WISCONSIN AIDS/HIV PROGRAM NOTES

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Implementing Fourth Generation Rapid HIV Testing in Wisconsin HIV Testing Sites

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In late 2015, the Wisconsin AIDS/HIV Program implemented a new rapid HIV test at publicly funded HIV testing sites that perform rapid testing. This involves a change from using the second generation *Clearview Complete*® HIV-1/2 antibody test to the fourth generation *Determine*™ HIV-1/2 Antigen/Antibody (Ag/Ab) Combo test. Both test devices are manufactured by Alere. Fourth generation HIV tests are differentiated from previous generations of tests by their ability to identify free p24 antigen in a blood or plasma sample in addition to HIV antibodies. First, second, and third generation tests could only identify HIV antibodies.

As CDC and other federal recommendations continue to emphasize finding undiagnosed HIV infection as early as possible and linking newly identified positive people to care, it is critical that state health departments use the most up-to-date HIV testing technologies in laboratory and point-of-care settings that are both clinical and community-based. The Wisconsin AIDS/HIV Program currently supports rapid HIV testing at 29 sites throughout the state, including health departments and community-based organizations. Introducing the fourth generation *Determine*™ HIV-1/2 Ag/Ab Combo test to these sites will potentially allow Wisconsin to diagnose more acute and early HIV infection at the point-of-care and link people to care sooner.

This article outlines what acute HIV infection means and why early detection of the virus is important, steps the Wisconsin AIDS/HIV Program has taken to detect more cases of acute infection leading up to implementing the new rapid HIV test, and background information and detail on the *Determine*™ HIV-1/2 Ag/Ab Combo test.

Acute HIV infection and the importance of early detection

Acute HIV infection (AHI) is the earliest stage of HIV, the period beginning immediately after a person becomes infected. During AHI, the body has not yet developed HIV antibodies and the newly infected person's viral load (amount of HIV in the blood and body fluids) is extremely high. When a case of AHI is identified, prompt intervention is needed because a high viral load increases the risk of transmission, and early HIV treatment can significantly improve long-term health.[1]

Because testing people at high risk for HIV and identifying cases of AHI are a priority, the AIDS/HIV Program implemented an HIV testing algorithm for suspected cases of AHI in mid-2012. The algorithm requires laboratory testing for suspected cases of AHI through the use of all three of the following tests:

[1] CTR Acute HIV Infection Quick Reference. Wisconsin AIDS/HIV Program. Available at https://wi-ew.lutherconsulting.com/Wisconsin/commonFiles/downloads/Acute%20HIV%20Infection%20Quick%20Reference%201-13-15.pdf

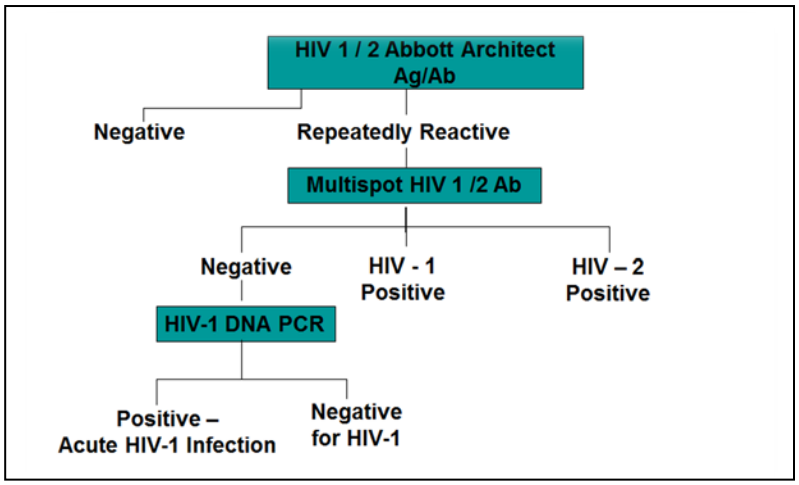
- The fourth generation laboratory-based Abbott Architect Antigen/Antibody (Ag/Ab) HIV-1/2 test.
- An antibody-only HIV-1/2 multispot test.
- An HIV-1 DNA polymerase chain reaction (PCR) test.

Under this testing protocol, HIV Counseling, Testing, and Referral (CTR) sites send a blood specimen to the Wisconsin State Laboratory of Hygiene (WSLH) for analysis. A specimen is considered positive for AHI when all of the following are found:

- The Ag/Ab result is repeatedly reactive (at least 2 of the 3 Ag/Ab results are reactive).
- The Multispot HIV-1/2 is non-reactive or indeterminate.
- The DNA PCR is reactive.

Under this algorithm (Figure 1), when the HIV is identified by the Ag/Ab and DNA PCR tests but antibody had not yet been detected by the Multispot test, these results indicate an early infection. Early infection is defined as having occurred less than two months prior to the test, when both free p24 antigen and HIV antibodies are present in the blood.

Figure 1: Acute HIV Testing Algorithm, 2012-2015



CTR sites using this algorithm were successful in identifying four people with AHI in 2014, all of whom were linked to medical care and HIV Partner Services.

While the algorithm can identify cases of AHI, it also has had limitations in the following areas:

- *Staff Training*—Many staff providing CTR services at community-based sites required phlebotomy training to be able to collect the volume of blood needed for the WSLH to conduct algorithm testing. Training can be time-consuming and costly.
- *Wait Time for Results*—None of the tests performed by the WSLH is a rapid test. Consequently, it can take several days before final test results are received by CTR sites and delivered to clients. This delays people with AHI from accessing HIV medical care in a timely manner.
- *Client Discomfort with Needles*—Many clients are not comfortable with venipunctures, which are required to produce enough samples for the laboratory-based tests in this algorithm. They would prefer a fingerstick or submitting an oral fluid sample as used with rapid HIV testing.

The acute HIV testing algorithm continues to play a significant role in the AIDS/HIV Program's efforts to detect HIV infection as early as possible. The city of Milwaukee Health Department (MHD) recently began using an Abbott Architect HIV-1/2 Antigen/Antibody laboratory-based screening machine. This allows the MHD to implement the AHI testing algorithm without forwarding samples to the WSLH.

To address limitations of the current AHI algorithm and to bring point-of-care rapid testing to the same level as laboratory-based testing, the AIDS/HIV Program is implementing the use of a rapid HIV test that can detect HIV infection much earlier than the current rapid test used by publicly funded CTR sites in Wisconsin. This will enable the CTR sites to identify potential acute and early infections as quickly as possible.

Rapid Antigen/Antibody Combo test

In 2013, the U.S. Food and Drug Administration (FDA) approved the first rapid HIV test for the simultaneous detection of HIV-1 p24 antigen and antibodies to both HIV-1 and HIV-2 in human serum, plasma and venous or fingerstick whole blood specimens.[2] Approved for use in diagnosing HIV-1 and HIV-2 infections, the Alere *Determine*™ HIV-1/2 Ag/Ab Combo test is the first FDA-approved test that distinguishes results for HIV-1 p24 antigen and HIV antibodies in a single test.

Detection of HIV-1 antigen permits earlier detection of HIV-1 infection than is possible by testing for HIV-1 antibodies alone. The period between the time of infection and when a test is capable of identifying infection is the "window period." Figure 2 (page 4) shows the detection window period for various generations of HIV tests.

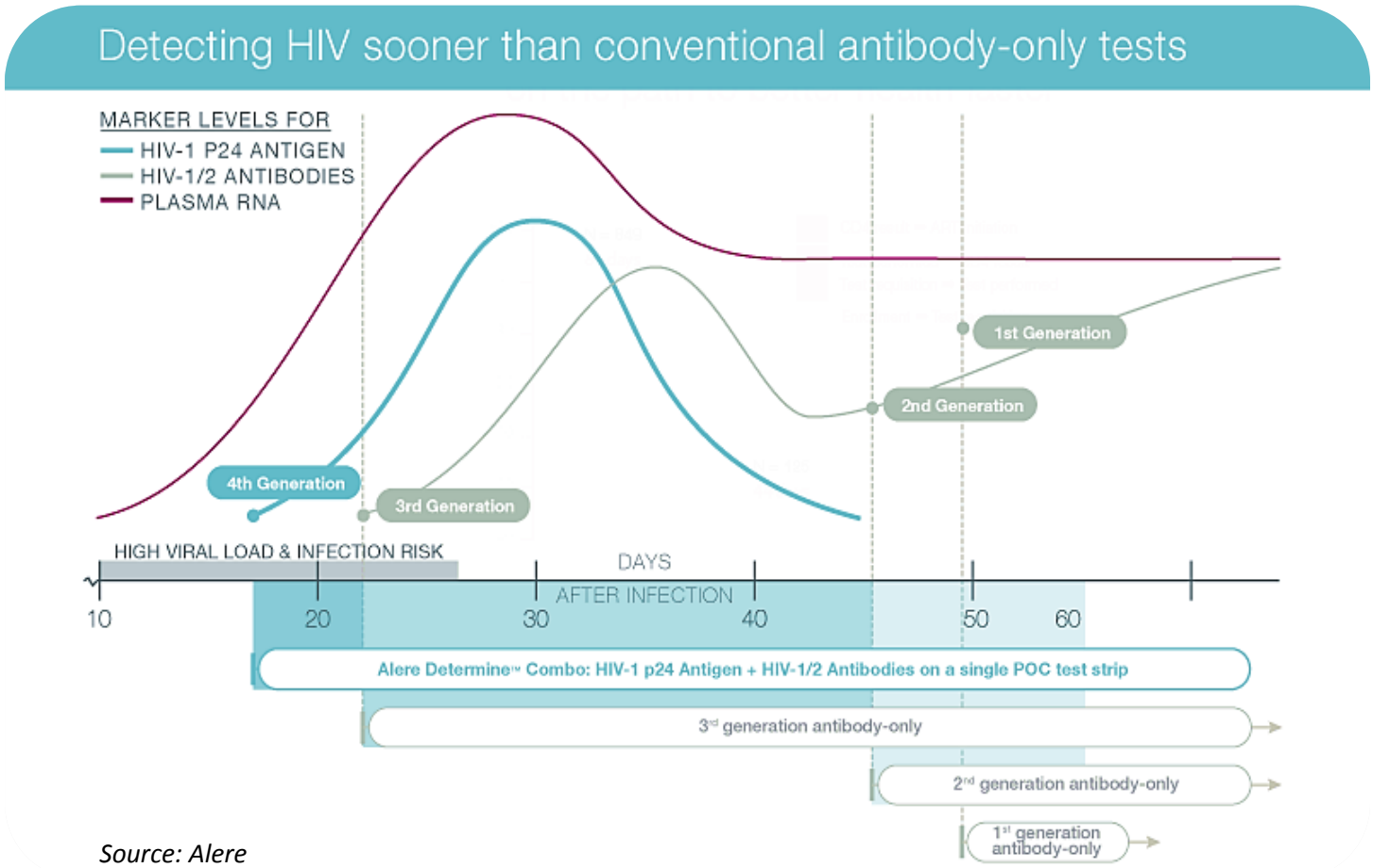
Currently, rapid testing sites in Wisconsin use the second generation *Clearview Complete* HIV-1/2 antibody rapid test, which can only detect HIV antibodies in an infected person. This assay has a window period of three months from initial infection to the time when it can detect the antibodies. This is well past the window period of fourth generation tests such as *Determine*. The fourth generation tests can detect HIV p24 antigen 15-30 days after initial infection, within the time period when an infected person has a very high viral load and is at increased risk of infecting others with the virus. It is during this time when it is crucial to link an infected person to medical care and initiate antiretroviral treatment.

AIDS/HIV Program staff gathered materials and lessons learned from three other states that have either implemented or are in the process of utilizing the *Determine* rapid test and integrated them into the training and technical assistance plan used to transition agencies to the new test.

The *Determine* test was successfully piloted at Public Health Madison-Dane County in August 2015. Rapid testing staff in Milwaukee were trained in September. The remaining CTR staff providing rapid testing will have been trained in October and November 2015, with full implementation beginning in November.

[2] FDA approves first rapid diagnostic test to detect both HIV-1 antigen and HIV-1/2 antibodies [Press release]. (2013, August 8). Retrieved from http://www.fda.gov/NewsEvents/Newsroom/PressAnnoucements/ucm364480.htm

Figure 2: Window periods of generations of HIV tests



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