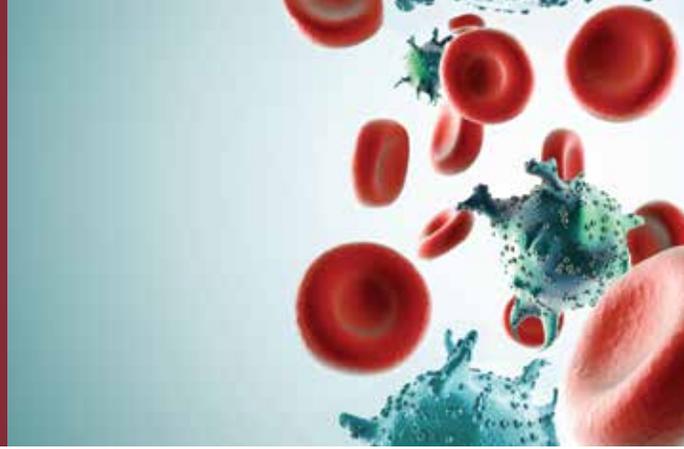


HIV-1/2 Antigen and Antibodies Fourth Generation, with Reflexes

Test Code 3682



Clinical Use

- Screen for and confirm HIV-1/HIV-2 infection, including acute infection
- Differentiate HIV-1 from HIV-2 infection

Clinical Background

More than 1.1 million people in the United States were living with HIV infection as of 2009, 18.1% of whom did not know they were infected.¹ Another ~50,000 individuals are newly infected each year.² Identification and treatment of HIV infection can lead to substantial benefits in terms of decreased transmission, morbidity, and death.³ The US Preventive Services Task Force thus recommends voluntary, opt-out, screening for all pregnant women and for individuals 15 to 65 years of age in regions where the prevalence of infection is $\geq 0.1\%$. Individual risk assessments determine the need for screening beyond this age range.³ The importance of detecting HIV during the acute phase (before seroconversion) is increasingly recognized; although brief, acute infection is marked by high viral load and appears to contribute disproportionately to transmission.⁴

The conventional HIV testing algorithm begins with a “third-generation” HIV-1/HIV-2 antibody immunoassay, followed by supplemental testing (eg, Western blot) to confirm repeatedly reactive results. This approach is highly sensitive and specific but has several drawbacks: it cannot detect acute infection; it does not readily differentiate between HIV-1 and HIV-2; and negative or indeterminate results on Western blots during early seroconversion can delay diagnosis. An alternative algorithm proposed by the CDC and adopted by the Clinical Laboratory Standards Institute (CLSI) is designed to avoid these drawbacks.⁵ The alternative algorithm begins with (preferably) a “fourth-generation” combination assay that detects HIV p24 antigen in addition to HIV antibodies. Because HIV p24 antigen is detectable before seroconversion, fourth-generation assays can detect HIV during acute

infection; the inclusion of HIV-1/HIV-2 antibodies allows detection after seroconversion, when p24 antigen becomes undetectable. Fourth-generation assays have $>99.7\%$ sensitivity and $>99.3\%$ specificity for HIV infection and can identify most ($>80\%$) acute infections that would otherwise require nucleic acid testing for detection.^{6,7} In general, they can detect infection 0 to 20 days (median, 5-7 days) before third-generation immunoassays.^{5,8,9}

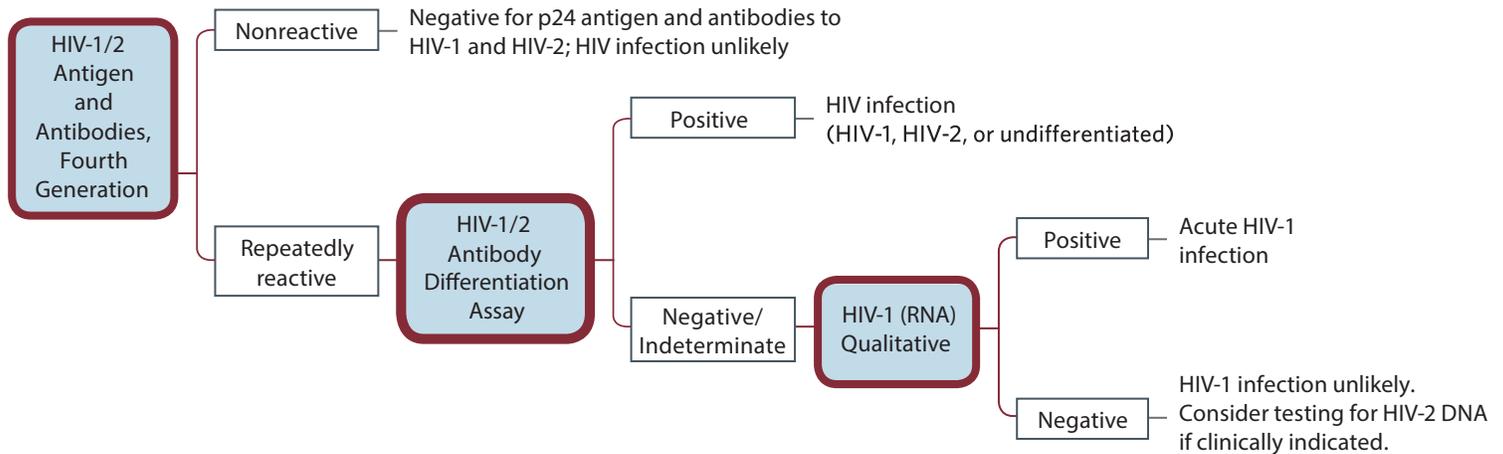
Repeatedly reactive results on fourth-generation screening tests require confirmation with a supplemental test, such as an HIV-1/HIV-2 antibody differentiation assay. Differentiation between HIV-1 and HIV-2 antibodies can have treatment implications, as HIV-2 does not respond to some antiretroviral agents. Differentiation tests also tend to detect antibodies earlier than Western blots.¹⁰ Like Western blot, HIV-1/HIV-2 antibody differentiation tests do not detect acute infection. HIV RNA testing is thus needed to resolve infection status in patients with positive results on the fourth-generation assay but negative results on the antibody differentiation test.

Quest Diagnostics, one of our parent companies, has collaborated with the CDC on key clinical studies supporting the alternative algorithm,^{6,10-12} which has demonstrated high sensitivity ($>99.7\%$) and specificity (100%).^{12,13} The HIV-1/2 Antigen and Antibodies, Fourth Generation, with Reflexes assay (Figure) is consistent with this algorithm.

Individuals Suitable for Testing

- Pregnant women
- Adolescents and adults 15 to 65 years of age, and beyond this range for those at increased risk
- Individuals with recent confirmed or suspected exposure to HIV-1 or HIV-2 infection
- Children 2 years of age or older with suspected HIV infection

Figure. Reflex Pathway for the “HIV-1/2 Antigen and Antibodies, Fourth Generation, with Reflexes” Assay (3682)



This algorithm depicts the testing pathway of the “HIV-1/2 Antigen and Antibodies, Fourth Generation, with Reflexes” test, which is consistent with reference 4. Although nonreactive results on the fourth-generation screening test and negative results on the HIV-1/HIV-2 differentiation test are consistent with absence of infection, they may also represent samples that were collected before development of detectable p24 antigen or HIV antibodies. Individual risk assessments may be helpful to determine the need for, and the frequency of, re-screening for patients with nonreactive/negative results.³

The algorithm is provided for informational purposes only and is not intended as medical advice. A physician's test selection and interpretation, diagnosis, and patient management decisions should be based on his/her education, clinical expertise, and assessment of the patient.

Methodology

- Chemiluminescent microparticle immunoassay specific for
 - HIV p24 antigen
 - HIV-1 (groups M and O) and HIV-2 antibodies
- Repeatedly reactive screening results are reflexed to the supplemental HIV-1/2 antibody differentiation test; negative HIV-1/2 antibody differentiation results are reflexed to the HIV-1 Qualitative RNA test. See the Figure for reflex pathway and reporting.

Specimen Requirements

3 mL refrigerated serum in a serum separator tube (2 mL minimum). Tube must be labeled with two patient identifiers and submitted only for HIV testing. Tube should be spun after clotting and remain unopened.

CPT Codes*

Screen: 87389; Reflex 1: 86701, 86702; Reflex 2: 87535

*The CPT codes provided are based on AMA guidelines and are for informational purposes only. CPT coding is the sole responsibility of the billing party. Please direct any questions regarding coding to the payor being billed.

Reference Range

Nonreactive

Interpretive Information

Interpretative information for the reflex pathway is depicted in the Figure.

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