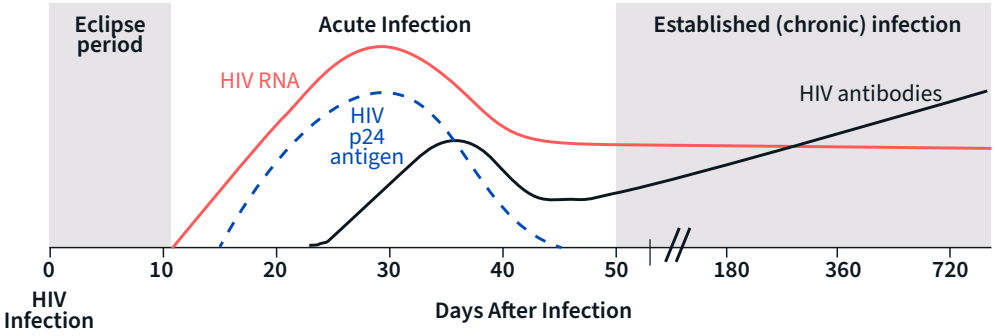
Human Immunodeficiency Virus (HIV) Screening and Diagnosis

In 2022, more than 31,000 estimated new HIV diagnoses were made in the United States.[1] Timely diagnosis of infection and linkage to care of all persons with HIV is crucial for achieving optimal clinical outcomes and preventing HIV transmission. The HIV diagnostic algorithm illustrated below relies on the detection of laboratory markers with distinct temporal kinetics.

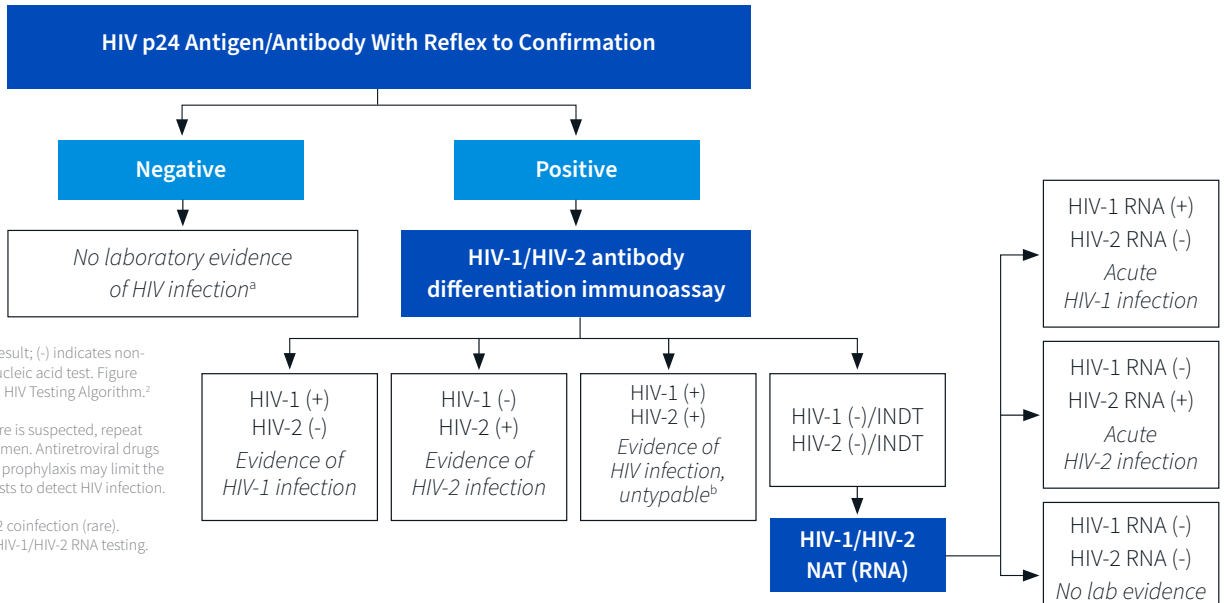
Temporal Appearance of Laboratory Markers of HIV Infection[2]



HIV Testing Algorithm

The HIV testing algorithm recommended by the U.S. Centers for Disease Control and Prevention (CDC) is a multistep process that identifies both chronic and acute (pre-seroconversion) HIV infection.[2] The first step of the algorithm is the HIV p24 antigen/antibody screen, which can detect the HIV-1 p24 antigen, and both IgG and IgM HIV-1 and HIV-2 antibodies. Repeated reactivity on the HIV antigen/antibody screen triggers a reflex to a secondary immunoassay that detects and differentiates between HIV-1 and HIV-2 antibodies. A positive secondary antibody assay is consistent with established HIV infection. If the secondary antibody assay is negative or indeterminate, a nucleic acid test (NAT) is performed for HIV-1 and HIV-2 RNA. A positive NAT, combined with a reactive screen and negative/indeterminate secondary antibody test, indicates acute infection. The complete algorithm and interpretations are illustrated below.[2] This testing cascade is available from Labcorp as part of the **HIV p24 Antigen/Antibody with Reflex to Confirmation [083935]** test.

HIV Testing Algorithm



(+) Indicates reactive result; (-) indicates non-reactive result; NAT, nucleic acid test. Figure adapted from the CDC HIV Testing Algorithm.[2]

a. If recent HIV exposure is suspected, repeat testing on a new specimen. Antiretroviral drugs taken for treatment or prophylaxis may limit the ability of diagnostic tests to detect HIV infection.

b. Possible HIV-1/HIV-2 coinfection (rare). Labcorp will reflex to HIV-1/HIV-2 RNA testing.

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HIV Testing Recommendations

General Population
Per CDC recommendations,[3] everyone ages 13-64 years old should get tested for HIV at least once using a reflexive algorithm such as Labcorp's HIV p24 Antigen/Antibody With Reflex to Confirmation [083935].

High-Risk Populations
People at high risk for HIV infection include men who have sex with men, people who inject drugs and their sex partners, people who exchange sex for money or drugs, sex partners of people with HIV, and those who have had or whose partners have had multiple sex partners since their most recent HIV test. All persons initiating treatment for tuberculosis or a sexually transmitted infection (STI) should also be screened for HIV. Per CDC guidelines,[4] annual HIV screening is recommended for these high-risk populations using HIV p24 Antigen/Antibody With Reflex to Confirmation [083935].

People Taking HIV Pre-Exposure Prophylaxis (PrEP)
The CDC has issued recommendations for baseline evaluation and ongoing monitoring of patients receiving PrEP.[5] Prior to initiating PrEP, patients should be screened for HIV infection using the HIV p24 Antigen/Antibody With Reflex to Confirmation [083935]. Because PrEP can alter the timing of laboratory markers of HIV infection,[5] the CDC recommends the addition of an HIV RNA test to baseline testing for patients who have taken PrEP/PEP (post-exposure prophylaxis) within three months or received a PrEP injection within 12 months. Addition of an HIV RNA test is also recommended for patients who have not taken PrEP but have reported possible exposure in the four weeks prior to their initial PrEP visit and have experienced signs/symptoms of acute HIV during that time.[5]

Guidance for laboratory monitoring of patients on HIV PrEP has been established and is tailored to each PrEP modality (oral or long-acting injectables).[5] Labcorp offers individual assays and panels to support the monitoring of patients on PrEP that can be found on our website (see HIV Screening and Diagnostic Testing Options table at https://www.labcorp.com/treatment-areas/virology-infectious-diseases/clinical-testing/hiv/prep/cdc-compliant-prep-test-panels).

The use of HIV RNA testing differs among clinicians. Labcorp offers alternative PrEP panels and individual assays to accommodate diverse clinical practices.

Recent Exposure
HIV RNA is the earliest detectable laboratory marker of HIV infection. When acute retroviral syndrome is suspected, the Human Immunodeficiency Virus 1 & 2 (HIV-1/HIV-2), Qualitative, RNA [139825] test may identify HIV infection earlier than the HIV p24 Antigen/Antibody Screen With Reflex to Confirmation test; therefore, the two tests should be used in conjunction in situations where recent HIV exposure may have occurred.[4,6]

Pregnant Women
Per guidelines from the U.S. Department of Health and Human Services (DHHS), pregnant women should be tested for HIV infection using HIV p24 Antigen/Antibody With Reflex to Confirmation [083935] as early as possible in pregnancy to minimize the risk of vertical HIV transmission. For women at increased risk of HIV acquisition, repeat testing is recommended during the third trimester. Repeat testing is also recommended for patients with an STI or signs/symptoms of acute HIV infection.[7]

Neonates
Because of transplacental transfer of antibodies from mothers with HIV to infants, serologic testing, including antigen/antibody testing, should not be used in infants less than 18 months old. Instead, assays that detect HIV nucleic acid should be used. HIV DNA and HIV RNA polymerase chain reaction (PCR) assays are recommended as preferred virologic assays by the DHHS guidelines; however, the guidelines also caution that maternal antiretroviral therapy or infant HIV prophylaxis may affect HIV-1 RNA and DNA test results.[8]

Please consult the CDC and DHHS guidelines for complete HIV testing recommendations.

HIV Testing Options

Test No.	Test Name	Intended Use	Specimen Type(s)*
083935	HIV p24 Antigen/Antibody With Reflex to Confirmation	Guideline-recommended algorithm for laboratory screening and diagnosis of HIV infection, including acute and primary infection	Serum
139825	Human Immunodeficiency Virus 1 & 2 (HIV-1/HIV-2), Qualitative, RNA	Aid in the diagnosis of HIV-1 and/or HIV-2 infection, including acute or primary infection. Aid in the diagnosis of HIV-1 and/or HIV-2 in individuals with indeterminate or inconclusive serologic test results. Aid in the diagnosis of HIV-1 and/or HIV-2 infection in infants under 18 months of age who are born to HIV-infected mothers	Plasma or serum
550430	Human Immunodeficiency Virus 1 (HIV-1), Quantitative, Real-time PCR (Nongraphical)	Detect and quantitate HIV-1 in plasma (viral load)	Plasma
550420	Human Immunodeficiency Virus 1 (HIV-1), Quantitative, Real-time PCR (Graphical)	Detect and quantitate HIV-1 in plasma (viral load)	Plasma
550880	Human Immunodeficiency Virus 1 (HIV-1), Quantitative, RNA (Abbott® RealTime)	Detect and quantitate HIV-1 in plasma (viral load)	Plasma, frozen

*Samples positive on the HIV Ag/Ab assay reflex to HIV antibody differentiation and HIV RNA as appropriate.
Note: For HIV PrEP testings optiions, visit our online Test Menu at Labcorp.com.

Frequently Asked Questions

Q: What is the rate of false-positives on the HIV p24 Antigen/Antibody Screen?
A: The false-positive rate of the HIV p24 Antigen/Antibody screen, which is the first step of the HIV p24 Antigen/Antibody With Reflex to Confirmation [083935] test, has been investigated in several studies and ranged from 0.035% to 0.223%.[9-14]

Q: What are possible reasons for false-positive HIV serology?
A: Possible triggers of false-positive HIV results include infections such as viral hepatitis,[15] Epstein-Barr virus (EBV),[16] cytomegalovirus (CMV),[17] babesiosis[18] and schistosomiasis[19]; malaria[20]; SARS-CoV-2[21-24]; syphilis[25]; autoimmune diseases including lupus,[26] rheumatoid arthritis[26] and autoimmune hepatitis[27-28]; malignancy including lymphoma[29-30] and cancer[16,25,31]; heterophilic antibody interference[32]; recent immunization[33]; pregnancy[25]; CAR-T cell therapy;[34-35] and investigational products administered in an HIV vaccine trial.[36]

Q: A patient previously diagnosed with HIV is on antiretroviral therapy (ART), but an attempt to confirm the diagnosis using serologic assays produced a negative result. What are the possible reasons for these findings? What tests are available for further evaluation of the patient's HIV status?
A: These findings may reflect a well-documented decline in HIV-1 antibodies (seroreversion) associated with early initiation of ART and prolonged viral suppression.[37-46] Erroneous initial HIV diagnosis is also possible. Qualitative and quantitative HIV-1 RNA tests may produce negative/undetectable results for patients on ART and therefore may not be suitable for confirming HIV diagnosis in such cases. Assays that detect HIV-1 DNA, which is less affected by ART,[47] may provide confirmation of infection. However, inability to produce a result on a DNA-based assay does not exclude HIV infection. In diagnostically challenging cases, consultation with the National Clinical Consultation Center (nccc.ucsf.edu, 844-ASK-NCCC) may help identify alternative diagnostic approaches. The final clinical assessment should be based on all available data including the patient's immune status, risk factors and history.

Q: Are there any special considerations when interpreting HIV testing in patients who have received CAR-T cell therapy?
A: Potential interactions between HIV assays and specific lentiviral vector-based CAR-T cell therapies have been identified that could lead to false-positive HIV-1 RNA results.[34-35] Due to the potential cross-reactivity between some NAT assays and certain lentiviral vector-based therapies, clinicians should exercise caution when ordering and interpreting HIV testing in patients who have received CAR-T therapy.

Q: Are there any special considerations when interpreting HIV testing in individuals on antiretroviral therapy (ART), including patients administered HIV preexposure prophylaxis (PrEP) and HIV post exposure prophylaxis (PEP)?
A: Interpretation of HIV testing in patients on PrEP can be challenging as PrEP and PEP can reduce HIV RNA levels early in infection, leading to false-negative results on nucleic acid tests (NAT) during acute infection. If HIV infection occurs while on PrEP or PEP, seroconversion may be delayed or incomplete, causing indeterminate or negative antibody/antigen tests. PrEP and PEP users may occasionally have false-positive antigen/antibody or HIV RNA results due to assay interference or altered seroconversion patterns.[25]

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