Experience with the Fourth Generation HIV Testing Algorithm in Saint Louis, Missouri

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Introduction

Diagnostic testing for Human Immunodeficiency Virus (HIV) is a multistep process requiring an initial highly sensitive screening test, followed by a secondary highly specific confirmatory test. In 2014 the Centers for Disease Control (CDC) updated recommendations for the diagnostic testing of HIV to a fourth generation screening algorithm. The revised algorithm consists of a new 4th generation screening assay, which is a combined p24 antigen/antibody detection test. All specimens that are reactive in this screening assay are tested by a secondary antibody assay that detects and differentiates HIV-1 and HIV-2 antibodies (the HIV1/HIV2 Multispot test). Multispot negative specimens are confirmed using nucleic acid amplification testing (NAAT). In October 2014 Barnes Jewish Hospital (Saint Louis, MO) transitioned to the new fourth generation testing algorithm to screen for HIV. The purpose of this study was to retrospectively gather data regarding our experience with the new testing algorithm.

Method

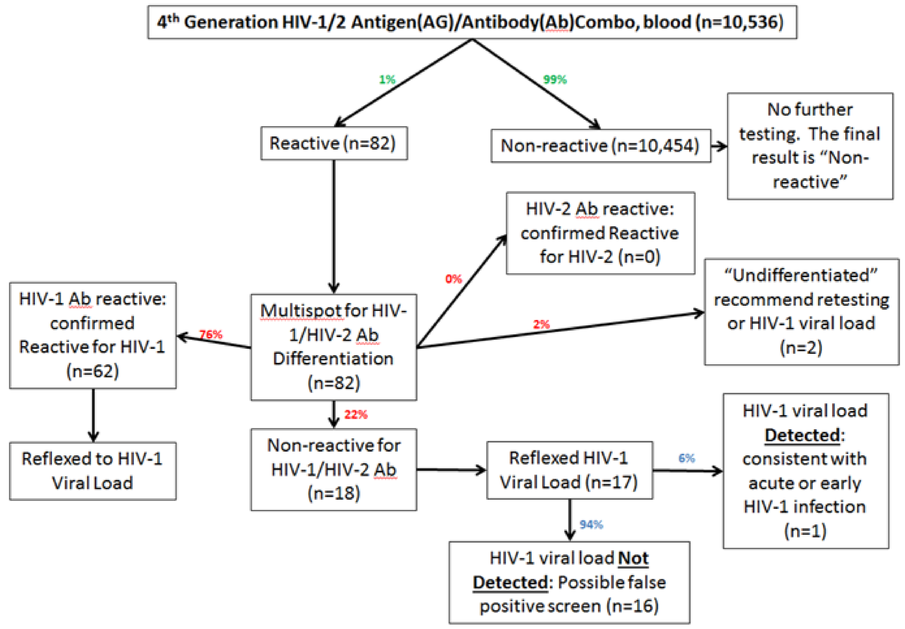
We retrospectively reviewed total test volumes and results for each test included in the fourth generation algorithm. Results from the antigen/antibody screen were classified as either "false positive" or "true positive" according to the remaining tests in the algorithm. A detailed chart review was performed on all patients with either "false positive" or "true positive" antigen/antibody screens. Data obtained from each patient included age, gender, comorbidities, pregnancy, and the presence or absence of HIV risk factors. Results were compared amongst the two groups.

Results

Test volumes and results are shown in Figure 1. Of the 10,536 patient specimens tested by the fourth generation algorithm, 1% (n=82) were positive by the antigen/antibody screen. Following Multispot testing, 72% (n=62) of screen positive specimens were positive for HIV-1. No specimens were positive for HIV-2 and only 2% (n=2) of screen positive specimens were classified as "undifferentiated" (reactive for both HIV-1 and HIV-2 targets). Negative Multispot results were obtained for 22% (n=18) of the screen positive specimens. Only 17 of these specimens were of sufficient volume for NAAT, of which only 1 specimen was positive by NAAT.

Chart review of patients with "true positive" initial screens (n=60) revealed that the diagnosis of HIV-1 was already known in 24 of the tested patients (testing only performed to re-establish care). Of the 36 patients with newly diagnosed HIV-1, 78% (n=28) had documented HIV-1 risk factors, 14% (n=5) had a documented lack of risk factors, and 8% (n=3) had no history available in the patient chart (Figure 2). None were pregnant or had autoimmune disease. In contrast, of the 14 patients with false positive screens, only 14% (n=2) had documented HIV-1 risk factors (Figure 3). Pregnancy and autoimmune disease was observed in 50% (n=7) of these patients. A detailed list of comorbidities and further test results in this population is shown in Table 1.

Figure 1. HIV Testing Algorithm Results



Legend: Green- Percentage of specimens tested by Antigen/Antibody Combo Screens, Red- Percentage of specimens tested by Multispot HIV-1/HIV-2 AB Differentiation Assay, Blue- Percentage of specimens tested by HIV-1 viral load

Table 1. Chart Review Data from Patients with False Positive Screens

Gender	Age	Comorbidities	HIV Risk Factors	Repeat Screen
Female	24 Years	History Not Available	History Not Available	yes (positive 1 day later)
Male	45 Years	Pancreatitis and Type 1 Diabetes	none	yes (negative 2 months later)
Female	35 Years	Polyarthralgias	None	yes (positive 6 months later)
Male	41 Years	Focal Segmental Glomerulosclerosis	None	yes (positive 3 months later)
Male	57 Years	Paraplegia Secondary to Brain Infarction	none	yes (positive 2 days later)
Female	30 Years	Type 2 Diabetes and Antiphospholipid Antibody Syndrome	none	no
Male	33 Years	None	none	no
Female	23 Years	Pregnant	none	no
Female	31 Years	Cystic Fibrosis with Bilateral Lung Transplant,	none	no
Female	25 Years	Pregnant	none	yes (positive 6 months later)
Female	38 Years	Hepatitis B and Hepatitis C Infection	yes (IV Drug Use)	no
Female	33 Years	Pregnant and Polycystic Ovarian Syndrome	none	no
Male	53 Years	Hepatitis C Infection and Squamous Cell Carcinoma of Head and Neck	yes (IV Drug Use)	yes (negative 4 days later)
Female	45 Years	Crohn's Disease	none	no

Figure 2. Risk Factors in Patients with Newly Diagnosed HIV (n=36)

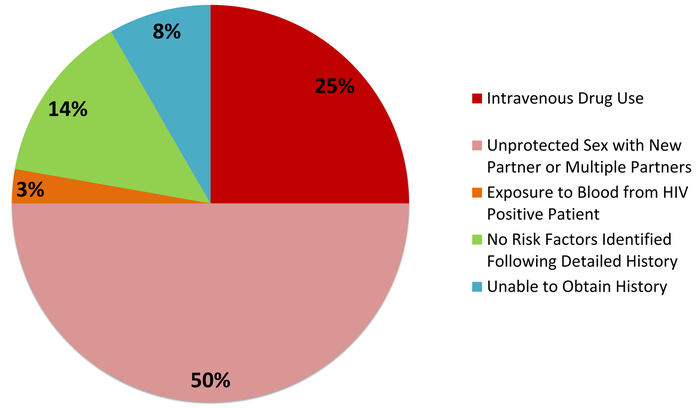
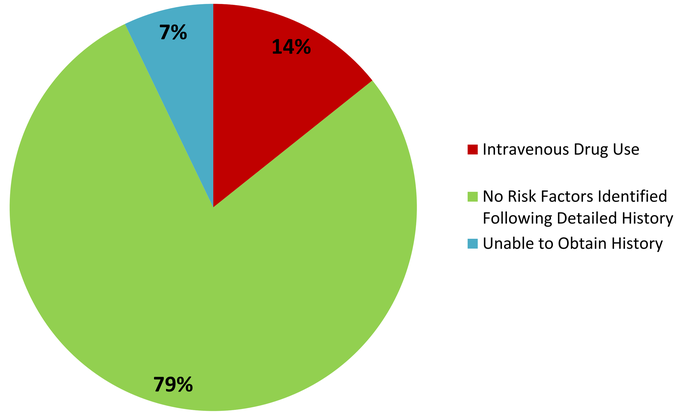


Figure 3. Risk Factors in Patients with False Positive Screens (n=14)



Conclusions

-In our patient population, approximately 20% of positive screens for HIV are determined to be false positives by the remaining algorithm. This highlights the importance of confirmatory testing prior to an official diagnosis of HIV infection.

- Patients with "false positive" screens often have very different clinical histories than those with "true positive" screens. Patients with "true positive" screens had a high percentage of documented risk factors (78%, 28/36). Patients with "false positive" HIV screens had a high percentage (50%, 7/14) of documented pregnancy and autoimmune diseases, conditions classically associated with false positive HIV screens.

-While awaiting results of confirmatory testing, the presence of HIV-1 risk factors may be a useful predictor of a "true positive" screen, whereas conditions such as autoimmune disease or pregnancy may be useful predictors of "false positive" screens. However, clinical history should not be used as a substitute for confirmatory testing.