

# Monitoring Tests for People with HIV

13.4  
183  
2129  
1236  
456  
51  
27  
54.6  
31.7  
11.7  
1.3  
0.7

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A wide variety of monitoring tests are available to help gauge HIV disease progression and the state of overall health. HIV viral load tests provide a picture of viral activity, while CD4 cell counts shed light on the status of the immune system and can help physicians predict—and therefore prevent—the development of opportunistic illnesses (OIs). These tests can help guide treatment decisions and indicate whether treatment is working. Viral load tests and CD4 cell counts offer a more accurate representation of HIV activity and disease progression than older, indirect surrogate markers—such as beta-2 microglobulin and neopterin—that are no longer commonly used.

In addition, general tests such as the complete blood count, the blood chemistry panel, and blood sugar and lipid (fat) tests can help keep track of side effects such as low blood cell counts, liver toxicity, and elevated triglyceride and cholesterol levels. Other tests, such as genotypic and phenotypic resistance assays and therapeutic drug monitoring, can help optimize anti-HIV therapy.

Almost all the laboratory tests described in this article require a blood sample; fortunately, a single sample often can be used for several different assays. Typically, a person with HIV or his or her physician will receive a report that combines several test results, along with normal or “reference” ranges. In many cases, a person should receive initial tests as soon as possible after an HIV diagnosis to establish a baseline against which future tests may be compared. In general, most monitoring tests should be performed every 3–6 months or so. Results obtained by different laboratories and different test methods can vary greatly, and results may even vary from day to day at the same lab. Tests should preferably be done at the same lab using the same procedure each time, to allow for more accurate comparisons.

Many factors—such as time of day, recent vaccinations, and concurrent infections such as the flu—may influence test results. A test that returns an unexplained or unexpected result should be repeated. A single abnormal lab result is not always cause for concern; upward and downward trends over time are usually more important. (The normal lab values given below and in the chart on page 38 represent typical reference ranges; values may vary considerably between laboratories.)

32.0-35.0  
11.0-15.0  
140-400  
1500-7800  
850-3900  
200-950  
15-500  
0-200

THOUS/NCL  
BILL/NCL  
G/DL  
X  
FL  
PG

## Complete Blood Count

Whole blood is made up of various types of cells suspended in a liquid called plasma. The complete blood count (CBC) is an inventory of the different cellular components of the blood: red blood cells, white blood cells, and platelets. This test is important because people with HIV may have low blood cell counts (cytopenias) due to chronic HIV infection or as a side effect of medications, particularly drugs that damage the bone marrow, where all blood cells are produced. Blood cell counts are typically reported as the number of cells in a cubic millimeter of blood (cells/mm<sup>3</sup>) or as a percentage of all blood cells. Most experts recommend that people with HIV should receive a CBC about every six months, and more often if they are experiencing symptoms or taking drugs associated with low blood cell counts.

### Red Blood Cells

Red blood cells (erythrocytes) carry oxygen from the lungs to the body's cells, bound to a molecule called hemoglobin. Anemia is a condition characterized by a reduction in the number of red blood cells, often leaving a person fatigued, weak, and short of breath. Anemia is common in HIV positive people. HIV itself and various OIs such as *Mycobacterium avium* complex (MAC) can affect red blood cells and their oxygen-carrying capacity. In addition, drugs such as AZT (zidovudine, Retrovir) may lead to low red blood cell counts due to bone marrow suppression, while other medications such as ribavirin (used to treat hepatitis C) can directly destroy red blood cells (hemolysis). Several tests are used to help diagnose various types of anemia.

**Red Blood Cell Count (RBC):** the total number of red blood cells in a quantity of blood. Normal ranges are 4.5–6.0 million cells/mm<sup>3</sup> for men and 4.0–5.5 million cells/mm<sup>3</sup> for women. (Women typically have lower counts than men due to the loss of blood through menstruation.)

**Hematocrit (HCT):** the proportion of red blood cells as a percentage of total blood volume. A normal hematocrit is 40–55% for men and 35–45% for women.

**Hemoglobin (HGB):** the number of grams of hemoglobin in a deciliter of blood (g/dL). Normal levels in healthy adults are 14–18 g/dL for men and 12–16 g/dL for women. As a rough guideline, hemoglobin should be about one-third the hematocrit.

**Mean Corpuscular Hemoglobin (MCH) and MCH Concentration (MCHC):** the amount or concentration, respectively, of hemoglobin in an average red blood cell.

**Mean Corpuscular Volume (MCV):** the average size, or volume, of individual red blood cells. Conditions such as iron deficiency can lead to smaller than normal red blood cells, while certain vitamin deficiencies and some drugs (including nucleoside reverse transcriptase inhibitors [NRTIs]) can produce larger than normal cells.

**Red Blood Cell Distribution Width (RDW):** a measure of the size and uniformity of red blood cells.

### White Blood Cells

White blood cells (leukocytes) carry out the body's immune responses. The CBC looks at numbers of various different types of white blood cells.

**White Blood Cell Count (WBC):** the total number of white blood cells in a quantity of blood. A healthy adult normally has 4,000–11,000 white blood cells/mm<sup>3</sup>. A WBC increase often indicates that a person is actively fighting an infection or has recently received a vaccine. Decreased WBC (leukopenia) can leave a person vulnerable to various pathogens and cancers.

**Differential:** a report of the proportions of different types of white blood cells as a percentage of the total number of white cells; these percentages may be multiplied by the WBC to obtain absolute counts. People with HIV should be especially concerned with neutrophil and lymphocyte levels, in particular CD4 and CD8 cell counts (discussed below).

**Neutrophils:** a type of cell that fights bacterial infections. Neutrophils normally make up about 50–70% of all white blood cells. Various anti-HIV drugs (especially AZT), OI medications (including ganciclovir [Cytovene], used to treat cytomegalovirus, or CMV), and cancer chemotherapies that suppress the bone marrow may lead to low neutrophil levels (neutropenia). The risk of bacterial infection increases when the absolute neutrophil count falls below about 500–750 cells/mm<sup>3</sup>.

**Lymphocytes:** there are two main types of lymphocytes. B cells produce antibodies that fight foreign invaders in the body, while T cells target infected or cancerous cells and help coordinate the overall immune response. A normal lymphocyte count is about 20–40% of all white blood cells. The typical differential does not include specific subsets of T cells, but because CD4 and CD8 cell counts are important to people with HIV, they are measured separately (discussed below).

**Monocytes:** a type of cell that fights pathogens by engulfing and destroying them. Monocytes circulate in the blood for about 24 hours; when they leave the bloodstream and migrate into the tissues, they mature into macrophages. Monocytes and macrophages normally account for 2–10% of all white blood cells.

**Eosinophils:** cells that play a role in defense against parasites and in allergic reactions. They normally make up 0–6% of all white blood cells.

**Basophils:** another type of cell involved in allergic reactions, in particular the release of histamine. They normally account for 1% or less of all white blood cells.

### Platelets

Platelets (thrombocytes) are necessary for blood clotting. A normal platelet count is about 130,000–440,000 cells/mm<sup>3</sup>. Low platelet counts (thrombocytopenia)—which can lead to easy bruising and excessive bleeding—may be caused by certain drugs, autoimmune reactions, accelerated destruction by the spleen, or HIV disease itself.

## CD4 and CD8 Cell Tests

### CD4 Cell Count

As noted above, T cells are types of lymphocytes that help the body get rid of infected or cancerous cells and help coordinate the immune response. CD4 cells (also known as T4 or T-helper cells) carry the CD4 receptor molecule on their surface and coordinate the cell-mediated immune response. Most CD4 cells reside in the lymph nodes, and various factors can cause them to enter or leave the bloodstream. A normal CD4 cell count in a healthy adult is about 600–1,200 cells/mm<sup>3</sup>; it tends to be somewhat higher in women than in men, and considerably higher in young children. CD4 cell counts often fluctuate due to factors including time of day (levels are usually higher in the morning), fatigue, stress, vaccinations, infections such as the flu, and monthly menstrual cycles in women.

HIV primarily targets CD4 cells. As HIV disease progresses, CD4 cell counts decline, typically by about 30–100 cells/mm<sup>3</sup> per year (depending on viral load), leaving a person increasingly vulnerable to infections and cancers. People with CD4 cell counts above 500 cells/mm<sup>3</sup> generally have relatively normal immune function and are at low risk for OIs.

When the CD4 cell count drops below 200 cells/mm<sup>3</sup>, an individual is prone to infections such as *Pneumocystis carinii* pneumonia (PCP). The risk is even greater when the CD4 cell count declines further; people with fewer than 100 cells/mm<sup>3</sup> may contract OIs such as toxoplasmosis and cryptosporidiosis, while those with fewer than 50–75 cells/mm<sup>3</sup> are at risk for MAC and CMV. A CD4 cell count below 200 cells/mm<sup>3</sup> or a CD4 percentage below 14% signals a diagnosis of AIDS.

The CD4 cell count is a valuable tool for gauging HIV disease progression. Along with viral load, it provides information about when anti-HIV therapy is indicated and how well it is

working; effective treatment can halt HIV replication and restore CD4 cell levels. Current U.S. HIV treatment guidelines recommend that people should consider starting anti-HIV therapy when their CD4 cell count falls below 350 cells/mm<sup>3</sup>. In 2001 this level was reduced from 500 cells/mm<sup>3</sup> after research showed little benefit to starting treatment in asymptomatic people with 350–500 cells/mm<sup>3</sup>, especially given the adverse effects, inconvenience, and cost of therapy. Studies are underway to assess the value of treatment in people with 200–350 cells/mm<sup>3</sup>.

Many people who have started combination anti-HIV therapy have seen dramatic increases in their CD4 cell counts and have been able to safely stop OI prophylaxis (preventive treatment). However, the CD4 cell count tends to eventually drop back to its previous lowest level—known as the nadir—if anti-HIV therapy is discontinued. Importantly, CD4 cell numbers do not tell the whole story: how well the cells function and what pathogens they target are also important. (Tests of T cell activation and proliferation are available as research tools, but are not widely used in clinical practice.)

Most experts recommend that the CD4 cell count should be measured when HIV is diagnosed, then every 3–6 months or so—closer to three months if the count is low or falling or a person is starting or changing treatment, and closer to six months if the count is high or has been stable for several months. An individual CD4 cell measurement is not as informative as downward or upward trends over time; any large or unexpected change should be confirmed with a repeat test.

### CD8 Cell Count

Two types of T cells carry the CD8 surface molecule: T-suppressor cells, which inhibit immune responses, and killer T cells (also known as cytotoxic T lymphocytes, or CTLs), which target and kill infected or cancerous cells. A normal CD8 cell count is about 200–1,000 cells/mm<sup>3</sup>. As with CD4 cells, a variety of factors can cause CD8

cell counts to fluctuate. CD8 cell counts typically rise over time in people with HIV, but (unlike CD4 cells) CD8 cell numbers do not independently predict disease progression, and their relation to immune status is not well understood.

### CD4 and CD8 Cell Percentage

Because absolute CD4 and CD8 cell counts are so variable, some physicians prefer to look at CD4 or CD8 cell percentages—that is, the proportion of all lymphocytes that are CD4 or CD8 cells. Percentages are usually more stable over time than absolute counts. A normal CD4 cell percentage in a healthy person is about 30–60%, while a normal CD8 cell percentage is 15–40%.

### CD4/CD8 Cell Ratio

The CD4/CD8 cell ratio will also be reported. This is calculated by dividing the CD4 cell count by the CD8 cell count. A normal CD4/CD8 cell ratio is about 0.9–3.0 or higher—that is, there are at least 1–3 CD4 cells for every CD8 cell. In people with HIV this ratio may be much lower, with many more CD8 cells than CD4 cells.

## Blood Chemistry Tests

The blood chemistry, or chem panel, measures many important substances in the blood. Although the chem panel does not directly measure HIV disease progression, it can help indicate how well various organs are functioning and provide valuable information about drug side effects. A chem panel should be done at least every six months, and more often in people who are experiencing symptoms or taking drugs that can adversely affect blood values. As noted previously, different laboratories have different reference ranges for what they consider normal values.

### Electrolytes

Electrolytes are positively or negatively charged molecules (ions) that play important roles in cellular activity and heart and nerve function. Normally electrolyte levels are regulated

by the kidneys, and any excess is excreted in the urine. Most healthy people can get all the electrolytes and other minerals they need by eating a balanced diet. Electrolyte imbalances may signal malnutrition, kidney problems, or dehydration (which may be caused by prolonged vomiting or diarrhea). Such imbalances are not uncommon in people with acute or chronic illnesses.

**Bicarbonate:** a form of carbon dioxide (CO<sub>2</sub>) in the blood. Bicarbonate acts as a buffer to help maintain the body's acid-base balance (pH). A normal bicarbonate level is about 22–33 millimoles per liter (mmol/L). A high level might indicate an “anion gap,” which may signify high lactate levels or lactic acidosis (an adverse effect associated with NRTIs).

**Calcium:** a major component of bones and teeth, calcium is also required for proper nerve and muscle function. A normal total serum calcium level is 8.5–10.5 milligrams/deciliter (mg/dL).

**Chloride:** sodium and chloride are often found together, and both help regulate the body's fluid balance. A normal chloride level is 95–105 mmol/L.

**Magnesium:** this mineral plays a role in nerve impulse transmission and muscle contractions. A normal range is 1.5–3.0 mg/dL.

**Phosphorus:** most of the body's phosphorus is located in the bones, but it also plays an important role in maintaining the body's pH balance. A normal level is 2.0–4.5 mg/dL.

**Potassium:** this mineral also plays a role in nerve impulse transmission and muscle function. A normal level is 3.5–5.0 mmol/L. Abnormal potassium levels may be related to kidney failure or dehydration.

**Sodium:** this mineral is important in maintaining the body's fluid balance and is involved in transmission of nerve impulses. A normal level is 135–145 mmol/L. Abnormal sodium levels may be due to dehydration, elevated lipid levels, or kidney dysfunction.

## Liver Function Tests

Liver function tests, also known as the hepatic panel, are laboratory tests that help measure how well the liver is working. The liver carries out many vital bodily functions; when it is not working properly, levels of various enzymes, proteins, and other substances in the blood may rise or fall. Elevated liver enzyme levels may be a sign of liver damage caused by factors such as viral hepatitis, heavy alcohol consumption, or drug toxicity. Because several anti-HIV medications are known to cause liver damage (hepatotoxicity), people taking antiretroviral therapy should have their liver function monitored regularly, about every two months. This is especially important for people coinfecting with the hepatitis B or C viruses.

**Alanine transaminase (ALT):** formerly called SGPT, ALT is an enzyme normally present in liver cells. When these cells are damaged, ALT is released into the bloodstream. A normal ALT level for adult men is 0–50 International Units per liter (IU/L); levels are somewhat lower in women. While mild elevations are common, an ALT level more than 2.5 times the upper limit of normal (ULN) is cause for concern. Recent research has shown that even moderately elevated ALT or AST levels in people with HIV are associated with a higher risk of death. In general, upward or downward trends in ALT are more informative than a single measurement.

**Aspartate transaminase (AST):** formerly called SGOT, AST is another liver enzyme that may spill into the blood when liver cells are damaged. AST levels may also be elevated in people with muscle damage. A normal AST level for adult men is 0–45 IU/L.

**Bilirubin:** bilirubin is a pigment released when red blood cells are broken down. A normal bilirubin level is 0.1–1.5 mg/dL. An elevated level (hyperbilirubinemia) may indicate liver damage, impaired bile flow, or excessive red blood cell destruction. High bilirubin levels can lead to

jaundice (yellowing of the skin and whites of the eyes).

**Alkaline phosphatase (AP):** elevated AP levels may signal obstructed bile flow or bone destruction. A normal level is 35–115 IU/L.

**Gamma glutamyl transpeptidase (GGT):** high GGT levels may also be a sign of impaired bile flow. A normal level is 30–60 IU/L.

**Blood clotting measures:** liver dysfunction may lead to impaired blood clotting as platelets are destroyed by an enlarged spleen and the liver is unable to produce adequate amounts of clotting factors. Platelet count (described above) and prothrombin time (PT) are two measures of blood clotting ability. PT is an indication of how long it takes the blood to clot; a normal value is about 10–12 seconds. Laboratories usually report PT in seconds and in terms of international normalized ratio (INR). PT is generally considered prolonged if it is 1.2 times normal or slower (INR greater than 1.2).

## Kidney Function Tests

Kidney function tests are important for people with HIV because certain anti-HIV drugs (e.g., tenofovir DF [Viread]) and medications used to treat OIs (e.g., foscarnet [Foscavir] for CMV) may cause kidney damage, especially in those with a history of kidney problems. To assess kidney function, urine is usually analyzed in addition to blood tests. The presence of protein, glucose, or red or white blood cells in the urine may be a sign of kidney damage or some other abnormal condition.

**Blood urea nitrogen (BUN):** nitrogen is a metabolic waste product that is normally filtered out by the kidneys and excreted in the urine. A normal BUN is 8–20 mg/dL. Elevations may indicate kidney dysfunction or a body fluid imbalance (e.g., dehydration).

**Creatinine:** this waste product of protein metabolism is also normally excreted by the kidneys. A normal blood creatinine level is 0.6–1.5 mg/dL. Elevated creatinine levels may indicate kidney damage.

% CD4 (HELPER CELLS)	
ABSOLUTE CD4+ CELLS	
THOUS/MCL	3.0-10.0
BILL/MCL	4.20-5.00
G/DL	13.2-17.1
X	38.5-50.0
FL	60.0-100.0
MG	27.0-33.0

## MONITORING TEST RESOURCES

### Understanding Your Lab Results (ACRIA)

[www.criany.org/treatment/treatment\\_edu\\_lab\\_results.html](http://www.criany.org/treatment/treatment_edu_lab_results.html)

*\*the print version, but not the web site, contains a sample lab report*

### The Blood Tests You'll Need

[www.aidsmeds.com/lessons/StartHere4.htm](http://www.aidsmeds.com/lessons/StartHere4.htm)

*\*includes a sample lab report*

### Blood Work (Project Inform)

[www.projinf.org/fs/HIVDiagTest.html](http://www.projinf.org/fs/HIVDiagTest.html)

### Laboratory Tests for Monitoring HIV-1 Infection

[www.hivandhepatitis.com/hiv\\_and\\_aids/test/lab1.html](http://www.hivandhepatitis.com/hiv_and_aids/test/lab1.html)

### Lab Tests Online

[www.labtestsonline.org](http://www.labtestsonline.org)

## Other Blood Tests

**Albumin:** one of the major blood proteins, albumin helps regulate the body's fluid balance and maintain normal blood volume. It also acts as a carrier protein for many drugs. A normal serum albumin level is 3.0–5.5 grams per deciliter (g/dL). An elevated level may be a sign of dehydration, while a low level may indicate malnutrition, liver disease, or kidney dysfunction. A recent study showed that low serum albumin levels are a strong predictor of disease progression and death in women with HIV.

**Amylase:** this enzyme is produced by certain digestive organs, especially the pancreas. A normal amylase level is 50–160 IU/L. A high level is often a sign of pancreatitis (inflammation of the pancreas). Some anti-HIV drugs (e.g., ddI [didanosine, Videx]) may cause pancreatitis; people taking such drugs should have their amylase levels checked if they experience unexplained symptoms such as abdominal pain.

**Creatine phosphokinase (CPK):** this enzyme may be released into the blood when muscles are damaged. A normal

level is 20–150 IU/L for men and 10–80 IU/L for women. Elevations may be due to heart muscle damage (such as a heart attack), excessive exercise, or muscle toxicity caused by drugs.

**Lactate (or lactic) dehydrogenase (LDH):** this enzyme is released from damaged cells. A typical reference range is 100–250 IU/L. Elevated levels may indicate widespread inflammation or cell death (necrosis), for example, due to a heart attack, PCP, or lymphoma (cancer of the lymphoid tissue).

**Testosterone:** both men and women produce this steroid hormone, and research suggests that levels are often decreased in people with HIV. The generally accepted testosterone range is 200–1,200 micrograms per deciliter (µg/dL) for men and 20–60 µg/dL for women. However, levels vary widely among individuals. Low testosterone levels may lead to loss of libido (sexual drive), fatigue, wasting, and depression.

**Sedimentation (sed) rate:** this test measures how rapidly red blood cells settle in a test tube. An elevated sed rate may indicate inflammation.

## Blood Sugar and Lipid Tests

Over the past several years increased attention has focused on unusual metabolic complications in people with HIV. It is still not definitively known whether these manifestations are related to long-term HIV infection itself, immune recovery, antiretroviral drugs, or a combination of these factors. However, dramatically elevated blood lipid (fat) and glucose (sugar) levels have been correlated with the use of protease inhibitors (PIs). Today, most physicians regularly monitor blood fat and sugar levels in their patients taking anti-HIV therapy, and may recommend antiretroviral regimen changes or lipid-lowering medications if levels get too high.

**Glucose:** sugar is carried in the blood in the form of glucose, which is broken down by cells to provide energy. A normal glucose level is 65–125 mg/dL. A persistently high glucose level is a sign of diabetes mellitus. It may indicate that the pancreas is not producing enough insulin (a hormone that allows the body to use glucose), or that the body is not responding normally to the insulin produced, a condition known as insulin resistance. Some anti-HIV drugs—particularly PIs—have been associated with insulin resistance and elevated glucose levels. In addition to tests that measure blood glucose at a single point in time, the hemoglobin A1c test can help assess the amount of glucose in the blood over several months.

**Triglycerides:** after eating, energy that is not needed immediately is converted into triglycerides and transported to fat cells for storage. A normal triglyceride level is about 45–150 mg/dL. Elevated levels (hypertriglyceridemia) are associated with increased risk of cardiovascular disease, especially when accompanied by high cholesterol levels. Extremely high triglyceride levels (greater than about 1,000 mg/dL) can cause pancreatitis. Triglycerides should be measured after fasting for at least eight hours.

**Cholesterol:** a fatty substance that circulates in the blood, cholesterol is an important component of cell membranes, certain hormones, vitamin D, and bile acids. A healthy total cholesterol level is 120–200 mg/dL. Elevated total cholesterol (hypercholesterolemia) is known to increase the risk of cardiovascular disease, but it is more useful to look at specific types of cholesterol. Low-density lipoproteins (LDL)—so-called “bad” cholesterol—can deposit cholesterol in artery walls, causing atherosclerosis (hardening of the arteries). But high-density lipoproteins (HDL)—so-called “good” cholesterol—help clear cholesterol from the body and may reduce the risk of cardiovascular disease. In some studies, higher HDL levels have been associated with more robust viral load reductions in people taking anti-HIV therapy. The National Cholesterol Education Program recommends that people try to achieve a total cholesterol level below 200 mg/dL, an LDL level below 100 mg/dL, and an HDL level of at least 40 mg/dL.

## Tests for Pathogens Other than HIV

Anyone being treated for HIV most likely will have already received antibody tests (usually an enzyme-linked immunosorbent assay, or ELISA, followed by a Western blot test) to confirm the presence of the virus. But providers may recommend additional tests to detect other pathogens.

Serologic (blood serum) tests detect antibodies in the blood that indicate that a person has been exposed to a microorganism and has mounted an immune response. Microbiological tests look for pathogens themselves or their genetic material. While many pathogens can be detected using blood tests, some require other bodily substances—for example, a sputum test for PCP, a stool (fecal matter) test for parasitic infections such as cryptosporidiosis, or a cerebrospinal fluid test (spinal tap) for brain infections such as cryptococcal meningitis.

In most cases, tests for pathogens are performed only if a person is experiencing symptoms of a specific infection. But other tests should be routinely offered to people with HIV. For example, many physicians recommend that people be tested for toxoplasmosis and syphilis when they are first diagnosed with HIV. And, because coinfection is so prevalent, the U.S. Public Health Service and the Infectious Diseases Society of America recommend that all people with HIV should be screened for viral hepatitis. Anyone with significantly elevated liver enzymes should be tested for hepatitis A, B, and C.

## HIV Viral Load Tests

Viral load tests measure the amount of HIV RNA (genetic material) in the blood. The presence of RNA indicates that the virus is actively replicating (multiplying). Along with the CD4 cell count, viral load is one of the most valuable measures for predicting HIV disease progression and gauging when anti-HIV treatment is indicated and how well it is working.

Viral load is expressed either as copies of RNA per milliliter of blood (copies/mL) or in terms of logs. A log change is an exponential or 10-fold change. For example, a change from 100 to 1,000 is a 1 log (10-fold) increase, while a change from 1,000,000 to 10,000 is a 2 log (100-fold) decrease. (For a more complete explanation of logs, see the sidebar on page 15.)

If the level of HIV is too low to be measured, viral load is said to be undetectable, or below the limit of quantification. However, undetectable viral load does not mean that HIV has been eradicated; people with undetectable viral load maintain a very low level of virus. Even when HIV is not detectable in the blood, it may be detectable in the semen, female genital secretions, cerebrospinal fluid, tissues, and lymph nodes.

Two types of viral load test are commonly used to measure HIV viral load: Roche’s Amplicor HIV-1 Monitor polymerase chain reaction (PCR) assay

and Bayer’s Quantiplex branched-chain DNA (bDNA) assay. Other viral load tests—Organon Teknika’s nucleic acid sequence-based assay (NASBA) and Digene’s DNA hybridization test—are newer and less widely used. Only the Amplicor test is currently approved by the U.S. Food and Drug Administration (FDA). While first-generation tests measured viral load down to about 400 copies/mL, the ultrasensitive second-generation tests in widespread clinical use today have a lower limit of detection of about 50 copies/mL; some research tests can measure as few as 5 copies/mL. The older-generation tests are better at measuring high viral loads, while the newer tests more accurately measure low viral loads. (The first-generation PCR test was more sensitive than the first-generation bDNA assay, but the newer versions of both tests are comparable.)

A viral load of 100,000 copies/mL or greater is considered high, while levels below 10,000 copies/mL are considered low. Research has consistently shown that higher viral loads are associated with more rapid HIV disease progression and an increased risk of death. Current U.S. HIV treatment guidelines recommend that people should consider starting treatment if their viral load is above 55,000 copies/mL (revised upward from 10,000 copies/mL in the previous guidelines). Importantly, most studies that have correlated viral load and HIV disease progression have been done in men; more recent research indicates that women may progress to AIDS at lower viral load levels, suggesting that the treatment threshold should perhaps be revised downward for women.

Effective anti-HIV treatment can often reduce viral load to low or undetectable levels. Therapy that does not produce an undetectable viral load is often said to be failing. Another warning sign is viral breakthrough, an increase in viral load following earlier suppression. Inability to achieve an undetectable viral load may mean that a person’s HIV is resistant to the drugs being used. Providers often take this as an indication to change or add new

% CD4 (HELPER CELLS)	
THOUS/MCL	3.0-10.0
MILL/MCL	4.20-5.00
G/DL	13.2-17.1
X	38.5-50.0
FL	60.0-100.0
W	77.0-90.0

## PAP SMEARS

Not all monitoring tests for people with HIV involve blood draws. Research has shown that women and men with HIV are at greater risk of developing genital and anal cancer than HIV negative people. Cervical, penile, and anal cancer are associated with certain strains of the human papillomavirus (HPV), and HPV disease progression appears to be more aggressive in people with HIV.

Pap smears, which are used to detect abnormal cell changes, have dramatically reduced the death rate due to cervical cancer. In a cervical Pap smear, a sample of cells is taken from the cervix (the lower part of the uterus) opening using a wooden spatula or brush and examined under a microscope. Experts recommend that HIV positive women should receive a Pap smear every 6–12 months—closer to six months if previous Pap test results were abnormal, and closer to annually if past tests were consistently normal. In March 2003 the FDA approved a new test to detect high-risk strains of HPV; the Digene HC2 HPV DNA assay is used in conjunction with a Pap smear, using the same sample of cervical cells.

Pap smears are not just for women: experts increasingly recommend that men who have sex with men—whether or not they are HIV positive—receive a yearly anal Pap smear.

If Pap smear results are abnormal, a follow-up test (in which the affected area is examined using a lighted magnifying device) is indicated.

drugs to a person's anti-HIV regimen. However, research suggests that therapy that substantially decreases HIV levels (especially if it reduces them to below 10,000 copies/mL) is likely to be beneficial even if it does not achieve the "gold standard" of undetectability.

Most experts recommend that a viral load test should be done when a person is first diagnosed with HIV to establish a baseline, then every 3–6

months or so. Tests should be done about four weeks after a person starts or changes anti-HIV therapy to monitor whether the new treatment appears to be working. Various factors—such as concurrent infections or recent vaccines—can affect viral load, and blips (brief increases) may occur that do not signal actual HIV disease progression. As with CD4 cell count, an individual measurement is not as useful as downward or upward trends over time.

## Treatment Monitoring Tests

As noted above, increasing viral load levels (viral breakthrough) and decreasing CD4 cell counts while a person is taking anti-HIV therapy are indications that adherence is not adequate or that the drugs being used are not effective and may need to be changed. In addition, today there are other tests that can help physicians determine whether current therapy is working or whether a treatment option under consideration is likely to work.

### Resistance Testing

HIV can develop drug resistance by mutating in such a way that the virus can continue to replicate despite the drug. (Nonmutated HIV is referred to as "wild-type" virus.) This usually occurs when a drug is not completely effective (due to poor adherence, sub-optimal drug levels, or other reasons), allowing HIV to multiply and mutate in the presence of the drug. Also, an increasing number of people are becoming infected with HIV that is already resistant to one or more drugs.

Several studies have shown that use of resistance testing to guide treatment decisions leads to more sustained viral load reductions. The ability to tell which drugs are no longer working provides the opportunity to change a specific drug, rather than tossing out an entire failing regimen. Resistance tests are increasingly being used in clinical practice, but they are not yet standardized and should be interpreted by an experienced physician. The tests work best when a person has a viral load of at least 1,000 copies/mL and is currently still on a failing anti-HIV drug regimen. Three types of tests are used to measure drug resistance. (For more information on resistance testing, see "Salvage Therapy," *BETA*, Winter 2003.)

**Genotypic tests:** these tests examine the genetic sequence of HIV's reverse transcriptase and/or protease enzymes to look for mutations that are known to be associated with resistance to particular drugs. For example, the K103N mutation

## Blood Cell Tests

Test	Normal Range
<b>Red blood cell count (RBC)</b>	Men: 4.5–6.0 million cells/mm <sup>3</sup> Women: 4.0–5.5 million cells/mm <sup>3</sup>
<b>Hematocrit (HCT)</b>	Men: 40–55% Women: 35–45%
<b>Hemoglobin (HGB)</b>	Men: 14–18 g/dL Women: 12–16 g/dL
<b>Mean corpuscular hemoglobin (MCH)</b>	27–33 picograms/red blood cell
<b>MCH concentration (MCHC)</b>	32–36%
<b>Mean corpuscular volume (MCV)</b>	79–100 femtoliters
<b>White blood cell count (WBC)</b>	4,000–11,000 cells/mm <sup>3</sup>
<b>Differential:</b>	
Neutrophils	50–70% of WBC
Lymphocytes	20–40% of WBC
Monocytes	2–10% of WBC
Eosinophils	0–6% of WBC
Basophils	0–1% of WBC
<b>Platelet count</b>	130,000–440,000 cells/mm <sup>3</sup>

## Blood Chemistry Tests

Test	Normal Range
<b>Electrolytes:</b>	
Bicarbonate	22–33 mmol/L
Calcium	8.5–10.5 mg/dL
Chloride	95–105 mmol/L
Magnesium	1.5–3.0 mg/dL
Phosphorus	2.0–4.5 mg/dL
Potassium	3.5–5.0 mmol/L
Sodium	135–145 mmol/L
<b>Liver function tests:</b>	
ALT (SGPT)	0–50 IU/L
AST (SGOT)	0–45 IU/L
Bilirubin	0–1.5 mg/dL
Alkaline phosphatase (AP)	35–115 IU/L
GGT	30–60 IU/L
<b>Kidney function tests:</b>	
Blood urea nitrogen (BUN)	8–20 mg/dL
Creatinine	0.6–1.5 mg/dL
<b>Other blood tests:</b>	
Albumin (total serum)	3.0–5.5 g/dL
Amylase	50–160 IU/L
Creatine phosphokinase (CPK)	Men: 20–150 IU/L Women: 10–80 IU/L
Lactate (lactic) dehydrogenase	100–250 IU/L
Testosterone	Men: 200–1,200 µg/dL Women: 20–60 µg/dL

## Common Monitoring Tests for People with HIV

### CD4 and CD8 Cell Tests

Test	Normal Range
<b>CD4 cell count</b>	600–1,200 cells/mm <sup>3</sup>
High	Above 500 cells/mm <sup>3</sup>
Medium	200–500 cells/mm <sup>3</sup>
Low	Below 200 cells/mm <sup>3</sup>
Treatment guidelines threshold	350 cells/mm <sup>3</sup>
<b>CD8 cell count</b>	200–1,000 cells/mm <sup>3</sup>
<b>CD4 cell percentage</b>	30–60%
<b>CD8 cell percentage</b>	15–40%
<b>CD4/CD8 cell ratio</b>	0.9–3.0

### HIV Viral Load

Level	Normal Range
High	100,000 copies/mL or greater
Low	10,000 copies/mL or less
Undetectable	below 400 or 50 copies/mL, depending on the test
Treatment guidelines threshold	55,000 copies/mL

### Blood Sugar and Lipid Tests

Test	Normal Range
<b>Glucose</b>	65–125 mg/dL
<b>Triglycerides*:</b>	
Normal	Less than 150 mg/dL
Borderline high	150–199 mg/dL
High	200–499 mg/dL
Very high	500 mg/dL or greater
<b>Total cholesterol*:</b>	
Desirable	Less than 200 mg/dL
Borderline high	200–239 mg/dL
High	240 mg/dL or greater
<b>LDL cholesterol*:</b>	
Optimal	Less than 100 mg/dL
Near optimal	100–129 mg/dL
Borderline high	130–159 mg/dL
High	160–189 mg/dL
Very high	190 mg/dL or greater
<b>HDL cholesterol*:</b>	
Low	Less than 40 mg/dL
Normal (acceptable)	40–60 mg/dL
High (desirable)	60 mg/dL or greater

(\* per the National Cholesterol Education Program)

confers resistance to current non-nucleoside reverse transcriptase inhibitors (NNRTIs).

**Phenotypic tests:** these tests are done by adding a medication to an HIV culture in the laboratory to determine how much drug is needed to inhibit viral replication. Resistance levels are usually reported in terms of how much drug is needed to inhibit viral replication by 50% or 90% (the  $IC_{50}$  or  $IC_{90}$ , respectively), compared with wild-type virus. Phenotypic tests provide a more direct measure of resistance, but are more difficult, time-consuming, and expensive.

**Virtual phenotype:** this is a new approach to estimating the viral phenotype using a large database of more than 18,000 pairs of genotypic and phenotypic data. HIV with a similar genotype is identified in the database, and the corresponding phenotypic information is used to estimate resistance. Preliminary research suggests that the virtual phenotype predicts treatment response about as well as a true phenotypic test.

## Therapeutic Drug Monitoring

Therapeutic drug monitoring (TDM) is used to help individualize anti-HIV therapy by measuring the amount of drug in an individual's blood. This is important because different people absorb, process, and eliminate drugs at different rates, and blood levels may vary considerably among individuals taking the same doses of the same medications. Ideally, the lowest plasma drug concentration between doses (the trough level, or  $C_{min}$ ) should still be high enough to inhibit HIV, but the highest concentration (the peak level, or  $C_{max}$ ) should not cause intolerable side effects.

Some, but not all, studies have shown that using TDM to guide treatment decisions increases the chance of successful viral suppression. However, drug level monitoring is not appropriate for all anti-HIV drugs. TDM has grown in popularity, especially for guiding salvage therapy, but it remains

controversial and is still not widely used in the U.S. (For more on TDM and the related topics of inhibitory quotient and viral fitness, see "Salvage Therapy," *BETA*, Winter 2003; and "Therapeutic Drug Monitoring," *BETA*, Autumn 2000.)

## Conclusion

Regular monitoring is an important way for HIV positive people to take control of their health. People with HIV should talk with their physicians about how often they should receive various monitoring tests. Interpretation of test results can be tricky and should be carried out by an experienced practitioner. (For this reason, we do not include a sample lab report here; some of the resources included in the sidebar on page 35 provide test result examples.)

Along with general health measures such as blood cell counts and liver enzyme levels, and specific measures of HIV disease progression such as viral load and CD4 cell count, new tests such as resistance assays and therapeutic drug monitoring may help individualize anti-HIV treatment and promote optimal outcomes.

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