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Detecting HIV earlier: Advances in HIV testing

By Len Tooley

How soon after a potential exposure can someone know their HIV status? Well, it all depends on the type of test used. This article will take you on a tour of the different types of HIV tests available and will walk you through how long it takes for each test to tell you accurately if someone has HIV.

Since the early days of the HIV epidemic, HIV tests have improved considerably. We now have multiple methods to test for HIV infection, and today's testing technologies are getting better at detecting new infections. This has led some HIV testing experts to suggest that we can detect the vast majority of HIV infections much earlier than many people realize. This article will review the scientific evidence on the early detection of HIV to help guide our messaging about HIV testing.

Why is it valuable to detect HIV infections as early as possible?

There are two major reasons why it is valuable to detect an HIV infection as soon as possible after it has occurred:

1. Early detection is good for people getting tested for HIV. HIV tests that provide an accurate result sooner after infection may significantly reduce the anxiety of "not knowing" that many people feel after they think they may have been exposed to HIV.

For those who test HIV-positive, testing early may give them a better sense of how and when they were exposed to HIV. It may also provide them with greater opportunities to access services and support that will help manage their health and well-being. Another distinct advantage of early diagnosis is that people can access anti-HIV treatment before their immune systems have been severely damaged, which can also improve their long-term health outcomes.

2. Early detection can help prevent new HIV infections. Research demonstrates that almost half of new HIV infections may come from individuals who have been newly infected.¹ This may be because people who are newly infected have significantly higher levels of the virus in their blood and genital tracts, which may make HIV transmission more likely to occur.^{2,3,4,5} People who are newly infected are also more likely to be unaware of their HIV status. Diagnosing HIV infection early allows a person to make more informed decisions (such as practicing safer sex and using drugs in a safer way). Research shows that when aware of their status, most HIV-positive people do take steps to prevent HIV transmission.^{6,7,8,9}

Being able to detect new HIV infections earlier is not only beneficial to people seeking testing and to the service providers offering testing services, but may also play a significant role in preventing further transmission of HIV within the population.

The HIV antibody test

Once a person becomes infected with HIV, a number of steps must take place before an HIV antibody test can detect infection. First, the virus infects more and more cells in the person's body. The person's immune system then responds by producing HIV antibodies, which are proteins that circulate in the blood to try to fight the HIV infection. It is these antibodies that the HIV antibody test detects, NOT HIV itself. If there aren't enough antibodies created by the body when the test is given, the result will be negative despite the person being infected with HIV.

In order for an HIV antibody test to detect an HIV infection, two conditions must be met:

- 1. **HIV antibodies must be present in the person's blood.** The amount of time it takes for the immune system to create HIV antibodies after HIV infection varies based on genetics, how transmission occurred (e.g. sex vs. shared needles), the amount of virus the person was exposed to, whether they underwent post-exposure prophylaxis (when someone takes a combination of anti-HIV medications within 72 hours of exposure to reduce the chances of becoming infected), and numerous other factors. For more on PEP, see Can we prevent infection with HIV after an exposure? The world of post-exposure prophylaxis (PEP).
- The HIV antibody test must be sensitive enough to detect the antibodies. Newer testing technologies can now detect HIV antibodies when there are lower concentrations in the blood and hence are able to detect an HIV infection much sooner.

The "window period" refers to the maximum amount of time it may take for a person's body to create HIV antibodies after HIV infection. HIV antibodies must be present in order for the HIV antibody test to accurately detect HIV antibodies in someone's blood. If someone is "in the window period," there is a chance that even though they may have been infected with HIV, the test won't be able to detect the infection and will give a negative result.

HIV antibody tests are the most widely used HIV tests. One of the main reasons they are so widely used is that once HIV antibodies are present in a person's blood, they will be there for the rest of that person's life (provided their immune system is functioning properly). This means that following the window period, an HIV antibody test will always give a positive result for someone who has been infected with HIV. This is important as many people are not diagnosed until several years after infection.

Older HIV antibody tests were significantly less able than newer tests to detect low levels of HIV antibodies in a person's blood, which is why in the past the window period was set at 6 months.

Across Canada, all labs use newer, more sensitive antibody tests (this includes rapid (point-of-care) HIV tests). For more on rapid HIV testing, see <u>A rapid approach to community-based HIV testing</u>. Research shows us that with these new tests, as many as 95% of people who test positive will do so within 34 days of exposure to HIV.<u>10</u> However, for the remaining 5%, the window period for these HIV antibody tests is generally accepted to be three months so as to ensure people who take longer to develop antibodies are not overlooked. This means that if someone tests negative for HIV antibodies during the window period, they should be re-tested three months after possible exposure, to fully rule out HIV infection.

There are some rare exceptions which may require someone to retest up to six months after exposure:

- People who have a severely impaired immune system may take longer to develop HIV antibodies.
- People who have taken post-exposure prophylaxis (PEP). This is a one-month course of anti-HIV drugs that, if started within 72 hours of potential exposure, may reduce the risk of HIV infection. If PEP does not successfully prevent HIV infection in someone, the presence of the PEP drugs may still reduce HIV replication until the drugs are finished. This may delay the time it takes for a person's body to create HIV antibodies. For more on PEP, see <u>Can we prevent infection with HIV after an exposure? The world of post-exposure prophylaxis (PEP)</u>.

It should be noted that if someone tests positive with an antibody test, the result should always be confirmed using a Western blot test to rule out the possibility of a false-positive result.

Tests that directly detect HIV

There are a number of technologies that detect HIV itself. However, at this time, these tests are not offered uniformly throughout Canada or within provinces and territories. It is important to do some research and find out which testing services are available for your clients to help ensure effective messaging for someone who thinks they have recently been exposed to HIV. The two most commonly used tests that detect HIV directly are the **p24 antigen test** and the **HIV nucleic acid amplification test (NAT)**.

The HIV p24 antigen test

The HIV p24 antigen test, the most widely available of the two, is designed to detect a protein (the p24 protein) associated with HIV. The p24 antigen test can detect the p24 protein on average 10 to 14 days after infection with HIV.^{2,3,11,12} One drawback of this test is that levels of the p24 protein peak at around three to four weeks after exposure to HIV and are usually not detectable after five to six weeks (and sometimes even earlier). A positive p24 test means that someone is HIV-positive. However, a negative p24 test can mean three things:

- the person is HIV-negative
- the person is HIV-positive but that the test could not detect the p24 protein because the person was infected more than four to six weeks earlier
- the levels of p24 antigen are too low to be detectable with current technologies.

Currently, the most advanced tests combine a p24 antigen test and an antibody test. While combination tests are available in some regions across Canada, they are not yet available everywhere. These tests are seen as beneficial because they combine the early detection abilities of the p24 antigen test with the accuracy of the newer antibody tests. It should be noted that a rapid (point-of-care) version of these tests is not yet available.

The HIV NAT test

The HIV NAT test is a very sensitive test designed to detect HIV RNA in blood. RNA is the viral equivalent to human DNA. The NAT test is able to detect HIV RNA as early as seven to 14 days after infection with HIV.^{2,3,11,12} Unlike the p24 test, the NAT test will always give a positive result as long as there is HIV in someone's blood.

NAT testing is currently being offered in six clinics in British Columbia as part of a five-year study called the Acute HIV Infection Study (<u>http://www.acutehivstudy.com</u>). One of the objectives of this study is to investigate the impact of new testing technologies on gay men's testing practices.

When are p24 antigen tests and HIV NAT tests used?

In places where p24 antigen tests or HIV NAT tests are available, these tests are often used for individuals who have recently had a high-risk exposure and are either (a) in the three-month window period of the antibody test, or (b) experiencing symptoms of a new HIV infection (most often flu-like symptoms, including a fever, diarrhea, rash and/or sore throat). The p24 antigen test is also used when indeterminate results are obtained from an HIV antibody test (the test couldn't give a clear answer).

Seroconversion symptoms

It is also important to talk about the symptoms of seroconversion when we talk about testing. Educating clients about the symptoms of seroconversion may increase the likelihood that they will get tested if they experience symptoms. Seroconversion symptoms can occur from two to four weeks after infection and may include flu-like symptoms, such as fatigue, fever, sore throat, swollen lymph nodes, headache, loss of appetite or skin rash. This illness usually lasts less than two weeks although it can last as long as 10 weeks. If a client has had a recent high-risk encounter and experiences any of these symptoms, they should be encouraged to have an HIV test. Depending on the time since infection, the antibody test may not give an accurate result. However, if available, the p24 antigen test will be able to give an accurate result two to four weeks following infection and the NAT test will be accurate in as little as seven to 14 days after infection.

What does all this mean for front-line workers?

The early detection of HIV is important because people who are newly infected are very infectious and may inadvertently transmit HIV to others. There is still a lot of misunderstanding about how soon one should get tested after potential HIV exposure. Many people still believe they have to wait three months. However, new and improved testing technologies are continually decreasing the amount of time it takes for a new HIV infection to be detected.

In the case of clients at high risk of HIV, testing can be done as early as one month after exposure for standard antibody assays and rapid point-of-care tests. Clients who test positive will know for certain they are HIV-positive. Of those who test negative, 95% are in fact negative. It is important to realize that up to 5% of people who test negative at one month could later test positive at three months. It is important to ensure that people testing negative at one month are advised to return for repeat testing once the three-month window period is covered.

The p24 antigen test and the HIV NAT test could be used to test for HIV in people who think they were recently exposed to HIV. These tests are useful for people who think they have recently seroconverted. As these tests may not be readily available in all cities and towns across Canada, it may be useful to find out when and where these new and improved testing technologies will be offered in your area.

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