Limitations for the Use of HIV-1 Western Blot in Plasma/Serum

Background

The Centers for Disease Control and Prevention (CDC) and the Association of Public Health Laboratories (APHL) published a new laboratory algorithm for the diagnosis of HIV in June 2014.[1] "Laboratory Testing for the Diagnosis of HIV Infection: Updated Recommendations"[1] supersedes all previous HIV laboratory testing guidelines.[2,3,4] The primary advantage of the new algorithm is the ability to identify HIV infection earlier.[5,6] This is critical because the risk of HIV-1 transmission from persons with acute and early infection is much higher than that from persons with established infections. Therefore, identifying these cases as early as possible and initiating antiretroviral therapy (ART) can benefit patients and reduce HIV transmission. The new algorithm takes advantage of the advances in HIV diagnostic testing by using a sequence of tests that concurrently detect HIV-1 and HIV-2 antibodies and HIV-1 p24 antigen. The algorithm also includes an HIV antibody differentiation assay as a supplemental test and HIV-1 RNA testing, as needed. This algorithm produces fewer indeterminate results and has a faster turnaround time for HIV-1 antibody positive samples compared to previous algorithms that utilized the Western blot (WB) for confirmation.[7]

Evidence Supporting Discontinuation of the HIV-1 WB for Plasma/Serum

The HIV-1 Western blot (WB), the historic gold standard for laboratory diagnosis of HIV-1 infection, is no longer part of the recommended algorithm. The two main reasons for this are the inability of the WB to detect acute infection and the potential to misclassify HIV-2 infection as an HIV-1 infection.

- The use of WB slows the process of HIV diagnostic testing, since laboratories typically need to batch or outsource samples for testing, delaying results for at least 48 hours; however, using the new algorithm screening and antibody confirmation can be performed as quickly as the same day thus reducing result turn-around time.[7,8]
- If WB is used as the confirmatory test for 3rd and 4th generation immunoassays, it could produce false-negative or indeterminate results during the acute phase of infection as well as in the early stages of seroconversion.[9,10]
- WB can misclassify HIV-2 infections as HIV-1.[11,12,13,14] Although HIV-2 infection is rare in the United States, correct diagnosis of HIV-2 is still imperative because some antiretroviral agents are effective only against HIV-1 and are not effective against HIV-2.[15,16]
- The HIV antibody differentiation assay is easier to interpret compared to WB and not only detects HIV-1 and HIV-2 it also differentiates between the two.[17]

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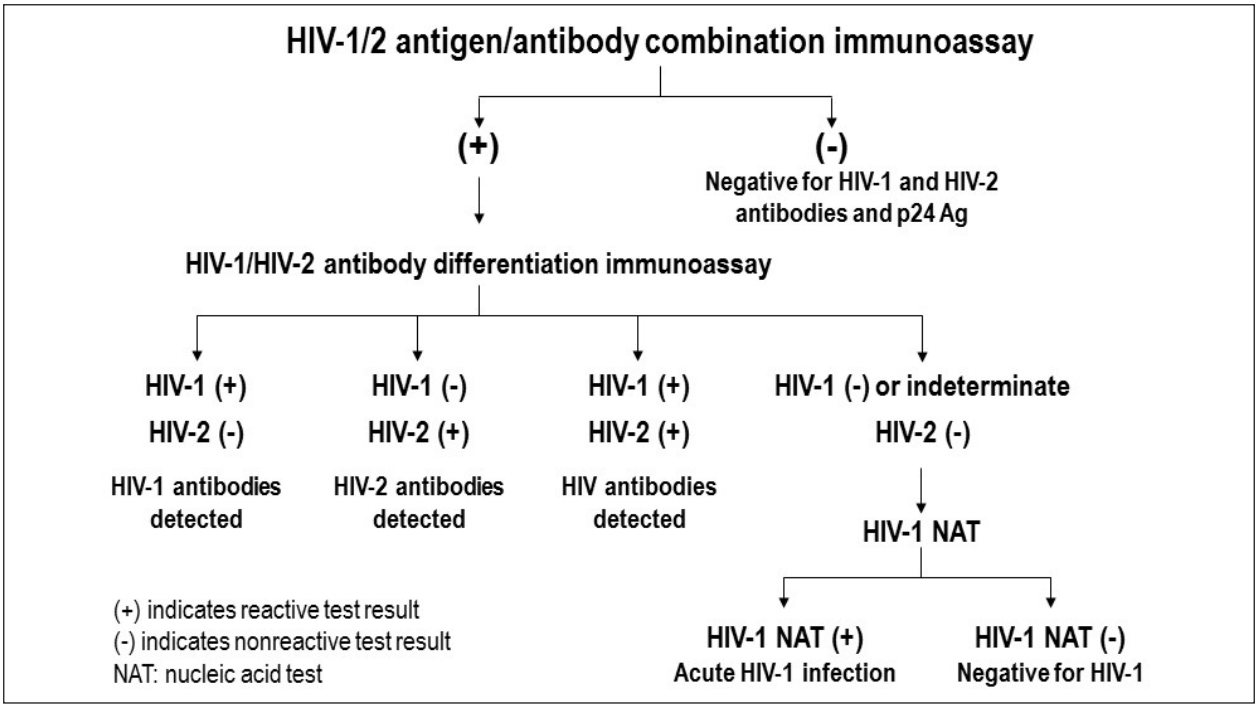
What is the Recommended Algorithm?



- Initial screen for all specimens: **FDA approved HIV-1/2 antigen/antibody combination immunoassay***
- Reactive specimens should be confirmed with: **FDA approved HIV-1/ HIV-2 antibody differentiation immunoassay**
- Negative or indeterminate specimens from differentiation immunoassay: **FDA-approved HIV-1 nucleic acid test (NAT)**

**Exception: As of April 2014, data are insufficient to recommend use of the FDA-approved single use rapid HIV-1/HIV-2 antigen/antibody combination immunoassay as the initial assay in the algorithm.*

This brief summary graphic of the recommended algorithm can be used as a reference. This algorithm applies to adults and children >24 months of age. For the complete recommendations and further information please consult the *Laboratory Testing for the Diagnosis of HIV Infection: Updated Recommendations*[1] which provides details and explanations for testing in special circumstances.

Considerations for Laboratories that Have Not Discontinued Using the HIV-1 WB

If your laboratory is using a HIV-1 WB or HIV-1 IFA for supplemental testing after a reactive screening assay and the result is negative or indeterminate, HIV-1 NAT should be conducted; if the HIV-1 NAT is negative, perform an HIV-2 antibody immunoassay. The only assays that have been FDA approved to differentiate HIV-2 from HIV-1 are the BioRad Multispot HIV-1/HIV-2 Rapid Test and Geenius™ HIV 1/2 Supplemental Assay. Both assays specifically detect antibodies to HIV-2; there are no FDA-approved HIV-2 NATs. Public health laboratories seeking assistance in evaluating suspect HIV-2 reactive specimens can contact Michele Owen (mowen@cdc.gov) or Tim Granade (tgranade@cdc.gov). Laboratories needing technical assistance in transitioning from the HIV-1 WB or HIV-1 IFA to the recommended algorithm can contact the Association of Public Health Laboratories (anne.gaynor@aphl.org).

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Monica Parker, PhD
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Bruce Robeson, MT (ASCP)
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Laura Wesolowski, PhD
Kelly Wroblewski, MPH

ASM

Susan E. Sharp, PhD, D(ABMM), F(AAM)
Melissa B. Miller, PhD, D(ABMM)
Eileen M. Burd, PhD, D(ABMM)
Stephen J. Cavalieri, PhD, D(ABMM)
Christine C. Ginocchio, PhD, MT (ASCP)
Paula Revell, PhD, D(ABMM)
James W. Snyder, PhD, D(ABMM), F(AAM)
Eric Weimer, PhD, D(ABMLI)
Amy L. Leber, PhD, D(ABMM)
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