State of Alaska Epidemiology Bulletin

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False-Positive 4th Generation HIV Screening Tests

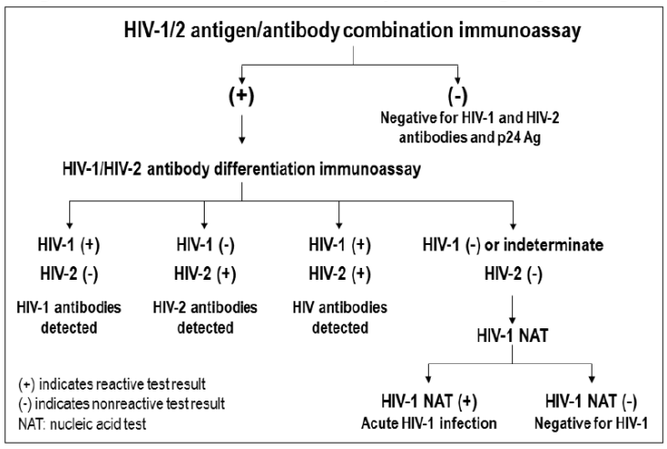
Background

Diagnostic testing technology for human immunodeficiency virus (HIV) infection is a rapidly evolving landscape. Newer, more sensitive HIV screening tests have been implemented, allowing for earlier detection of HIV infection. The high sensitivity of these HIV screening tests can lead to elevated false-positive error rates in areas of low HIV incidence such as Alaska.[1] In 2014, the Centers for Disease Control and Prevention (CDC) published updated HIV testing recommendations in response to the changes in HIV testing technologies.[2] We describe here a summary of false-positive HIV screening test results reported in Alaska during 2017 and a review of CDC's recommended HIV testing algorithm.

Laboratory Testing for HIV

The first step of CDC's Laboratory HIV Testing Algorithm involves a 4th Generation antigen/antibody combination immunoassay (Ag/Ab Combo), which detects HIV-1 and HIV-2 antibodies and the HIV-1 p24 antigen (Figure). If this test is positive, the laboratory will reflex to the second step for confirmation with an HIV-1/2 antibody differentiation assay (note: the Western Blot test is no longer recommended for confirmation of a positive screening test and is not used by most laboratories). If the initial screening test is reactive and the antibody confirmation test is non-reactive, the third step is to perform a nucleic acid test (NAT) polymerase chain reaction (PCR) test to rule out acute HIV infection. *If both the antibody confirmation test and the PCR test are negative, the initial screening test was a false-positive.* Most laboratories that perform HIV tests on specimens from Alaska patients (e.g., the Alaska State Virology Laboratory, Quest Diagnostics™, and LabCorp) will routinely reflex to the third step in the CDC algorithm with the submitted specimen; however, some laboratories (e.g., Mayo Medical Laboratories) require the provider to submit a new specimen to request the HIV-1 NAT (PCR).

Figure. CDC's Recommended Laboratory HIV Testing Algorithm[2]



Methods

The Alaska Section of Epidemiology (SOE) receives all positive HIV screening test results and subsequent confirmatory results (both positive and negative) performed on Alaska residents. Reactive HIV screening test results that are determined to be false-positives on subsequent confirmation tests are retained during the calendar year in which they are reported. Paper copies of the laboratory results reported from January 1 through July 31, 2017 were reviewed to determine the number of false-positive reports. Results were reported from nine laboratories that use either a point-of-care or an automated 4th Generation Ag/Ab Combo test for HIV screening.

Results

From January 1 through July 31, 2017, 22 confirmed cases of HIV and 46 false-positive 4th Generation HIV-1/2 Ag/Ab Combo screening tests were reported to SOE. False-positive tests were observed both in the automated tests (27; 59%) and the point-of-care Alere Determine™ HIV-1/2 Ag/Ab Combo test (19; 41%).

Of the 46 specimens with false-positive screening tests, 12 (26%) did not go through CDC's three step algorithm (7 did not receive the antibody confirmation test but were negative on the PCR, and 5 did not receive a PCR test following a negative antibody confirmation test).

Case Study

A teenaged girl presented to her health care provider for sexually transmitted infection screening. The provider included a 4th Generation HIV-1/2 Ag/Ab Combo test as part of the panel. The test was repeatedly reactive, but confirmation testing by HIV-1/2 antibody differentiation assay and PCR was negative. The provider misinterpreted the test results and told the patient that they were HIV-positive. The provider informed SOE staff of the new case. SOE staff reviewed the patient's test results and informed the provider that the initial screening test was a false-positive. The patient was notified that the initial test was a false-positive.

Discussion

This report highlights the potential for false-positive results with the Alere Determine™ point-of-care and the automated 4th Generation HIV-1/2 Ag/Ab Combo tests.[3,4] To date, SOE staff are aware of at least four patients who were mistakenly told they were positive for HIV due to incomplete follow-up testing or misinterpretation of the recommended HIV testing algorithm results. To avoid misdiagnosis, it is important to order the appropriate HIV screening test and to review all reported results in the testing algorithm prior to making a final HIV diagnosis.

Recommendations

1. Routinely screen for HIV in patients aged 13–64 years using a 4th generation HIV-1/2 Ag/Ab Combo test according to current CDC recommendations.[5]
2. Interpret a reactive 4th generation HIV screening test with caution due to the possibility of a false-positive result, and ensure that all steps in CDC's recommended HIV testing algorithm have been completed prior to making a final interpretation and a diagnosis of HIV infection.
3. For patients with symptoms consistent with acute HIV infection and a negative HIV-1/2 Ag/Ab Combo test, consider ordering the HIV-1 RNA PCR test, which has greater sensitivity during the first 2 weeks of infection.
4. Call the SOE at 907-269-8000 for assistance with interpreting results and to report confirmed and suspected cases of HIV (within 5 working days).

References

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