

Human Immunodeficiency Virus 1/0/2 Cascade Fourth-generation Antigen/Antibody Detection

The CDC estimates that 1.1 million individuals are infected with human immunodeficiency virus (HIV-1) in the United States and that approximately 16% of those infected are unaware they are infected.¹ Between 2008 and 2010, an estimated average of 50,000 new infections occurred each year in the US.¹

HIV infections disproportionately affect several populations in the United States, including gay and bisexual men, IV drug users, and (increasingly) racial and ethnic minorities.² Identification of infection and referral to care have become key strategies in domestic (National HIV/AIDS Strategy) and global initiatives to reduce HIV incidence.^{3,4}

The CDC recommends routine HIV screening for all individuals between 13 and 64 years of age, with repeat annual screening for those at high risk. Routine HIV screening is also recommended for all pregnant women, regardless of risk status.³

Detection of Acute HIV Infection

Several studies have demonstrated the importance of increased awareness of HIV status and referral to treatment in decreasing overall transmission of HIV.^{5,7} Early infection, especially prior to seroconversion, is a time of high infectivity that disproportionately contributes to dissemination of HIV in the population.^{7,8}

HIV antigen/antibody combination assays are particularly helpful in identifying HIV infection in high-risk populations, where the incidence of acute infection may be as high as 10%.⁹ Early diagnosis of HIV infection during the acute phase of the disease represents an excellent opportunity for treatment and prevention interventions.

Efforts to close the HIV EIA seroconversion window, estimated at 25 days (22–37 range) using third-generation HIV-1/HIV-2 IgG-sensitive and IgM-sensitive antibody tests, have led to the development of fourth-generation assays that are able to detect HIV antibody (IgG/IgM) and HIV p24 antigen simultaneously.¹⁰

The antigen/antibody combination assays have been shown to reduce the seroconversion window by an estimated seven days

(range 0–20 days)¹¹⁻¹² and are expected to identify 80% to 90% of acutely infected individuals who would otherwise be missed by a third-generation EIA assay.¹³ The p24 antigen component of the test is sensitive to a viral concentration of approximately 14,000 and 30,000 viral copies/mL.¹³

Fourth-generation Confirmatory Algorithms

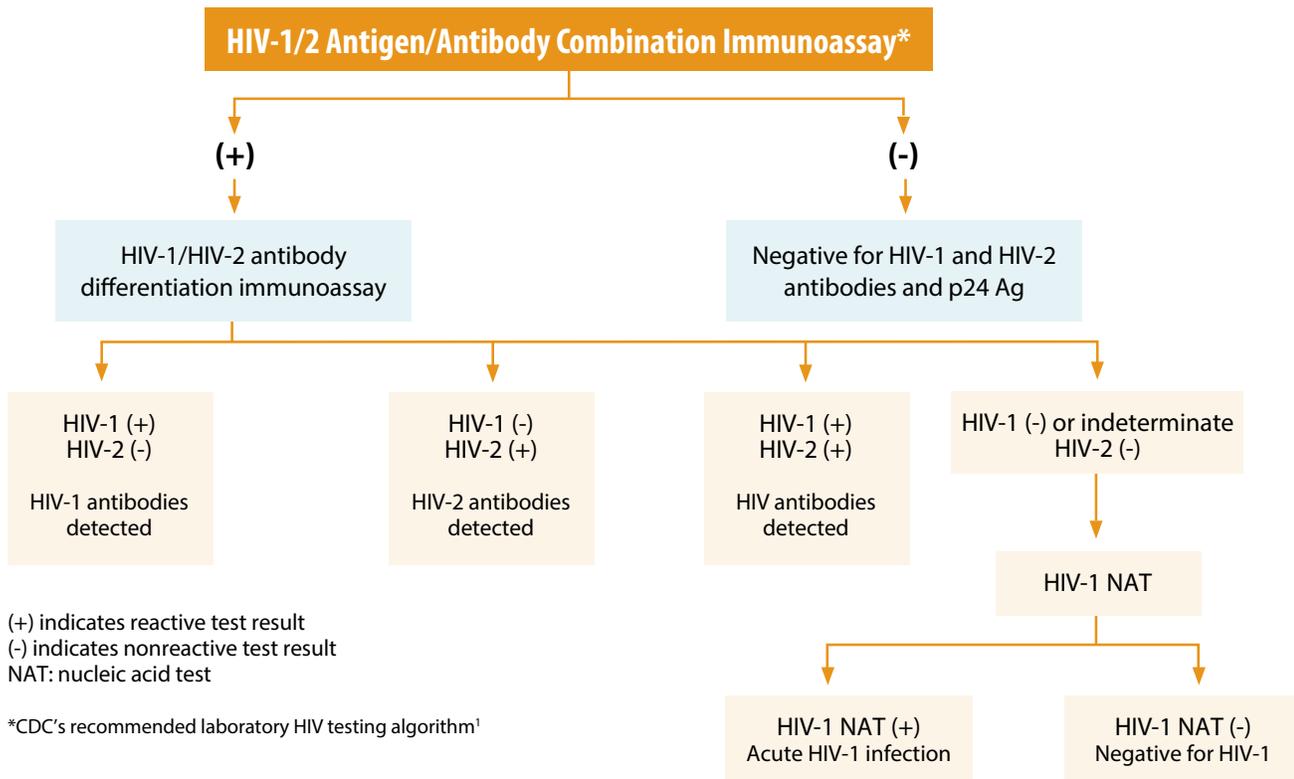
Improvements in sensitivity of the third-generation assays and the addition of antigen detection in fourth-generation assays present challenges for the use of standard HIV confirmatory Western blot assays. Since full reactivity on a Western blot assay may vary from 27 to 154 days following infection, nonconfirmatory Western blot test results may be obtained despite true repeat reactivity on third- and/or fourth-generation assays.^{10,14}

The Centers for Disease Control and Prevention (CDC) has released updated recommendations for laboratory testing for the diagnosis of HIV infection. These updated recommendations include a sequence of tests used to improve the accuracy of laboratory diagnosis of HIV. The updated recommendations include tests for HIV antigens and HIV nucleic acid to increase detection of HIV and no longer recommend the use of Western blot.¹

LabCorp's fourth-generation HIV antigen/antibody assay is available with a CDC-recommended supplemental algorithm (see figure). Repeat reactive specimens (due either to the presence of antigen or antibody) will be reflexed to a confirmatory EIA assay capable of differentiating HIV-1 reactivity from HIV-2 reactivity. Discrepant findings, consisting of a repeat reactive fourth-generation assay followed by a nonreactive confirmatory HIV-1/HIV-2 differentiation EIA result, are further resolved by NAT testing to identify potential acute infection and HIV RNA. Because fourth-generation assays detect both HIV p24 antigen as well as IgG and IgM antibody, preliminary data suggest that the number of repeat reactive specimens may be increased when compared to current third-generation antibody-only assays.^{12,15} Repeat reactive specimens will be resolved using supplemental testing per the reflex algorithm described on the next page.

Conclusion

Fourth-generation HIV screening and associated supplemental testing is a valuable addition to the HIV screening tools especially for use in high-risk populations where it will have its greatest impact. Detection of acute infections using the fourth-generation HIV screening assay provides an opportunity for early therapeutic intervention and the potential to reduce transmission rates.



Test Name	Test Number
Human Immunodeficiency Virus 1/O/2 Antigen/Antibody (Fourth Generation) Preliminary Test With Cascade Reflex to Supplementary Testing	083935

For the most current information regarding test options, including specimen requirements and CPT codes, please consult the online Test Menu at www.LabCorp.com.

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