

# Days at the lab

Find out what they're looking for in your blood and why it matters so much **by Dr. Marianne Harris**

**When you have HIV, you become a frequent visitor to the lab in your local clinic or hospital to have different tests done. Most of these tests serve to monitor the state of your HIV infection, which can be affected by the virus, by other diseases and by your body's defense system.**

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## **HIV diagnosis**

A screening test called ELISA (enzyme immunoassay) is done to make the initial diagnosis of HIV. If this is positive (meaning antibodies against HIV are detected), there's a small chance the result could be wrong (a "false positive") so the lab will automatically do a more specific test called a Western blot to confirm the diagnosis. If both the ELISA and Western blot are positive (confirming the presence of HIV antibodies), you're considered to have HIV. Note that a "positive" test means you have HIV while a "negative" test means you don't.

Both of these tests detect levels of HIV antibodies, which are proteins made by the body's immune system in response to the virus. Because it takes some time for the body to make antibodies, there's a "window period" of about four to six weeks (but sometimes as long as six months) after exposure to HIV during which the antibody tests will falsely show negative results. During the window period a person can be highly infectious, even though they're unaware they have HIV and their tests are still negative.

## **Tests for other infections after diagnosis of HIV**

Once the diagnosis of HIV is made, a number of tests are done to check whether other diseases may also be present. Decisions about treating other infections and taking preventive measures will be made on the basis of these tests.



## Viral hepatitis

- **Hepatitis A virus (HAV):** The anti-HAV test looks for antibodies to hepatitis A. If this test is negative that means you've never been exposed to the virus and should receive the hepatitis A vaccine (given in two or three doses), especially if you're in one of the following risk groups: injection drug users, men who have sex with men, persons with hemophilia or other clotting disorders, or chronic liver disease (including hepatitis B or C).



- **Hepatitis B virus (HBV):** Anti-HB tests can show whether you have chronic hepatitis B infection. If the tests are positive you may need treatment for hepatitis B. If negative, you should receive 3 doses of HBV vaccine (at 0, 1, and 6 months).
- **Hepatitis C virus (HCV):** Testing for anti-HCV antibodies determines whether you've been exposed to HCV, in which case you may or may not have chronic HCV; further blood tests will be done to see whether you need treatment for HCV. Unfortunately, there's no vaccine to protect against getting HCV.

## Toxoplasmosis and CMV tests

Before the advent of HAART, tests were done to detect the risk of developing toxoplasmosis (which can cause lesions in the brain) and CMV (cytomegalovirus) infection (which can affect a number of organs including the eyes, lung and bowel). Fortunately these infections are seen only when the CD4 cell count gets very low (below 100) and are unusual with modern HIV treatments. However, if for some reason you have a low CD4 and can't take HAART right away, testing can show whether you're at risk. If so, you can take medication to prevent toxoplasmosis and have frequent eye exams to monitor for CMV eye disease, which can lead to vision loss and blindness if it isn't detected and treated soon enough.

## Syphilis test (VDRL or RPR)

Since both HIV and syphilis can be transmitted sexually, people who have HIV are also at risk for syphilis. In fact, there's been a recent epidemic of syphilis among the HIV+ population in many cities. This test should be repeated annually or more frequently if you have many sexual partners. Syphilis can be treated with antibiotics such as penicillin. People who have been treated for syphilis may still test positive on the VDRL test, but are no longer contagious.

## Tuberculosis (PPD or tuberculin test)

A skin test for tuberculosis (TB) should be done after diagnosis with HIV and should be repeated every year if you're at high risk of being exposed to TB. For this test, two visits two or three days apart should be scheduled to inject the tuberculin beneath the skin and then examine the reaction.

## Other tests

If you have many sexual partners, you will usually be tested for other sexually transmitted infections (such as chlamydia and gonorrhea). Women should

## Test schedule\*

Test	Interval
ELISA/Western blot	Only at diagnosis
Hepatitis A and B	At diagnosis; vaccinated if never exposed
Hepatitis C	At diagnosis and then every year, depending on risk
TB	At diagnosis and then every year
CD4 cell counts	At diagnosis, every 3 to 6 months before starting therapy, every 4 to 6 weeks after starting therapy until viral load is undetectable, every 2 to 4 months after the viral load reaches undetectable levels.
Viral load	At diagnosis, every 3 to 6 months before starting therapy, every 4 to 6 weeks after starting therapy until viral load is undetectable, every 2 to 4 months after the viral load reaches undetectable levels.
Resistance tests	At diagnosis to see if you were infected with a resistant strain, or if treatment fails.

\* Note that these intervals are only meant as a rough guideline. Many factors will influence the timing of tests and produce significant variations.

have a pelvic exam and cervical Pap smear every six to 12 months. Some centres offer an anal Pap smear to check for cancer for men who have sex with men. In some cases, abnormal smears require further follow-up.

### Tests to find out more about HIV infection

An increasing number of tests are available to find out more about your particular HIV infection: what effect it's had on your immune system so far, how virulent it is and whether it's likely to be resistant to any particular drugs. This information is needed before you and your doctor can decide whether to start treatment and which antiretrovirals (ARVs) are likely to be most effective.

### CD4 cell counts

CD4 cells, also called T4 cells, are a type of white blood cell that are attacked and killed by HIV. A healthy CD4 cell count can be anywhere from 400 to 2000 cells per mm<sup>3</sup> of blood, depending on the lab. Because the lymphocyte (overall white cell) count can vary quite widely and affect the absolute CD4 cell count, it's also important to look at the CD4 fraction, meaning the percentage of lymphocytes which are CD4 cells. This is normally 27-60%.

People with HIV are at risk for developing AIDS-related infections (such as *Pneumocystis carinii* pneumonia) if their CD4 count drops below 200, and especially if it's below 100. For this reason, most doctors recommend starting treatment with ARVs if the CD4 is consistently below 200-250 and/or if the fraction is below 15%. Many will also consider treatment if the CD4 is in the 250-350 range. A number of factors can affect the CD4 count, which varies according to time of day and season, so it's important to look at trends in the CD4 count and fraction rather than rely on single measurements.

### HIV viral load

Since 1996, labs have been able to directly measure the amount of HIV virus in the blood with a test called HIV RNA PCR (polymerase chain reaction), more commonly known as viral load. Depending on the specific type of test used, this can measure levels from 50 to more than 750,000 copies of virus per mL of blood (although the viral load can actually be much higher than that, up in the millions per mL, particularly in the very early and very late stages of infection). In general, the higher your viral load, the faster your rate of CD4 cell loss and the faster you would be expected to develop AIDS without treatment.

## Testing for allergy to HIV meds

An experimental test now offered in some provinces can detect whether or not you're likely to have an adverse reaction to abacavir (Ziagen®). This test looks for a variant in your genes called HLA Class I B\*5701 variation, present in about 5% of Caucasians. If you have the B\*5701 variant and go onto an anti-HIV therapy which includes abacavir (Ziagen®, also found in Trizivir™ and Kivexa®), then you're about 100 times more likely to have an allergic reaction to this drug. If you don't have the B\*5701 variation, you're unlikely to have a bad reaction to this drug. This test isn't appropriate if you've already had a reaction to abacavir, since you shouldn't go back onto this medication regardless, because the reaction will be much more severe (and possibly fatal) the second time around. The test only needs to be done once, because your HLA type won't change.

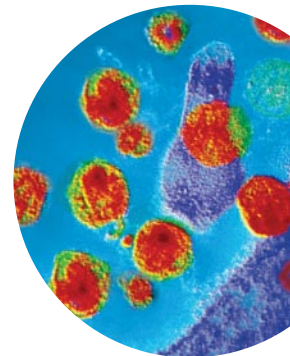
Fortunately, modern HAART regimens can halt this trend by driving the viral load down to very low levels, thus preventing and even reversing CD4 cell loss. The goal of HAART is to get the viral load to less than 50 or "undetectable," meaning that the amount of virus is so low that the test cannot measure it, NOT that the virus is absent. The viral load can vary about three-fold, especially down near 50, and can increase temporarily during infections or after immunizations such as the flu shot (especially in people not receiving HIV therapy).

An increasing number of tests are available to find out more about your particular HIV infection: what effect it's had on your immune system so far, how virulent it is and whether it's likely to be resistant to any particular drugs

### Monitoring the immune system and viral load

If you and your doctor decide you're not ready (or don't need) to start HIV treatment yet, your CD4 and HIV viral load, as well as some other tests such as the complete blood count (CBC), should be monitored every three to six months as long as your CD4 is over 350. These tests may be watched more often if your CD4 is lower.

When you start a new HIV therapy, or change to a new regimen, your doctor will want to measure your CD4 and viral load four to six weeks after the change and then about every three months until the viral load is undetectable (or less than 50), which is the target for effective antiretroviral therapy. (Some labs are using a different



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test on which undetectable means less than 500.) Depending what your viral load was to begin with, this may take two to six months. Once the viral load is undetectable and the other labs are stable, all the blood tests can generally be done every two to four months. Monitoring may need to be more frequent in certain situations, such as with complex, multiple drug regimens.

### **Danger signs**

If the viral load doesn't come down to less than 50 within six months after starting a new treatment regimen, or increases above 50 twice in a row after being undetectable, your current treatment may not be working. This should prompt an investigation into the possible reasons for so-called "treatment failure," which may include not taking your drugs correctly, interactions with other drugs, and resistance of the HIV to some of the drugs you are taking. An HIV resistance test should be ordered to rule out the latter and help design your next drug regimen.

## **Resistance testing is most often done when a treatment has failed to bring or keep your viral load under control**

### **HIV resistance tests**

HIV resistance testing can be done on the same blood sample as the viral load, to see if the virus you've acquired is resistant to any antiretroviral drugs. (You can be infected with resistant virus so this should be checked even before you take any treatment.) The test most commonly used in Canada is called a genotype, which is an indirect measurement of HIV resistance to antiretroviral drugs. This measures mutations in the HIV genome that are associated with reduced susceptibility to antiretrovirals. This test will help identify which drugs are less likely to be effective for you. However, even when no resistance to a certain drug is detected, that drug is not guaranteed to be effective against your HIV.

Resistance testing is most often done when a treatment has failed to bring or keep your viral load under control, and helps determine the cause of failure and design the next treatment regimen excluding drugs to which resistance is present. Drug-resistant virus can be transmitted, and around 10% of HIV+ Canadians who have never received antiretroviral therapy have some level of HIV drug resistance. Therefore, it's currently recommended that resistance testing be done before your first

HIV treatment. Some special situations where resistance testing is also highly recommended include acute HIV infection and pregnancy.

### **Drug level or therapeutic drug monitoring (TDM)**

This test is available in some provinces only, sometimes on an experimental basis. Blood levels of protease inhibitors (PIs) and non-nucleoside reverse transcriptase inhibitors (NNRTIs) — but not nucleoside reverse transcriptase inhibitors (NRTIs) — can be measured and compared with "normal" levels seen in a large number of people receiving the same drugs. Often, a number of blood samples need to be taken at different times during the day in relation to when you take your medications. This test may be useful in monitoring drug interactions in complicated multiple-drug regimens, side effects that may be caused by drug levels being too high, and lack of efficacy due to drug levels that are too low. However, use of TDM is somewhat controversial and interpretation of the results isn't standard. For many drugs, the ideal "target" drug levels aren't well defined.

This sounds like a lot of tests! Remember, some of them only need to be done once, when you're first diagnosed with HIV, or maybe once a year (see Table on page 8 for approximate test schedules). Some of them need to be done more regularly for your safety, especially if you're taking HIV medications. The specific tests you get each time depend on any background conditions you may have, your risk for other diseases, and what specific medications you're taking. Remember to ask your doctor if you don't understand why a test is being done or what the results mean for you. **R**

