Identification, Investigation and Impact of False Positive HIV Diagnostic Testing Algorithm Results - New York State Experience

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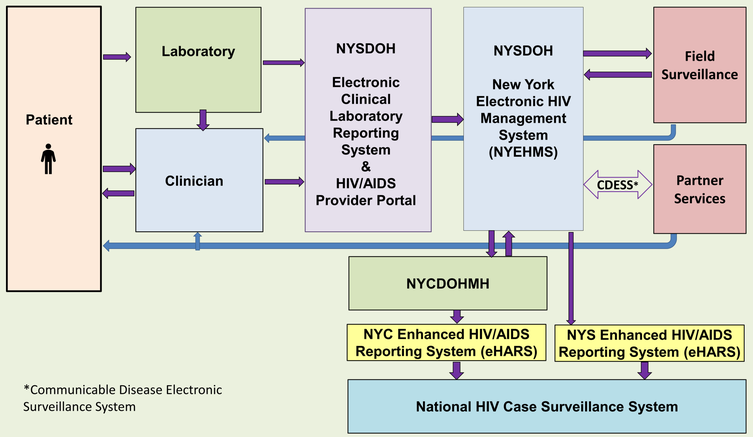
BACKGROUND

- New York State (NYS) Public Health Law requires laboratories conducting HIV-related testing for NYS clinicians and/or residents to electronically report any laboratory test, tests or series of tests approved for the diagnosis of HIV or for the periodic monitoring of HIV infection.
- Laboratories report using the Electronic Clinical Laboratory Reporting System (ECLRS), a single secure platform for all laboratory reporting to NYS.
- In June 2014, the Centers for Disease Control and Prevention (CDC) and the Association of Public Health Laboratories recommended the HIV Diagnostic Testing Algorithm (DTA) be for the diagnosis of HIV infection.
- In NYS, HIV Surveillance and Partner Services are initiated for persons with a new diagnosis of HIV.
- Surveillance collects and verifies case defining information while Partner Services interviews the person to assure appropriate follow-up and linkage to care of the individual and their exposed partner(s).
- Though HIV is reportable to the State, surveillance investigations are conducted separately by the NYS Department of Health (DOH) and the New York City (NYC) Department of Health and Mental Hygiene (DOHMH).
- This project focuses on the HIV DTA results for persons residing in NYS outside of NYC.

PROJECT

The HIV Laboratory DTA is a sequence of tests in which the final algorithm interpretation relies on the assay results from up to three distinct tests. The NYSDOH investigates all reports of suspected new diagnoses of HIV, and consequently identifies laboratory algorithm interpretations showing evidence of HIV infection as well as subsequent DTA testing that does not show evidence of HIV infection.

Figure 1: Process of HIV Laboratory Reporting from Patient to NYSDOH through Reporting to the National HIV Surveillance System



ISSUE

- Discordant diagnostic test results can confuse the ordering clinician as well as distress the individual being tested and their notified sexual or needle sharing partner(s).
- Significant staff resources are required to resolve the discordant diagnostic test results.
- Discordant results are often identified by Partner Services during field investigation. Field investigations are initiated for an individual and their partner(s) who may have a false positive result.

ACKNOWLEDGEMENT

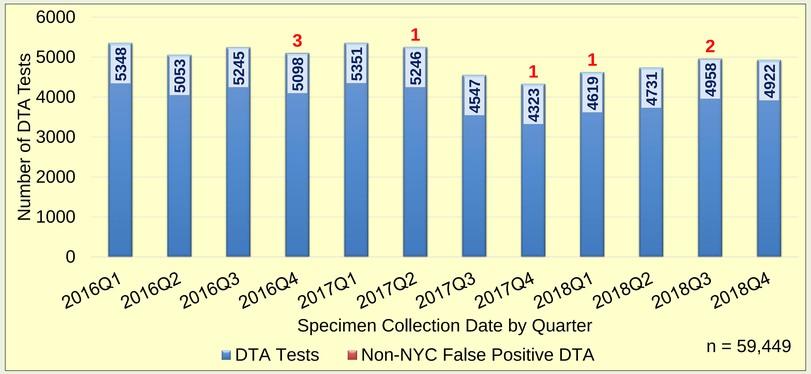
This analysis was made possible through the support of the Centers for Disease Control and Prevention PS18-1802 Integrated Human Immunodeficiency Virus (HIV) Surveillance and Prevention Programs for Health Departments. The content of this poster is solely the responsibility of the authors and does not necessarily represent the official views of the CDC.

RESULTS

Between November 2016 and August 2018, eight HIV DTA interpretations showed evidence of HIV infection and were reported to the NYSDOH. The eight specimens had similar assay results for each test in the HIV multi-test algorithm; HIV Ag/Ab immunoassay "reactive", HIV-1/HIV-2 antibody differentiation immunoassay "negative" and HIV-1 nucleic acid test (NAT) "positive". New specimens were obtained and all eight individuals were later found to not have HIV infection. The eight specimens will be referred to as "False Positive DTA".

- The eight false positive DTA specimens were from white, middle-aged women who live close to New York City

Figure 2: Temporal Distribution of False Positive DTA Results by Specimen Collection Date



Laboratory Handling of the Eight False Positive DTA Specimens:
- DTA testing was ordered by eight different providers
- For all eight, the original false positive DTA was performed on a single specimen
- Testing for seven occurred at the same national laboratory
- For one false positive DTA, the HIV-1/2 antigen/antibody and differentiation immunoassays were conducted at one lab and the HIV-1 NAT testing was conducted by a referral lab

How the Surveillance Unit was Alerted to Investigate Potential False Positive Diagnostic Testing Algorithm Results:
- Partner Services staff alerted the Surveillance Unit (n=4)
- Internal investigation within the Surveillance Unit:
  - Follow-up on report of apparent early/acute HIV infection (n=1)
  - Discordance between DTA results and provider report (n=1)
  - Analysis of discordant surveillance field investigation and Partner Services outcome (n=2)

Figure 3: Time Frame from Specimen Collection to Surveillance Unit Notification and Surveillance Assignment Closure (n=8)

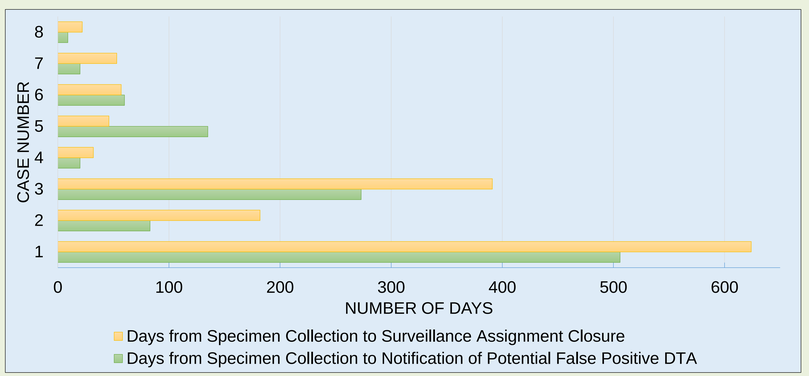


Table 1: Patient HIV Laboratory Testing History (n=8)

Case No.	Specimen Collection Date of DTA Interpretation "Evidence of HIV"	Specimen(s) Collected for Follow-up HIV Testing	HIV Laboratory Testing	Laboratory Test Results	Number of Days from Initial DTA to Lab Results Showing No Evidence of HIV
1	4Q2016	1	HIV-1 RNA PCR Viral Load Quantitative	Not Detected	69
2	4Q2016	1	HIV 1-2 Ag/Ab Immunoassay	Non-Reactive	11
3	4Q2016	1	HIV-1 RNA Viral Load Quantitative CD4 Absolute CD4 Percent	<20 Not Detected 1100 57.9%	14
		2	HIV 1-2 Ag/Ab Immunoassay HIV 1/2 Ab Differentiation HIV-1 RNA NAT Qualitative	Reactive HIV Negative Negative	
4	2Q2017	1	HIV 1-2 Ag/Ab Immunoassay	Non-Reactive	7
		2	HIV-1 RNA Viral Load Quantitative	<40 c/mL	
5	4Q2017	1	HIV-1 RNA Viral Load Quantitative HIV-1 RNA Viral Load Quantitative CD4 Absolute CD4 Percent	<200 c/mL <40 c/mL 1418 52%	16
6	1Q2018	1	HIV 1-2 Ag/Ab Immunoassay HIV 1/2 Ab Differentiation HIV-1 RNA NAT Quantitative	Reactive HIV Negative Not Detected	8
		2	HIV-1 RNA Viral Load Quantitative HIV-2 Proviral DNA, Qualitative	<20 Not Detected Not Detected	
		3	HIV-1 RNA Viral Load Quantitative HIV-1 RNA NAT Qualitative	<20 Negative	
7	3Q2018	1	HIV-1 RNA NAT Qualitative HIV-1 RNA Viral Load Quantitative CD4 Absolute CD4 Percent	Negative <20 794 44.1	13
8	3Q2018	1	HIV 1-2 Ag/Ab Immunoassay (Lab A) HIV-1 RNA NAT Qualitative (Lab A) HIV 1-2 Ag/Ab Immunoassay (Lab B)	Non-Reactive Not Detected Non-Reactive	10

The average number of days from specimen collection of the DTA to follow-up testing to conclude the algorithm result was a false positive result is 18.5 days, with a range of 8-69 days.

Laboratory Feedback Received for Various Specimens:
- Laboratory suggested to retest the individual if the DTA test result did not align with expectation
- Specimen contamination at draw site could impact DTA results
- Specimens were discarded so unable retest the specimens
- Lab conducted an in-depth investigation; specimen review identified the serum separator tubes were sent to the lab's external site for HIV-1 NAT testing. There was no pour-off. The lab reviewed the runs, quality control and results from worksheets and compared them to their Laboratory Information System and all results were confirmed to be accurate.
- Partner Services had a new specimen drawn and tested by the NYSDOH Public Health Lab which confirmed the individual had no laboratory evidence of HIV

Anecdotal Findings from the Field:

Provider: *Annoyed, wants an explanation of how this could happen*

Patient: *Upset, confused, unhappy with testing*

Partner Services: *Confused, apprehensive, not sure what to tell provider or patient*

Staff Involved in Investigation and Documentation of False Positive Results:
- **Partner Services Staff:** County Supervisor, Program Manager, Regional Coordinator, Regional Disease Investigation Specialist, Bureau of HIV/STD Field Services Director
- **Surveillance Staff:** Surveillance Coordinator, Laboratory Team Lead, Evaluation Specialist, Surveillance Field Staff, Bureau of HIV/AIDS Epidemiology Director
- **Laboratory:** NYSDOH Public Health Laboratory, Testing Laboratory Director

Surveillance Systems: Once the diagnostic testing algorithm is confirmed to be a false positive result, documentation compiled and the case is removed from the NYS HIV registry.

LESSONS LEARNED

- Need for systematic alert and review process for the identification and investigation of potential false positive DTA results
- Time consuming and multiple follow-up steps are necessary to resolve false positive HIV DTA results
- Negative HIV screen results are not currently reported to NYSDOH; investigation into discordant results would be more efficient and timely if negative results were reported to determine true negative status
- While the number of false positive results is small, the impact on the individual and staff is substantial.
- Need to re-educate clinicians that when a diagnostic testing algorithm interpretation result seems questionable, diagnostic testing should be repeated