Evaluation of FDA-approved rapid HIV tests for laboratory diagnosis of HIV infection

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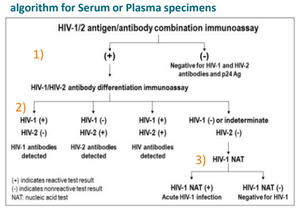
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Background

In 2014 the Centers for Disease Control and Prevention and Association of Public Health Laboratories published updated recommendations for the laboratory testing for diagnosis of HIV infection. This includes:

1. Screening with a test that detects both HIV antigen and antibody (Ag/Ab screening test)
2. Following reactive screening tests with a test capable of differentiating HIV-1 from HIV-2
3. Following a negative or indeterminate differentiation test with an HIV-1 nucleic acid test

Figure: Recommended Laboratory HIV testing algorithm for Serum or Plasma specimens



At the time the recommendation was published (2014) the Multispot test (Table 1) was the only test capable of differentiating HIV-1 from HIV-2.

The Multispot was replaced by the BioRad Geenius test in Summer 2016; the Multispot test is no longer being sold in the United States

None of the other FDA-approved rapid tests differentiate HIV-1 from HIV-2.

Objective

We investigated the performance of other FDA-approved single use rapid HIV tests (Table 1) when used as the 2nd test in the HIV testing algorithm.

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Table 1: Characteristics of rapid HIV tests

Test Name	Time to test result	Sensitivity for established HIV-1 infection % (95% CI) [a]	Specificity % (95% CI) [a]	Approved specimen types for CLIA-moderate settings and specimen volume	Shelf life	Median (Interquartile range) Window period (days)[a]
Bio-Rad Geenius HIV-1/HIV-2 Supplemental assay	20 min	Serum 99.33(97.59-99.82) EDTA Plasma 99.34 (96.34-99.88)	NA[c]	Serum/plasma 5 µl whole blood 15 µl	12 months	33 (28-39)
Chembio DPP HIV-1/2	15 min	Serum/plasma 99.9 (99.4-99.9)	Serum/plasma 99.9 (99.7-99.9)	Serum/plasma/whole blood 10 µl or oral fluid swab	23 months	30 (25-36)
Chembio SURE CHECK HIV 1/2 Assay	15 min	Serum/plasma 99.7 (98.9-100.0)	Serum/plasma 99.9 (99.6-100.0)	Serum/plasma/whole blood 2.5 µL	24 months	31 (27-38)
Clearview HIV 1/2 STAT-PAK	15 min	Serum/plasma 99.7 (98.9-100.0)	Serum/plasma 99.9 (99.6-100.0)	Serum/plasma/whole blood 5 µL	24 months	31 (26-37)
Determine HIV-1/2 Ag/Ab Combo Test	20 min	Serum/plasma 99.9 (99.4-100)	Plasma: Low risk subjects 100 (99.6-100) High-risk subjects 99.2 (98.2-99.7)	Serum/plasma/whole blood 50 µL	14 months	19 (15-25)
INSTI HIV-1/HIV-2 Rapid Antibody Test	<2 min	Plasma 99.9 (99.5-100)	Plasma 100 (99.7-100)	Plasma/whole blood 50 µl	12 months	26 (22-31)
MedMira Reveal G3 Rapid HIV-1 Antibody Test	<2 min	Serum 99.8 (99.2-100) Plasma 99.8 (99.0-100),	Serum: 99.1 (99.8-99.4) Plasma 98.6 (98.4-98.8),	Serum/plasma 30 µl	12 months	30 (26-36)
Multispot HIV-1/HIV-2 Rapid Test This test is no longer available	20 min	Serum/plasma 100 (99.9-100)	Serum/plasma 99.9 (99.8-100)	Serum/plasma 30 µl	12 Months	34 (29-40)
OraQuick ADVANCE Rapid HIV-1/2 Antibody Test	20 min	Plasma 99.6 (98.9-99.8)	Plasma 99.9 (99.6-99.9)	Plasma/whole blood 5µl	12 months	35 (29-42)
Uni-Gold Recombigen HIV	10 min	Serum/plasma 100 (99.5-100.0)	Serum/plasma 99.8 (99.3-100)	Serum/plasma/whole blood 50 µL	12 months	33 (27-39)

Table 1 is adapted from information available at www.cdc.gov/hiv/testing [a]As reported in FDA-approved package inserts [b]As reported in Delaney et al CID 2017 https://academic.oup.com/cid/article/64/1/53/2194435/Time-Until-Emergence-of-HIV-Test-Reactivity [c]NA= Not applicable. The Geenius test is only intended to be used with specimen that have been pre-screened and found to be reactive for HIV antibodies. Specificity when used with specimens from uninfected participants was not reported in the package insert for the Geenius test.

Methods

Stored plasma or serum collected in a study conducted in Los Angeles, California from 2003-2007 were tested with FDA-approved Ag/Ab screening tests (n=5), HIV-1 Western blot, Aptima HIV-1 RNA Qualitative Assay (APTIMA), Geenius and up to 8 other rapid HIV tests (Table 2). The study included:

- 5,470 persons screened for HIV, and 403 recruited with known HIV infection
  - 707 specimens reactive on at least one FDA-approved Ag/Ab screening test
    - 656 with established infection –HIV-1 Western blot positive
    - 9 with early infection – HIV-1 Western blot negative, APTIMA positive
    - 42 with false-reactive screening test results – HIV-1 Western blot and APTIMA negative

Algorithms were constructed from individual test results as if following the recommended algorithm (Figure); specimens with non-reactive results on the 2nd test were categorized as HIV-infected or false-reactive on the screening test based on the APTIMA result.

Table 2: Comparison of rapid test results when performed after reactive Antigen/Antibody screening tests in the CDC/APHL Algorithm for Laboratory Diagnosis of HIV infection

	CDC/APHL laboratory algorithm result					
	Negative		Early infection		Established infection	
	Rapid test result					
Rapid HIV Test	False Positive[a]	True Negative	False Negative[b]	True Positive	False Negative[b]	True Positive
Total[c]		42		9		656
Geenius HIV-1/HIV-2	0	37	8	0	0	655
DPP HIV-1/HIV-2	2	14	9	0	1	655
StatPak HIV-1/HIV-2	0	37	8	0	8	636
Determine HIV-1/HIV-2 Combo	3	39	3	5	1	651
Insti HIV-1/HIV-2	4	12	4	5	1	655
Reveal HIV-1	0	36	8	0	1	646
Multispot HIV-1/HIV-2	1	39	8	0	1	626
Oraquick HIV-1/HIV-2	0	42	9	0	4	651
Unigold HIV-1	0	37	8	0	4	642

[a]This would end the algorithm and results would be reported (incorrectly) as HIV-positive.
[b]These specimens would continue in the algorithm to nucleic acid testing and be resolved at that step
[c] Not all specimens could be tested with every rapid test, missing results can be calculated by summing the false and true results columns and subtracting from the overall total for each of the three CDC Algorithm results

Results and Discussion

- Among specimens from persons without early infection all FDA-approved rapid tests performed similarly to the Geenius test
- The Insti HIV-1/HIV-2 antibody test and Determine HIV-1/HIV-2 Combo correctly identified 5 of 8 early infection specimens; all early infection specimens were non-reactive using Geenius and all other rapid tests.
  - This result is consistent with published estimates of time to first test reactivity (Table 1), which suggest these tests detect infection sooner than other rapid tests
- However, these two tests also returned reactive results in 3-4 specimens (<1/1000 screened) that were HIV-1 Western blot and Aptima negative.
  - These specimens would have been incorrectly classified as HIV-1 antibody positive based on the current algorithm

All FDA-approved rapid tests could serve the role of a supplemental test in the HIV-1 diagnostic algorithm.

- Although they don't differentiate HIV-1 from HIV-2, HIV-2 remains rare in the US and would be identified when a quantitative HIV-1 viral load was performed at HIV care initiation.
- Likewise, the few false-reactive rapid tests could also be resolved during clinical follow-up.
- Less sensitive rapid tests would flag more specimens for NAT testing, and identify more cases of early infection for clinical follow-up

Factors such as speed with which results can be returned and simplicity of both testing and result reporting make these other rapid tests good alternatives for the second step in the HIV diagnostic algorithm.

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The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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