or b, d) neither a nor b.

5. Some researchers have speculated that certain individuals may not seroconvert within six months for which of the following reasons? a) they may have a slightly different HIV strain, b) they may have a lower concentration of HIV in their blood, c) the virus may not have activated their immune system, d) all of the above.

6. True or False: Through the use of PCR tests, it may be possible to detect HIV, even when antibodies have not been produced.

7. True or False: Several studies have found that silent infection is an infrequent occurrence.

8. True or False: Tests for T-helper cells can be used to determine impaired immune system functioning, but they are not specific to HIV.

DISCUSSION QUESTIONS

- People have traditionally considered the antibody test the most effective method for detecting HIV infection in large numbers of people. How can counselors discuss the need for alternative tests without reducing the credibility of antibody tests?
  - In what circumstances should a counselor discuss silent infection? In what cases should a counselor avoid raising the issue of silent infection with a client? In such instances, what counseling can be offered?
    - How can counselors be sure their referrals for follow-up testing will be sensitive to an individual’s HIV concerns, and will provide counseling and other services appropriate to the situation?
      - What counseling can be offered to an individual at very low risk for infection who has returned for a follow-up test, but does not believe in the validity of a negative result?
    - Discussion of silent infection can produce a high level of anxiety and fear in many people; in what ways can the counselor try to avoid or reduce this anxiety or fear?

Answers to “Test Yourself”

1. A. 95%.
2. False. Silent infection refers to a condition in which individuals have been infected with HIV for an extended period but have not developed antibodies to the virus.
3. B. Silent infection is a phenomenon that occurs, but is rare.
4. D. Neither A nor B.
5. D. All of the above.
6. True. PCR is a highly sensitive, experimental laboratory test that is capable of detecting HIV even when antibodies have not been produced. PCR results must be interpreted with a great deal of caution.
7. True.
8. True.

How to Use PERSPECTIVES: PERSPECTIVES is designed as an easy-to-read educational resource for antibody test counselors and other health professionals. Each issue presents a relevant topic with a "Research Update" and an "Implications for Counseling" section.

The Research Update reports and analyzes recent research related to the main topic. Implications for Counseling, the research is applied to the counseling session, and a case study is offered. PERSPECTIVES also includes two sets of questions, one to test yourself on the material presented, and another to discuss with others or consider alone.

Each issue can be filed and referred to as an instant resource in the future.

HIV Counselor PERSPECTIVES

Volume 1, Number 3 – June 1991

PERSPECTIVES is an educational publication from the California Department of Health Services, State Office of AIDS, and is written and produced by the AIDS Health Project, affiliated with the University of California San Francisco. Permission to reprint any part of PERSPECTIVES is granted, provided acknowledgement is given to the Department of Health Services. Addresses: Department of Health Services, State Office of AIDS, P.O. Box 942732, Sacramento, CA 94234, (916) 445-0653. UCSF AIDS Health Project, Box 0964, San Francisco, CA 94143, (415) 476-6430.

Director, AIDS Health Project: James W. Dilley, MD. Writer and Editor, PERSPECTIVES: John Charles Tighe.

Technical Production: Joseph Wilson.

Many people, including antibody test counselors, contributed information to PERSPECTIVES. Among those who had a significant influence on this issue are: Steve Hamilton, Graciela Morales and Tony Gonzalez.