Rapid HIV screening: missed opportunities for diagnosis and prevention

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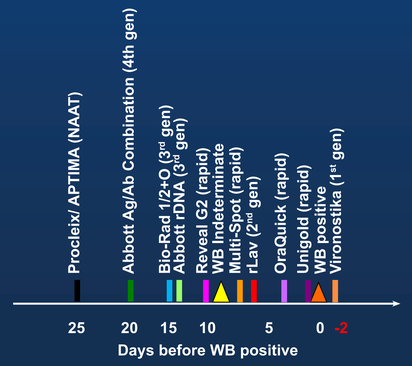
Background

- Rapid HIV tests offer several advantages because they are simple and easy to use; can be used in outreach, point-of-care, and nonclinical settings; and return results faster than conventional tests, usually in 30-40 minutes.
- Therefore, rapid HIV tests can be used to increase the number of persons tested for HIV and the number of persons who receive their HIV test results.
- Rapid HIV tests are widely used in venues that reach persons at high-risk for HIV infection; therefore, it is important to determine whether rapid tests can detect early HIV infection when viral transmission may be highest.
- Because persons who learn they are infected substantially reduce behaviors that are likely to transmit HIV, tests that can detect HIV as soon as possible after exposure can help interrupt further HIV transmission.
- Although rapid HIV tests increase the number of persons who are aware of their HIV status, they may have limited sensitivity for the diagnosis of early HIV infection, resulting in missed opportunities for HIV prevention.
- The figure below depicts the time at which HIV infection can be detected by several different HIV tests in relation to the Western blot (WB).
- Many rapid tests, including Unigold, which uses an "antigen sandwich" technique that can also detect IgM antibodies against HIV which develop earlier after infection, seem to detect HIV only a few days before the WB.
- However, many more sensitive assays, such as third- and fourth- generation enzyme immunoassays (EIAs) and nucleic acid amplification tests (NAAT), can detect HIV well before the WB.
- A few studies have shown that NAAT can detect early/acute HIV infection less sensitive assays have missed. However, a thorough evaluation of the sensitivity of rapid tests compared with NAAT for early infection has not been done.

Figure. Sequence of positivity of various HIV tests



Courtesy of Michele Owen, PhD. REF: Owen et al. Alternative Algorithms for Human Immunodeficiency Virus Infection Diagnosis Using Tests That Are Licensed in the United States. J Clin Micro; 2008:1588-95.

Objective

To determine the sensitivity for early HIV infection of several rapid tests and third- and fourth-generation assays compared with nucleic acid amplification testing (NAAT).

Methods

- In the CDC Acute HIV Infection (AHI) study, persons underwent routine HIV antibody screening at 80 public health clinics in 4 Florida counties; 12 county sexually transmitted disease (STD) clinics and one community clinic serving homosexuals in Los Angeles; and 3 municipal STD clinics in New York City from April 24, 2006 through March 28, 2008.
- Each project area used a different screening assay: Florida used Genetic Systems 1/2 +O® (third-generation EIA), Los Angeles used Vironostika HIV-1 Microelisa System (first-generation EIA), and New York City used Oraquick Advance Rapid HIV 1/2 (rapid test).
- To identify AHI, specimens that were negative by serologic testing underwent pooled NAAT, followed by individual NAAT of positive pool members.
- All NAAT-positive specimens underwent third-generation testing with Genetic Systems 1/2 +O®, viral load quantification, and rapid testing with Multispot HIV-1/HIV-2.
- A subset of specimens with adequate quantity for further testing was also tested with four other rapid tests: Clearview Complete HIV 1/2 Assay, Unigold Recombigen HIV, Clearview HIV 1/2 Stat-Pak Assay, and Oraquick Advance Rapid HIV-1/2 Antibody Test and tested with the Architect HIV Antigen/Antibody Combo®.

Results

- Of 99,111 specimens screened from April 2006 to March 2008, 60 were NAAT-positive/ seronegative by one of three different immunoassays and 2 were NAAT-positive/ Western blot indeterminate.
- The comparative results of all HIV testing done in this study of the AHI panel are seen in Table 1.
- Third-generation testing correctly detected antibody in 34 of 62 specimens (55%; 95% confidence interval (CI): 42-67); Multispot detected antibody in 16 (26%; 95% CI: 16-38). Of the 62 specimens, 33 (53%) had sufficient quantity for further testing.
- The sensitivity for acute HIV infection of the different HIV tests examined in the AHI panel of 33 specimens are summarized in Table 2.
- The rapid tests correctly detected antibody in 37 to 47% of cases detected by third-generation testing.

Table 1. Comparative HIV test results with an acute HIV infection panel.

Sample ID #	Initial EIA	NAAT	Third generation	Fourth generation	Rapid Tests					Viral Load
	NYC = Oraquick LA = Vironostika FL = Genetic Systems HIV 1/2+O	GenProbe Aptima HIV-1	BioRad Genetic Systems HIV 1/2 + O ®	Abbott Architect Antigen/ Antibody Combo®	Multispot	Oraquick	Unigold	Statpak	Clearview complete	Bayer Versant bDNA (copies/ mL)
NYC 1	NR	R	NR	QNS	NR	QNS	QNS	QNS	QNS	> 500,000
NYC 2	NR	R	R	QNS	R	QNS	QNS	QNS	QNS	42,074
NYC 3	NR	R	R	QNS	R	QNS	QNS	QNS	QNS	> 500,000
NYC 4	NR	R	R	QNS	R	QNS	QNS	QNS	QNS	180,586
NYC 5	NR	R	R	R	R	NR	NR	NR	NR	92
NYC 5-2	NR	R	R	R	R	NR	R	NR	NR	< 75
NYC 6	NR	R	R	R	R	R	R	R	R	732
NYC 7	NR	R	R	R	R	R	R	R	R	31,260
LA 1	NR	R	R	R	NR	NR	NR	NR	NR	> 500,000
LA 2	NR	R	NR	R	NR	NR	NR	NR	NR	> 500,000
LA 3	NR	R	NR	NR	NR	QNS	NR	QNS	QNS	1827
LA 3-2	NR	R	R	R	NR	NR	NR	NR	NR	> 500,000
LA 4	NR	R	NR	QNS	NR	QNS	QNS	QNS	QNS	> 500,000
LA 5	NR	R	R	R	NR	NR	NR	NR	NR	> 500,000
LA 6	NR	R	R	QNS	R	QNS	QNS	QNS	QNS	> 500,000
LA 7	NR	R	R	QNS	NR	QNS	QNS	QNS	QNS	> 500,000
LA 8	NR	R	R	QNS	NR	QNS	QNS	QNS	QNS	> 500,000
LA 9	NR	R	R	QNS	NR	QNS	QNS	QNS	QNS	301,417
LA 10	NR	R	NR	QNS	NR	QNS	QNS	QNS	QNS	> 500,000
LA 10-2	NR	R	R	R	NR	NR	R	NR	NR	> 500,000
LA 11	NR	R	NR	QNS	NR	QNS	QNS	QNS	QNS	> 500,000
LA 12	NR	R	NR	QNS	NR	QNS	QNS	QNS	QNS	109,697
LA 12-2	NR	R	R	QNS	NR	QNS	QNS	QNS	QNS	> 500,000
LA 13	NR	R	R	QNS	NR	QNS	QNS	QNS	QNS	59,184
LA 14	NR	R	NR	QNS	NR	QNS	QNS	QNS	QNS	> 500,000
LA 15	NR	R	NR	QNS	NR	QNS	QNS	QNS	QNS	37,378
LA 16	NR	R	R	QNS	NR	QNS	QNS	QNS	QNS	> 500,000
LA 17	NR	R	NR	QNS	NR	QNS	QNS	QNS	QNS	303,046
LA 18	NR	R	R	QNS	NR	QNS	QNS	QNS	QNS	1,520
LA 19	NR	R	NR	QNS	NR	QNS	QNS	QNS	QNS	21,116
LA 20	NR	R	NR	QNS	NR	QNS	QNS	QNS	QNS	> 500,000
LA 21	NR	R	NR	QNS	NR	QNS	QNS	QNS	QNS	> 500,000
LA 22	NR	R	NR	QNS	NR	QNS	QNS	QNS	QNS	477,386
LA 23	NR	R	R	QNS	NR	QNS	QNS	QNS	QNS	> 500,000
LA 24	NR	R	NR	QNS	NR	QNS	QNS	QNS	QNS	298,154
LA 24-2	NR	R	R	QNS	R	QNS	QNS	QNS	QNS	> 500,000
LA 25	NR	R	R	QNS	NR	QNS	QNS	QNS	QNS	> 500,000
LA 26	NR	R	R	QNS	NR	QNS	QNS	QNS	QNS	> 500,000
LA 27	NR	R	NR	QNS	NR	QNS	QNS	QNS	QNS	> 500,000
LA 28	NR	R	NR	R	NR	NR	NR	NR	NR	47,818
LA 29	NR	R	R	R	R	R	NR	R	R	98,989
LA 30	NR	R	NR	R	NR	NR	NR	NR	NR	> 500,000
LA 30-2	NR	R	R	R	R	R	R	R	R	16,258
LA 31	NR	R	R	R	R	R	R	R	R	173,725
LA 32	NR	R	R	R	R	NR	NR	NR	NR	> 500,000
LA 33	NR	R	R	R	NR	NR	NR	NR	NR	> 500,000
LA 34	NR	R	NR	NR	NR	NR	NR	NR	NR	21,548
LA 35	NR	R	NR	R	NR	NR	NR	NR	NR	224,103
LA 35-2	NR	R	R	R	R	R	R	R	R	> 500,000
FL 1	NR	R	NR	R	NR	NR	NR	NR	NR	1,381,600
FL 2	NR	R	NR	NR	NR	NR	NR	NR	NR	8,700
FL 3	NR	R	NR	R	NR	NR	NR	NR	NR	204,100
FL 4	R (WB-I)	R	R	R	R	R	R	R	R	1,024,000
FL 5	NR	R	NR	NR	NR	NR	NR	NR	NR	9,900
FL 6	R (WB-neg)	R	R	R	R	NR	R	NR	NR	47,700
FL 7	R (WB-neg)	R	R	R	NR	NR	NR	NR	NR	138,126
FL 8	NR	R	NR	R	NR	NR	NR	NR	QNS	241,547
FL 9	R (WB-I)	R	R	QNS	NR	NR	NR	QNS	QNS	6,334,400
FL 10	NR	R	NR	R	NR	NR	NR	NR	R	111,127
FL 11	NR	R	NR	R	NR	NR	NR	NR	QNS	341,312
FL 12	NR	R	NR	R	NR	NR	NR	NR	QNS	43,200
FL 13	R	R	R	R	NR	NR	NR	NR	QNS	3,397,000

EIA = enzyme immunoassay; NAAT = nucleic acid amplification test; NR = nonreactive; R = reactive; QNS = quantity not sufficient; WB-I = Western blot indeterminate; WB-neg = Western blot negative.

Table 2. Sensitivity for acute HIV infection of different HIV assays.

HIV screening assay	Test type	Clinical laboratory	Number of specimens that tested positive	Total number of specimens tested	Sensitivity for Acute HIV Infection (%)	95% Confidence Interval
Architect HIV-1 Ag/Ab Combo®	4th generation	N/A*	28	32	87.5	(72.6 – 95.9)
Genetic Systems HIV 1/2 + O ®	3rd generation	Highly complex	19	33	54.8	(42.4 – 66.9)
Multispot HIV-1/ HIV-2 Rapid Test	rapid	Moderately complex	11	33	33.3	(18.9 – 50.4)
Clearview Complete HIV 1/2 Assay	rapid	waived	8	27	29.6	(14.8 – 48.6)
Unigold Recombigen HIV	rapid	waived	8	33	24.2	(11.9 – 40.9)
Clearview HIV 1/2 Stat-Pak Assay	rapid	waived	7	31	22.6	(10.5 – 39.6)
Oraquick Advance Rapid HIV-1/2 Antibody Test	rapid	waived	7	32	21.9	(10.1 – 38.6)

*This assay is not FDA-approved.

Conclusions

- Many FDA-approved rapid HIV tests failed to detect half of the early HIV infection cases in whom antibody was present and at least two-thirds of the cases detectable by NAAT.
- Rapid test sensitivities for early HIV infection ranged from 22 to 33% compared with 55 to 57% for the third-generation assay and 88% for the fourth-generation assay.
- Programs that screen high-incidence populations with rapid tests should consider supplemental testing with NAAT.
- These data support the need for more sensitive antigen-based point-of-care screening tests for early HIV infection.

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