T-HELPER CELLS

T-helper cells, also known as CD4 cells, are white blood cells of the body's immune system that help the body fight disease. For a person with HIV, a decline in the number of T-helper cells is one of a number of markers that HIV disease has progressed, and it indicates a risk of future progression. T-helper cell counts are measured by laboratory blood tests. Other markers of HIV disease progression measured by laboratory tests and used in clinical practice include beta-2 microglobulin, neopterin, p24 antigen and p24 antibody. These markers are explained in greater detail beginning on page 4.

RESEARCH UPDATE

T-Helper Cells

T-helper cells are one of several kinds of white blood cells in the body and they are the immune system's primary line of defense in fighting infections, including HIV. While a decline in T-helper cell counts is an indicator of a suppressed immune system, it is not proof that a person is ill or is going to develop serious illness. In addition, fluctuations in T-helper cell counts are not specific to HIV infection; rises and falls occur in people who are not infected with HIV.

A healthy body has an enormous number of T-helper cells. When an organism, such as a common flu virus, invades the immune system of someone who is not infected with HIV, T-helper cells coordinate the body's response to fight and eventually eliminate the organism.

When a person is infected with HIV, the virus selectively invades T-helper cells, and becomes a part of these cells. At this stage, T-helper cells may slow HIV from advancing, but they are unable to eliminate HIV from the cells that are already invaded. Treatments can aid in slowing the progression of the virus and increasing the number of T-helper cells. However, during an extended period, which may stretch for several years, HIV gradually becomes more aggressive and spreads to a larger number of cells. These cells are unable to defend against HIV, they are eventually destroyed and the immune system becomes increasingly weakened. Opportunistic infections take advantage of the weakened immune system to cause disease.

T-helper cell counts measure the number of T-helper cells in a cubic millimeter of blood. In healthy people who are not infected with HIV, T-helper cell counts normally range between 700 and 1,300. In a person with HIV, a decline reveals that these cells have been eliminated — most likely because HIV has infected additional T-helper cells — and therefore, the body's immune system has weakened and is less able to defend itself against infections.

T-helper cell counts are considered the best test to evaluate the health of the immune system for a person with HIV. Many researchers consider T-helper cell counts the "most important feature in predicting short-term risk of developing clinical signs of disease." A conference on the use of the antiviral drug zidovudine (AZT) in early HIV disease concluded that the T-helper cell count is the only laboratory test necessary in deciding when to begin treatment with AZT.

Clinicians use T-helper cell levels to determine the degree to which infection has progressed, and to determine appropriate interventions. Researchers and clinicians have arrived at the following general guidelines as a result of studying T-helper cell levels in people who have developed illness.

- 500 or more. A T-helper cell count of at least 500 is considered to be above the range for which HIV treatments are recommended by physicians as a standard practice. At this level, immune-related diseases are extremely rare. Most people with HIV maintain T-helper cell counts of at least 500 for
T-Helper Cell Counts and AIDS Risk

Subjects with HIV Who Developed AIDS Three Years after Entering Study

- **200-499.** Antiviral treatment is recommended when T-helper cell counts fall below 500. Studies have found the drugs AZT and didanosine (ddI) to be beneficial in delaying disease progression for people with T-helper cell counts below 500. AZT has been shown to boost T-helper cell levels for an indefinite period that may extend several years. For most people not taking treatment, T-helper cell counts steadily fall. Even with treatment, T-helper cell counts usually decline over time.

Preventive, or prophylactic, treatment against the opportunistic infection *Pneumocystis carinii* pneumonia (PCP) is suggested for people with T-helper cell counts below 250. Most serious HIV-related diseases do not develop in people with T-helper cell counts between 200-499. However, T-helper cell counts between 200-499 are interpreted with caution because they show increased immune suppression and risk of further decline. T-helper cell tests for people with counts between 200-499 should be measured every three months.

Clinical signs of disease generally are not detected until a person's T-helper cell count falls below 500. Clinical markers, which can be used to measure a person's immune status, include oral candidiasis, also known as thrush; hairy leukoplakia; herpes zoster; and lymphoma-like symptoms such as drenching night sweats, sustained weight loss and persistent high-grade fever or diarrhea.

- **50-199.** As part of a recently expanded definition of AIDS proposed by the federal Centers for Disease Control (CDC), a person would be diagnosed with AIDS when his or her T-helper cell count falls below 200. This proposed change has been delayed indefinitely. A T-helper cell count between 50-200 is considered a danger sign for developing illness. In a recent study of gay men with HIV, 87% of those with T-helper cell counts of 200 or less at the start of the study developed AIDS within three years, compared to 16% of those with counts greater than 400. Illnesses occur with increasing frequency for people with T-helper cell counts between 50-200, and it is at this point that a person should have his or her health monitored at least every two months, and consider prophylactic treatment for other opportunistic infections, including cytomegalovirus (CMV), toxoplasmosis and *mycobacterium avium intracellulare* (MAI or MAC).

- **Less than 50.** In some cases, serious cases of life-threatening HIV-related illnesses do not develop until a person's T-helper cell count has fallen below 50; one study of patients receiving thorough treatment found it extremely rare for HIV-related death to occur before this time. Some people with HIV may have T-helper cell counts below 50, yet not have serious illnesses. This is often because infections are being successfully prevented by prophylaxis.

**Variable Results**

T-helper cell counts can vary dramatically for reasons that appear to have little to do with overall health status.

For instance, differences in laboratory techniques can result in counts that differ by as much as 20%. In addition, T-helper cell counts vary naturally in any person over time — even from day to day — for reasons that are independent of HIV infection, but which are poorly understood. For example, normal variation would allow for a T-helper cell count of 500 at one time and perhaps 400 or 600 on a follow-up test. Test results can vary based on the time of day they are performed; the existence of other medical conditions, such as colds; the presence of medications; and vigorous exercise.

To reduce variations, success-
A Related Issue: 
Defining AIDS — The Role of T-Helper Cells

The Centers for Disease Control (CDC) has proposed new criteria for its AIDS case definition. The CDC’s existing definition assigns an AIDS diagnosis only in the presence of at least one of a number of opportunistic infections, such as Pneumocystis carinii pneumonia (PCP), Kaposi’s sarcoma (KS), or toxoplasmosis. The proposed criteria expand the definition to include either one of these diseases or a T-helper cell count below 200. The definition, first proposed in the summer of 1991, was repeatedly postponed and in June 1992 its implementation was postponed indefinitely. Some believe the proposal to be cancelled. Regardless, the attempt to give merit to laboratory markers such as T-helper cells is significant. And, it signals the growing importance of looking at such markers, and not only the presence of certain opportunistic diseases, in viewing HIV infection.

The CDC sought to expand its definition in part to more accurately count the number of people with advanced signs of HIV disease. While the CDC has changed its definition of AIDS several times since the original definition was established in 1982, the proposed revision is the first to include a laboratory marker of progression such as a T-helper cell count. Earlier definitions were made at a time when little was known about laboratory markers, and they were based on diseases seen in homosexual men. They did not include conditions commonly seen in injection drug users and women, who have been increasingly affected by HIV.

The definition change has drawn criticism from some who believe it does not include all people at advanced stages of HIV infection. Specifically, the new definition does not include pulmonary tuberculosis, seen often in injection drug users, and vaginal candidiasis, which is common among women with HIV. Advocates say many people suffer these and other non-AIDS defining illnesses despite T-helper cell counts greater than 200.

If additional diseases were considered, doctors may recognize conditions as being associated with HIV disease, advise HIV antibody testing, and help patients develop HIV treatment plans earlier in the course of disease.

Some people also believe the new definition places too great an emphasis on T-helper cell counts, and that a combination of markers should be used. Despite the drawbacks, the focus on T-helper cell testing means that more asymptomatic people who would otherwise avoid treatment would be prompted to seek treatment when they receive an AIDS diagnosis. While this may ultimately be beneficial, especially as treatments improve, it is important to note that the definition in and of itself does not change people’s health. People with T-helper cell counts of less than 200 are no less healthy with an AIDS diagnosis than they are without one.

The Effect on Benefits

While some had hoped a definition change would broaden the number of people eligible to receive public benefits, the Social Security Administration has established separate criteria to determine when a person with HIV is eligible for benefits. This eligibility is based, not on a person’s T-helper cell count, but on factors more closely tied to whether a person is healthy enough to work. Physicians can make such claims on behalf of patients. Under the definition for these benefits, a person who has fewer than 200 T-helper cells but is healthy enough to work, may not qualify.

While it is likely that more people will qualify for benefits under the new benefits criteria, it is unlikely that financial support from the government will increase. Therefore, it may be more difficult to receive benefits.
counts greater than 500. Clinical evidence has found that some people have maintained T-helper cell levels higher than 500 for longer than 10 years after being infected.

T-Helper Cell Percentages or Ratios

While T-helper cells are most commonly reported in absolute numbers, they can be reported as a percentage of all T-lymphocytes. In healthy, uninfected individuals, T-helper cells generally make up more than 30% of all T-lymphocytes. Treatment with AZT is often recommended when the T-helper cell proportion falls below 25%. The percentage is used because it varies less from day-to-day than the absolute number of T-helper cells.

Other Markers

In addition to T-helper cell counts, other markers are used to evaluate the health of the immune system and show whether HIV is actively replicating within the body.

Because no single lab test, including a T-helper cell count, can be considered completely accurate in determining the health of a person’s immune status, it is useful to consider several different test results together. As with T-helper cell testing, the results of other tests are affected not only by HIV but also by the presence of drugs and medications and other infections. Most often, clinicians use T-helper cell counts with either beta-2 microglobulin or neopterin tests.

Beta-2 microglobulin

Beta-2 microglobulin is a molecule released into the bloodstream when a cell dies. Beta-2 microglobulin tests, which measure the molecule in milligrams per liter of blood, can detect cell loss in people with HIV. Levels below 3 are considered normal in healthy individuals. When the beta-2 microglobulin level rises above 3, the risk of HIV progression increases. The risk of progression is especially increased at levels higher than 3.5. One study found declines in beta-2 microglobulin levels in people who began therapy with AZT.

Neopterin

Neopterin is a substance that is released into the blood by cells called macrophages in the presence of a foreign agent such as HIV. In people who are not infected with HIV, the neopterin level is generally about 5.4 milligrams per liter. Like the beta-2 microglobulin level, neopterin levels reflect stimulation of the immune system. Increases in neopterin levels are a reliable indicator of the presence of a foreign agent, but neopterin can increase for reasons unrelated to HIV. Clinicians generally do not test for both neopterin and beta-2 microglobulin because these tests usually produce the same results. Neopterin tests are generally less available than beta-2 microglobulin tests.

P24 Antigen

P24 is the core protein of HIV. When p24 antigen is detected, it is a sign that HIV is actively replicating in the body. P24 antigen is often present in the period immediately after HIV infection and shortly before a person develops antibodies to HIV. It then disappears for several years and reappears when HIV begins progressing more rapidly. It is rarely detected in asymptomatic people with HIV after they have seroconverted, or started producing antibodies. Therefore, it is generally not a useful test for someone in the early stages of infection.

P24 Antibody

A p24 antibody test measures the amount of this specific HIV antibody produced in response to
p24 antigen. A person with reduced levels of p24 antibody is more likely to develop signs of HIV-related disease. An antibody decline is often detectable before p24 antigen increases.

**T-Killer Cells**

T-killer, or CD8, cells are white blood cells capable of attacking HIV-infected cells, and either killing them or suppressing the virus within them. According to a presentation at the Eighth International Conference on AIDS in July 1992, a drop in the number of these cells is followed by an onset of HIV symptoms. This finding is preliminary. Tests for T-killer cells are not yet in widespread use.

**Other Lab Tests**

In addition to markers of progression, many other laboratory tests evaluate general health or specific infections. They include tests for kidney and liver function, syphilis, tuberculosis infection and complete blood count (CBC). A CBC is a general purpose laboratory test used as part of the evaluation of almost any condition. A CBC counts the number of red blood cells, white blood cells, and platelets.

**References**


**IMPLICATIONS FOR COUNSELING**

Markers of progression are relevant to the antibody test counseling session because they are a client's "next step" after receiving a positive antibody test result. After an antibody test determines a person is infected, T-helper cell counts and other laboratory markers of progression can provide specific information about the status of a person's immune system.

Counselors can address the importance of markers of progression briefly in pre-test counseling by stating that clients who receive positive test results can proceed to manage infection with the help of medical intervention, which includes tests for T-helper cells.

Discuss markers of progression in a post-test counseling session by first determining a client's knowledge of the steps to take to manage HIV infection and receive health care. Make no assumptions about a client's knowledge related to markers of disease progression; clients may know a great deal about HIV infection, yet know little about tests beyond the HIV antibody test.

A discussion about markers of progression need not be lengthy. Present them as a valuable tool for clients to gauge their health status and maintain some control of their health. Specifically, results of laboratory tests are useful in making informed decisions about whether to enter clinical trials, and accept prophylactic and antiviral treatment.

Present the following information:

- Review the basics about the activity and progression of HIV. Explain that T-helper cells are the body's primary defense against HIV, and that T-helper cell counts are the most often used marker of HIV progression.
- Tests are available to determine a person's immune status, and these tests are a valuable part of medical care for someone with HIV. Emphasize that once people...
are aware of their antibody status, the next step is to determine immune system status.

- While a client's personal perceptions of how well he or she feels at the moment are important, laboratory tests can go beyond this to measure the degree to which the virus has weakened the immune system.
- Tell clients they can obtain T-helper cell counts from physicians. If they are interested, send or escort antibody positive clients to on-site health centers — where available — for T-helper cell testing after post-test counseling. If such sites are not available, offer referrals to area medical providers for these tests.

In many cases, it will not be necessary to discuss markers of progression in any further detail. Discussing this technical issue may confuse some clients, especially after antibody test result disclosure when many clients are overwhelmed and not necessarily ready to hear about or take additional steps. However, many clients will find it useful to talk in more detail. This is especially true for clients who raise questions or concerns about markers of progression, or those who wish to know more about their health status and about taking control of their health care.

Some clients may place excessive trust in laboratory markers. Even if they feel healthy and have no clinical signs of disease, they may believe that only their T-helper cell result is significant. State to clients that no laboratory marker or combination of markers can definitively determine a person's health and prospects for the future, and that caution should be used in interpreting any result. Put laboratory tests in proper perspective by stating that how a person feels is significant regardless of laboratory test results. Explain that T-helper cell counts can fluctuate broadly for reasons unrelated to significant changes in health, and that tests need to be performed more than once.

Resistance

Seropositive clients may resist seeking medical care or a T-helper cell test after antibody testing. They may feel that seeking further health care is an acknowledgement that they are ill, or they may fear being told they are sick.

Anticipate this resistance, and recognize that clients may not be ready to manage infection. Remind these clients that they have already taken the first significant step in learning about their health and that failing to manage HIV infection is dangerous. Empathize with clients who are unwilling to go further. These clients may be willing to seek education or psychosocial support. Recommend that they enter support groups for people with HIV. They can also visit early intervention sites for health education or one-on-one counseling about their health without receiving primary medical care. These clients may also be willing to set a time for themselves when they will begin to manage infection.

Often, clients have many questions about their health and they believe these can be answered by a T-helper cell test result. Be prepared with answers or appropriate referrals for clients' questions. The following are common questions asked by clients:

- "If my T-helper cell count is low, how can I get it higher?"

A primary purpose of T-helper cell testing is to know when to begin treatment. For someone whose immune system is suppressed, treatment with antivirals such as AZT or ddI may help sustain and perhaps boost T-helper cell counts. Exercise, stress management and proper nutrition and rest may also help boost T-helper cell levels. Poor nutrition and consumption of alcohol and other drugs may suppress the immune system and lower a person's T-helper cell count.

- "Why do I need follow-up tests right away?"

The sooner a person seeks such tests, the sooner he or she may be able to regain some control over his or her health and take the steps necessary to stay healthy. By seeking such tests, a person may learn he or she is at a stage of disease at
Case Study

David is a 33-year-old who has tested antibody positive. He is aware of the significance of T-helper cell levels. David is unwilling to see a physician for a follow-up exam to learn more about his health status. After further discussion with his counselor, David says it is enough to know he is infected, and he is not ready to deal further with his infection: “I don’t want somebody to do a (T-helper cell) test on me and tell me I’m sick and I’m going to die.”

Counseling Intervention

Recognize the source and significance of David’s fear. Because follow-up care can reveal David’s stage of infection, and may even show that he has an AIDS diagnosis, David may fear discovering that he is sicker than he feels or thinks he is.

Begin by assuring David that laboratory tests, including T-helper cell counts, are only a general indicator of immune status, and that a T-helper cell count, whether it is 500 or 50, does not mean that a person is necessarily going to become symptomatic. Help David see a T-helper cell count not as a test delivering a death sentence, but as a tool he can use to evaluate the overall status of his immune system, gain greater control over his health and determine when to begin appropriate interventions.

Describe HIV infection as a condition spanning a wide spectrum, from early to more advanced stages that may stretch over many years. T-helper cell counts usually decline gradually, and it is usually several years after after being infected before a person’s T-helper cell count falls to a point at which the immune system is severely suppressed. Reminder David that HIV antibody and T-helper cell test results do not reveal when he was infected.

Ask David about his health and energy level, and tell him these are important indicators of his general health. Help David see the importance of using his own feelings about his health in combination with laboratory tests, such as T-helper cell counts, and clinical signs of infection. Beyond this, describe the concept of health care for HIV infection and provide medical referrals so that David has this knowledge when he is ready to consider medical care.

Stress that a great deal about the management of HIV disease has been learned since the beginning of the epidemic, and the trend is to begin treatment at earlier stages of infection. With T-helper cell testing, David can have the chance to learn if he is at a stage in which he can benefit from intervention. If he is unwilling to seek health care at this time, accept this decision, and state the value of accepting the knowledge of his infection until he is ready to seek follow-up care.

Suggest that even without seeking a T-helper cell count, David can seek follow-up counseling or medical care. By doing this, he can talk with a clinician or counselor about his thoughts and concerns regarding his health while being monitored for clinical signs of disease. Provide him with referrals, and advise him to return to the test site if he needs more information. Strongly encourage David to talk with other people who are infected with HIV, and encourage him to involve others, such as friends or family in his decision-making. David needs support to make the decision to seek follow-up care; the counselor and other individuals can provide that.

which antiviral treatment will be most effective. At a later stage of infection, such treatments may be less successful at keeping a person healthy.

• “How do I know when to start taking AZT or another drug?”

Therapy with AZT or another antiviral is often recommended when a person’s T-helper cell count falls below 500. It is at this point that a person’s immune system is suppressed to the level where treatment is beneficial. However, not all physicians agree with the recommendation to use AZT when T-helper cell counts fall below 500. Clients can consult with their physicians for further direction.

• “What is the virus doing to my immune system right now?”

The virus may be relatively inactive and may remain this way indefinitely. Or, it may be active, and therefore weakening the immune system and eliminating T-helper cells. Such activity will be undetectable if there are no clinical signs of disease, or if a person feels healthy. The effect of HIV on the immune system can be determined by measuring T-helper cell counts, or other laboratory markers of progression.

In many cases, clients may ask these questions about the virus only after the test counseling session. Provide referrals who will later be able to answer questions.
TEST YOURSELF

1. True or False: T-helper cell counts are considered the most valuable laboratory marker in predicting short-term health risk for a person with HIV.

2. Antiviral treatment is generally recommended when T-helper cell counts fall below what level? a) 1,000, b) 50, c) 500, d) none of the above.

3. T-helper cell tests can show varying results for what reasons a) cell counts fluctuate naturally each day, b) laboratories measure results differently, c) both a and b can occur, d) none of the above.

4. True or False: A study found that beta-2 microglobulin levels fell, indicating a reduced risk of HIV progression, when people began taking AZT.

5. Drug treatments such as AZT are believed to have what effect on T-helper cell levels? a) they boost levels for an extended period, b) they cause levels to consistently fall, c) they have no effect.

6. True or False: Falling T-helper cell counts definitively mean a person will soon become symptomatic.

7. True or False: Most people with HIV have normal T-helper cell levels for several years after infection.

8. The following are used as markers of HIV disease progression: a) p24 antigen, b) beta-2 microglobulin, c) neopterin, d) all of the above.

QUESTIONS FOR DISCUSSION

- Clients may resist health care after receiving test results because knowledge of infection and health status is overwhelming. How can a counselor present a discussion of follow-up care and T-helper cells for these clients? How can a counselor know whether such information is overwhelming?

- Markers of infection other than T-helper cells are important, but may not be required discussion for post-test counseling sessions. When might a discussion of these tests be useful? How might these other markers be presented?

- How much information should antibody test counselors provide about markers of infection? Are there some antibody positive clients for whom it might be more useful not to talk about markers?

- In what ways can counselors help clients see the value in seeking follow-up medical care and lab tests?

- Because the new definition of AIDS proposed by the Centers for Disease Control is based on part on T-helper cell counts, clients may fear they will qualify for an AIDS diagnosis at the time they test antibody positive. How can counselors help clients view this possibility as being a stage in the spectrum of HIV infection, instead of as a sign that they will soon become ill?

PERSPECTIVES is designed as an easy-to-read educational resource for antibody test counselors and other health professionals. Each issue explores a single topic with a “Research Update” and an “Implications for Counseling” section. The Research Update reviews recent research related to the topic. In Implications for Counseling, the research is applied to the counseling session, and a case study is presented. PERSPECTIVES also includes two sets of questions to consider yourself or discuss with others.

HIV Counselor PERSPECTIVES

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