

False-Positive Fourth-Generation HIV Screening with Low-Level Viremia in Pregnancy: A Diagnostic Challenge

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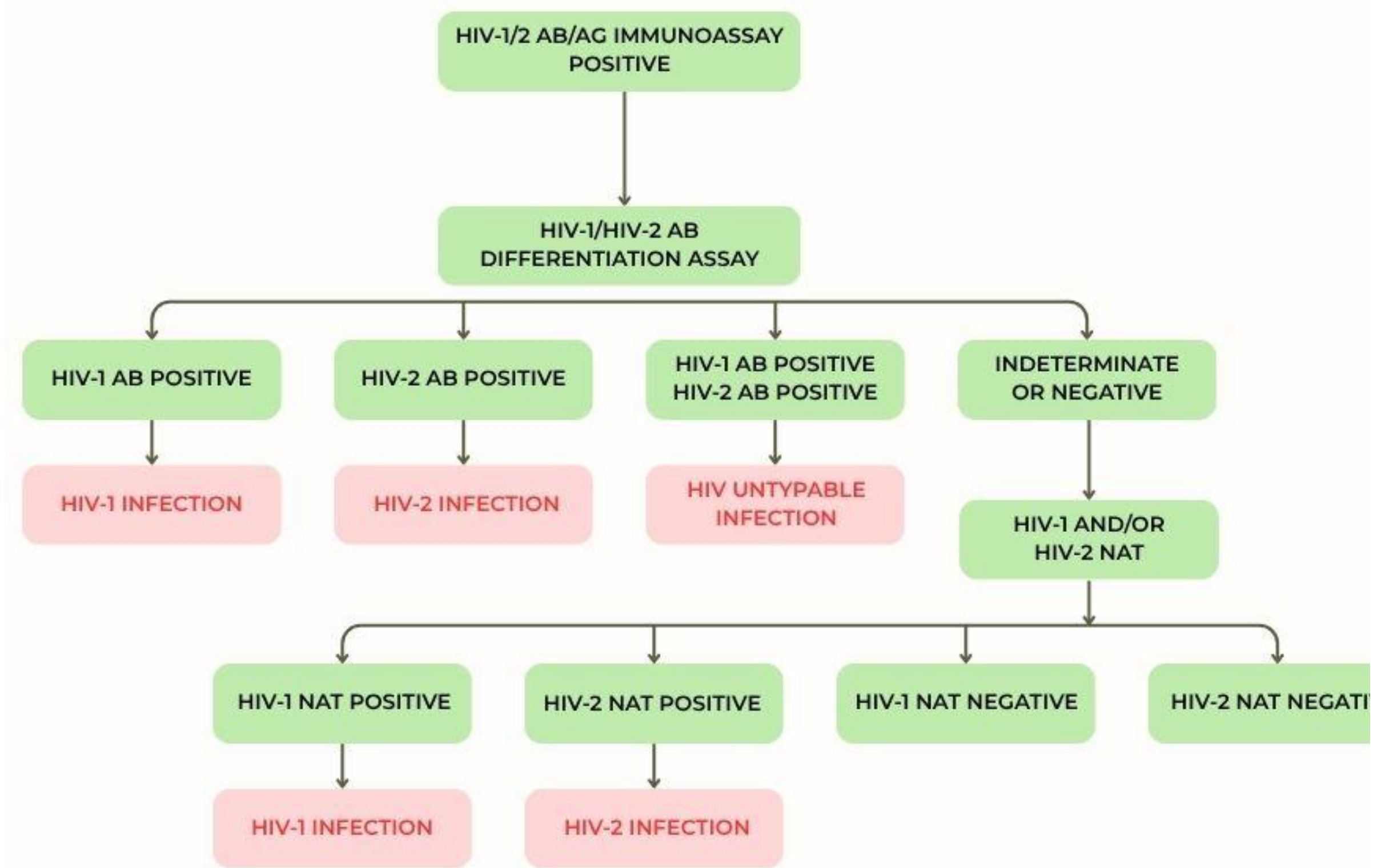
BACKGROUND

Fourth-generation HIV antigen/antibody testing is recommended for HIV screening during pregnancy and provides high sensitivity for early infection. A reactive screening test followed by a negative HIV-1/HIV-2 antibody differentiation assay requires HIV nucleic acid testing to distinguish acute infection from a false-positive screening result.

Discordant results can create particular challenges during pregnancy because delayed recognition of acute maternal HIV infection may increase the risk of vertical transmission, while an incorrect diagnosis may result in unnecessary antiretroviral and neonatal treatment and significant psychosocial consequences.

We describe an unusual case of discordant HIV testing during pregnancy in which two reactive fourth-generation screening results were followed by an isolated low-level detectable HIV-1 RNA result, despite subsequent testing failing to confirm HIV infection.

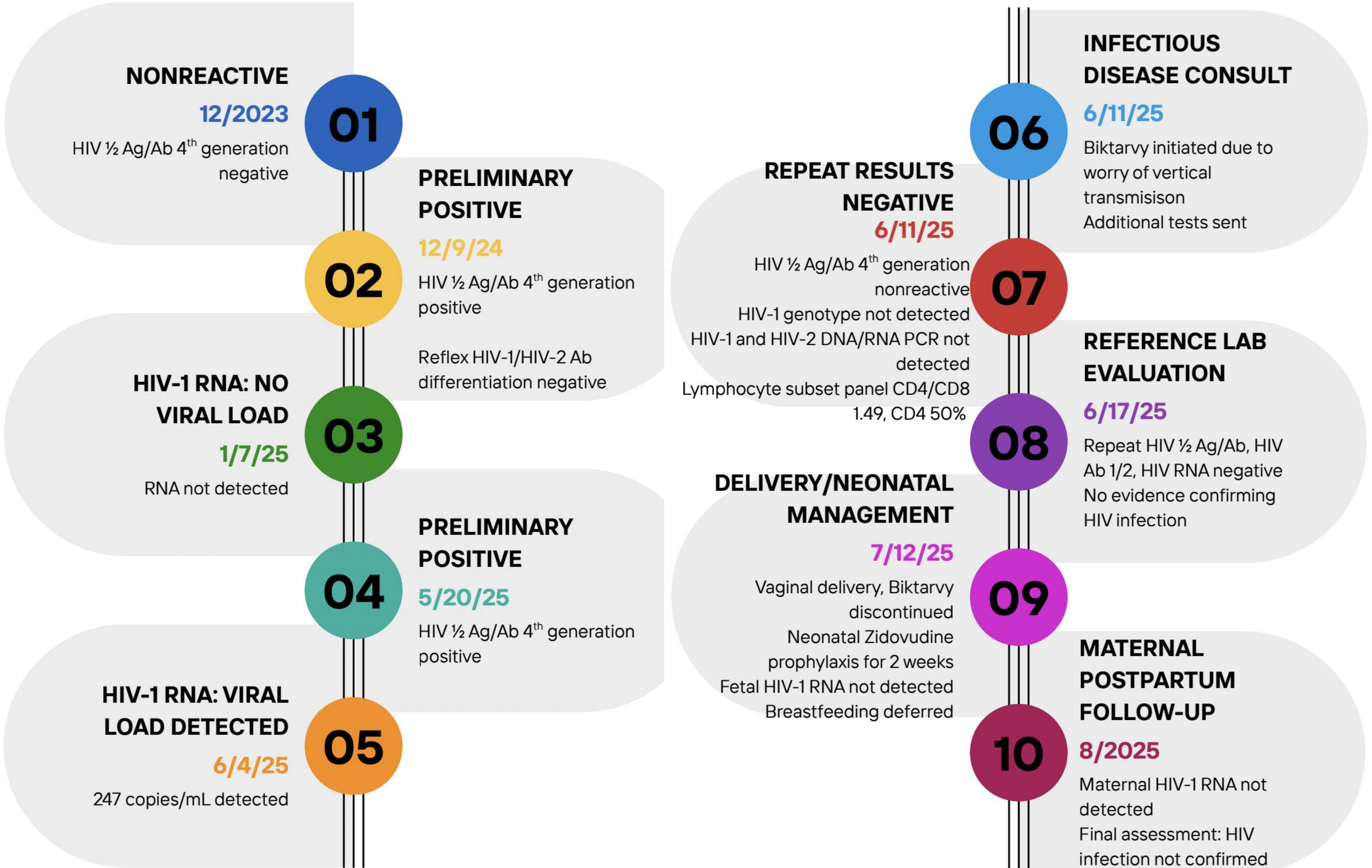
DIAGNOSTIC ALGORITHM FOR HIV WITH LAB TESTING PER THE CDC



WORK-UP

Date	Test	Result	Clinical significance
12/2023	HIV-1/2 Ag/Ab, 4th generation	Nonreactive	Documented negative pre-pregnancy baseline
12/2024	HIV-1/2 Ag/Ab, 4th generation	Reactive	Initial prenatal screening abnormality
12/2024	HIV-1/HIV-2 antibody differentiation	HIV-1 negative; HIV-2 negative	Did not confirm HIV infection
01/2025	HIV-1 RNA PCR	Not detected	Acute HIV infection not demonstrated
05/2025	HIV-1/2 Ag/Ab, 4th generation	Reactive	Recurrent reactive screen in the third trimester
06/2025	HIV-1 RNA PCR	247 copies/mL	Raised concern for acute HIV infection
06/2025	Repeat HIV-1 RNA PCR	Not detected	Low-level RNA result was not reproduced
06/2025	Repeat HIV-1/2 Ag/Ab, 4th generation	Nonreactive	Discordant with prior reactive screening results
06/2025	HIV-1 DNA PCR	Not detected	Additional testing did not support HIV-1 infection
06/2025	HIV-2 DNA/RNA PCR	Not detected	No evidence of HIV-2 infection
08/2025	Postpartum maternal HIV-1 RNA PCR	Not detected	Persistent absence of detectable viremia after ART discontinuation supported absence of established HIV infection

PATIENT TIMELINE



TAKEAWAY POINTS

SYSTEMATIC CONFIRMATION

A reactive fourth-generation screen with negative HIV-1/HIV-2 differentiation testing requires nucleic acid testing to evaluate for acute infection.

INTERPRET THE COMPLETE DIAGNOSTIC PICTURE

An isolated low-level detectable HIV RNA should be interpreted in the context of the complete diagnostic evaluation. When subsequent results are discordant, repeat and complementary testing may be necessary before establishing a definitive diagnosis.

BALANCE COMPETING RISKS IN PREGNANCY

When acute HIV infection cannot initially be excluded, clinicians must balance timely prevention of vertical transmission against the consequences of unnecessary maternal and neonatal treatment. Multidisciplinary management and careful patient counseling are essential.

REFERENCES

- 1 CDC. HIV Diagnoses, Deaths, and Prevalence [Internet]. HIV Data. 2025. Available from: <https://www.cdc.gov/hiv-data/nhss/hiv-diagnoses-deaths-prevalence.html>
- 2 Townsend CL, Byrne L, Cortina-Borja M, Thorne C, de Ruiter A, Lyall H, et al. Earlier initiation of ART and further decline in mother-to-child HIV transmission rates, 2000–2011. AIDS [Internet]. 2014 Apr 1;28(7):1049–57. Available from: https://journals.lww.com/aidsonline/FullText/2014/04240/Earlier_initiation_of_ART_and_further_decline_in.14.aspx
- 3 Prenatal and Perinatal Human Immunodeficiency Virus Testing [Internet]. www.acog.org. Available from: <https://www.acog.org/clinical/clinical-guidance/committee-opinion/articles/2018/09/prenatal-and-perinatal-human-immunodeficiency-virus-testing>
- 4 Bernard M. B, S. Michele O, Laura G. W, Berry B, Barbara G. W, Kelly E. W, et al. Laboratory testing for the diagnosis of HIV infection : updated recommendations. Centers for Disease Control and Prevention [Internet]. 2014 Jun 27; Available from: <https://stacks.cdc.gov/view/cdc/23447>
- 5 Kim S, Lee JH, Choi JY, Kim JM, Kim HS. False-Positive Rate of a “Fourth-Generation” HIV Antigen/Antibody Combination Assay in an Area of Low HIV Prevalence. Clinical and Vaccine Immunology. 2010 Aug 4;17(10):1642–4.
- 6 Adhikari EH, Macias D, Gaffney D, White S, Rogers VL, McIntire DD, et al. Diagnostic accuracy of fourth-generation ARCHITECT HIV Ag/Ab Combo assay and utility of signal-to-cutoff ratio to predict false-positive HIV tests in pregnancy. American Journal of Obstetrics and Gynecology. 2018 Oct;219(4):408.e1–9.
- 7 Wormser GP, Schneider LM. False-Positivity of an HIV Antigen/Antibody Assay for HIV p24 Antigen in Active SARS-CoV-2 Infection. The American Journal of Medicine. 2024 Jan;137(1):8–9.
- 8 Liu P, Jackson P, Shaw N, Heysell S. Spectrum of false positivity for the fourth generation human immunodeficiency virus diagnostic tests. AIDS Research and Therapy. 2016 Jan 5;13(1).
- 9 Rapid Testing for HIV - Counseling Protocol for Rapid HIV Testing Sessions [Internet]. Ny.gov. 2026 [cited 2026 Apr 30]. Available from: <https://www.health.ny.gov/diseases/aids/providers/testing/rapid/protocol.htm>