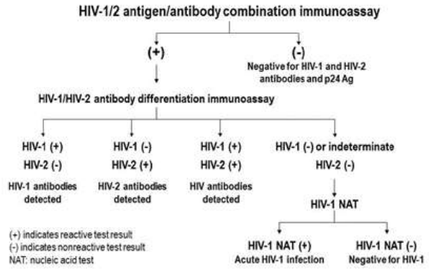
569 EVALUATION OF THE CDC/APHL HIV DIAGNOSTIC ALGORITHM WITH RECENTLY FDA-APPROVED ASSAYS

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BACKGROUND

- In 2014, CDC updated the recommendations for laboratory testing for the diagnosis of HIV infection



- **Since 2014, two new HIV assays were approved by FDA:**
  - **BioPlex 2200 HIV Ag-Ab screening assay**
    - detects and differentiates p24 antigen (Ag) and HIV-1 and HIV-2 antibodies (Ab)
    - Final interpretation R or NR and p24, HIV-1 Ab and HIV-2 Ab results
  - **Geenius™ HIV-1/2 supplemental assay**
    - differentiates HIV-1 from HIV-2 Ab
    - Eight final interpretations based on combinations of results of two analytes

OBJECTIVE

To evaluate the performance of these two newer assays in HIV-1 seroconverters (SC) and HIV-2 infections with the current HIV diagnostic algorithm

HIV SAMPLES AND METHODS

- 501 sequential plasma specimens were available from 49 U.S. HIV-1 seroconverters (SC), with 67 collected before first detectable nucleic acid test (NAT) and 134 collected during antiretroviral therapy (ART)
- 100 HIV-2 Ab-positive plasma were collected in the U.S. (n=16) and Ivory Coast (n=84)
- Samples were tested blinded with BioPlex Ag-Ab at Bio-Rad Laboratories and with Geenius at the CDC laboratory
- NAT was done in singlet with APTIMA HIV-1 RNA qualitative assay for 497 SC samples and with the Roche COBAS AmpliPrep/TaqMan HIV-1 v2.0 test for four

RESULTS

Table 1. Bioplex Ag-Ab Performance on Samples Collected Sequentially from 49 HIV-1 Seroconverters

HIV-1 RNA result	BioPlex Ag-Ab Reactive	BioPlex Ag-Ab Nonreactive	Total
Positive	407*	27**	434*
Negative	0	67	67
Total	407	94	501

* includes 134 samples collected during ART
**includes four in a secondary negative diagnostic window

- **BioPlex Ag-Ab sensitivity: 93.8%**
- **BioPlex Ag-Ab specificity: 100%**

Table 2. Example of Bioplex Ag-Ab Secondary Diagnostic Window

Sample ID	Collect date	BioPlex Ag-Ab test results: Final Interpretation	Ag	HIV-1 Ab	HIV-2 Ab	APTIMA HIV-1 RNA
9032-07	7/28/1998	NR	NR	NR	NR	REACTIVE
9032-08	7/30/1998	R	R	NR	NR	REACTIVE
9032-09	8/4/1998	NR	NR	NR	NR	REACTIVE
9032-10	8/11/1998	R	NR	R	NR	REACTIVE
9032-11	8/13/1998	R	NR	R	NR	REACTIVE

- **BioPlex Ag-Ab had a secondary negative diagnostic window in three seroconverters**

Table 3. HIV Diagnostic Algorithm using Bioplex Ag-Ab and Geenius Assays on HIV-1 Seroconverters

BioPlex Ag-Ab test: Final Interpretation	Ag	HIV-1 Ab	HIV-2 Ab	Total	Geenius HIV-1/2 supplemental test: HIV-1 positive	HIV-1 indeterminate	HIV-negative		HIV-1 RNA result: reactive	nonreactive
NR	NR	NR	NR	27*						
R	R	NR	NR	41	0	0	41	⇨⇨	41	0
R	R	R	NR	46	22	9	15		22	2
R	NRDTHAL	R	NR	30	30	0	0		n/a	n/a
R	NR	R	NR	290	263	22	5		25**	2
Total				434	315	31	61	92	88	4
(%)				(100)	(77.4)	(7.6)	(15)	(100)	(95.7)	(4.3)

R: reactive; NR: nonreactive: NRDTHAL: not reportable due to high antibody titers; n/a: not applicable
* 27 HIV-1 NAT positive (includes four from secondary negative phase and two Roche viral load instead of APTIMA)
** Two were only tested with Roche VL

- **Algorithm sensitivity in early HIV-1 infections: 92.9%**

Table 4. HIV Diagnostic Algorithm using Bioplex Ag-Ab and Geenius Assays on HIV-2 Ab-positive samples

BioPlex Ag-Ab test: Final Interpretation	Ag	HIV-1 Ab	HIV-2 Ab	Total	Geenius HIV-1/2 supplemental test: HIV-2 positive	HIV-2 positive w/XR HIV-1	HIV-2 indeterminate	HIV untypable	HIV indeterminate	HIV negative
R	NR	NR	R	16 (US)	8	5	2			1
R	NR	NR	R	79 (IVC)	26	42		9	1*	1
R	NR	R	R	5 (IVC)	1	4				
Total				100	35	51	2	9	1	2
(%)				(100)	(35)	(51)	(2)	(9)	(1)	(2)

US: United States; IVC: Ivory Coast; *sample was not repeated as indicated in package insert

- **Geenius supplemental assay was HIV-2 positive in 86% of HIV-2 Ab-positive samples**

RESULTS

1. In SC, Bioplex was non-reactive in 94 samples
   - 67 of which were collected before the first NAT reactive (HIV-negative samples)
   - 27 were NAT-only positive including samples from a secondary diagnostic window (3 seroconverters)
2. BioPlex Ag-Ab combo test in early HIV-1 infections
   - Sensitivity: 93.8% (95% CI: 91.1- 95.7%)
   - Specificity: 100% (95% CI: 94.6- 100%)
3. Geenius identified 78% (315/407) of early HIV-1 infections as HIV-1 positive and 86% (86/100) of HIV-2 Ab-positive samples as HIV-2 positive including five BioPlex Ag-Ab undifferentiated
4. Limitations of the study are long-term storage of samples at -80C and HIV-2 RNA was not performed in all samples to calculate the algorithm sensitivity in HIV-2 infections
5. All BioPlex Ag-only reactives were Geenius HIV-negative, but were HIV-1 RNA-positive
6. Overall, the HIV diagnostic algorithm detected 92.9% (403/434) of samples during early stages of HIV-1 seroconversion
7. HIV-1 RNA was nonreactive in 4.3% (4/92) samples including one with viral suppression due to ART (BioPlex Ag-Ab-reactive/Geenius HIV-1 indeterminate)
8. In 134 samples collected during ART, the algorithm detected 133 (99.3%)

CONCLUSION

- **The BioPlex Ag-Ab assay performed well and detected Ag in early HIV-1 infections**
- **Ag-only reactive samples could be confirmed directly with NAT**
- **BioPlex Ag-Ab differentiated HIV-1 from HIV-2 antibodies in most cases, but in combination with more Geenius results, the possible number of final interpretations increased**
- **These results provide important data for potential updates to the CDC/APHL recommendations for HIV diagnostics**

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