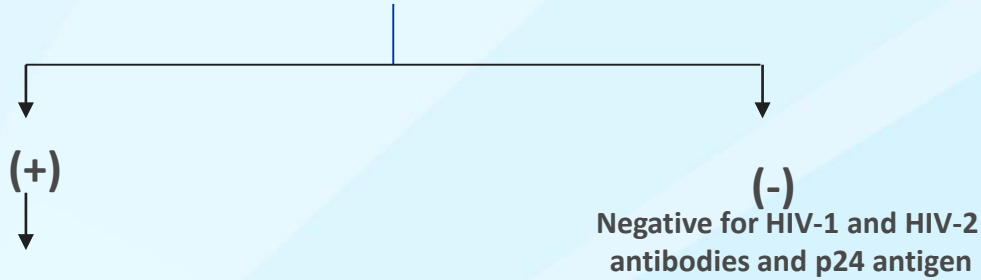# Feedback Session: New Technology and its Impact on the CDC/APHL Laboratory Testing Algorithm
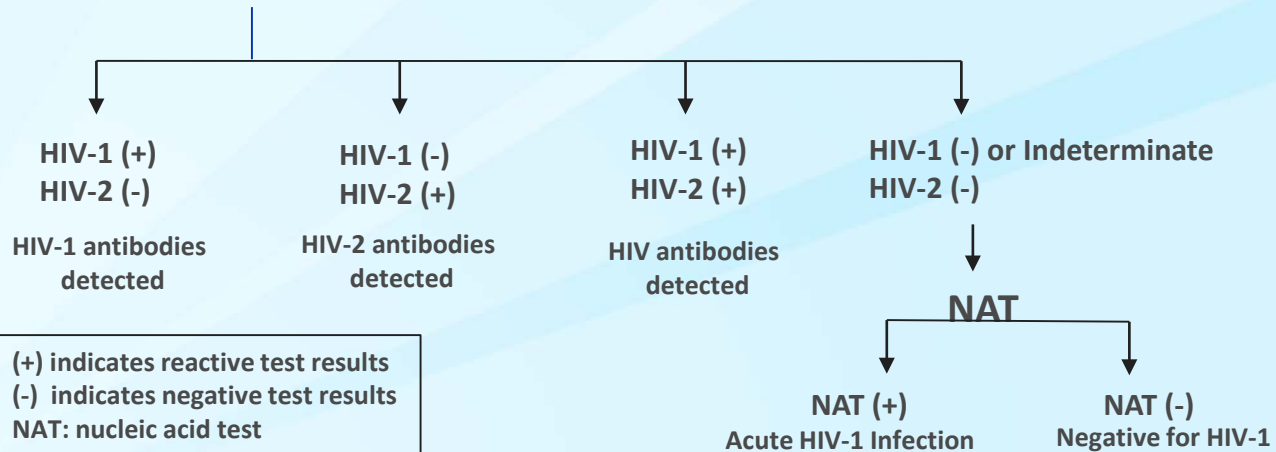
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Michele Owen, Ph.D.

March 24, 2016

HIV-1/2 Ag/Ab combination immunoassay

(+)

(-)
Negative for HIV-1 and HIV-2
antibodies and p24 antigen

HIV-1/HIV-2 antibody differentiation immunoassay

HIV-1 (+)
HIV-2 (-)

HIV-1 antibodies
detected

HIV-1 (-)
HIV-2 (+)

HIV-2 antibodies
detected

HIV-1 (+)
HIV-2 (+)

HIV antibodies
detected

HIV-1 (-) or Indeterminate
HIV-2 (-)

NAT

NAT (+)
Acute HIV-1 Infection

NAT (-)
Negative for HIV-1

(+) indicates reactive test results
(-) indicates negative test results
NAT: nucleic acid test

http://www.cdc.gov/hiv/testing/lab/guidelines/

Geenius HIV 1/2 Supplemental Test

- Rapid test with automated reader; differentiates HIV-1 from HIV-2.
  - Additional results
    - HIV-2 indeterminate
    - HIV indeterminate
    - HIV-2 positive, HIV-1 cross reactivity
  - Established HIV-1, 100% concordance Multispot; 1.6% HIV positive untypable (Bennett, Dx conference)
  - No false-positive algorithm results Ag/Ab and Geenius (Delaney, Dx conference)

Geenius HIV 1/2 Supplemental Test

- HIV-2 indeterminates?
  - Delaney: 3 HIV-2 indeterminates
    - 2 from 165 false positive Ag/Ab or IgM Ab (gp140 only)
    - **1 acute HIV-1** (gp140 only)
  - Bennett: 2 HIV-2 indeterminates
    - 2 from 60 false positive Ag/Ab (gp140 only)
  - Luo: 8 HIV-2 indeterminates
    - 2 HIV-2s (gp36 only)
    - **3 acute HIV-1** (gp140 only)
    - 3 false pos Ag/Ab (gp140 only)

Geenius HIV 1/2 Supplemental Test

- Data needs
  - Cost data for Geenius compared to Multispot
  - HIV indeterminates
  - Performance on whole blood
  - If Geenius HIV-2 IND or HIV IND, conduct HIV-1 NAT. If HIV-1 NAT negative, test with HIV-2 test.

Determine HIV-1/2 Ag/Ab Combo Use in Laboratory

- Rapid test, distinguishes Ag from Ab, interpreted subjectively (i.e., no reader)
  - 100% sensitivity established infection serum/plasma/whole blood
  - Specificity
    - 100% low risk subjects
    - 98.9% (serum) to 99.7% (whole blood), high risk subjects

SP = Sample Pad; CP = Conjugate Pad; LTA = Lower Test Area; UTA = Upper Test Area;   CA = Control Area

Determine HIV-1/2 Ag/Ab Combo Use in Laboratory

- Early infection
  - Plasma
    - Ag not detected, most acutes (Laperche, Rosenberg, Kilembe, Duong, Conway, Faraoni)
    - Ag detected at about 3 million copies/mL (Pandori, Dx conference)
    - Detects infection earlier than IgM-sensitive assays, not as early as lab-based Ag/Ab assays (Masciotra, JCV)
    - Detected 40-54% early infections (Delaney, Masciotra, Dx conf)
  - Whole blood
    - 0% Ag sensitivity, acutes (Lewis, AIDS)
    - Detects infection 2 days after plasma (Masciotra, CROI)

Determine HIV-1/2 Ag/Ab Combo Use in Laboratory
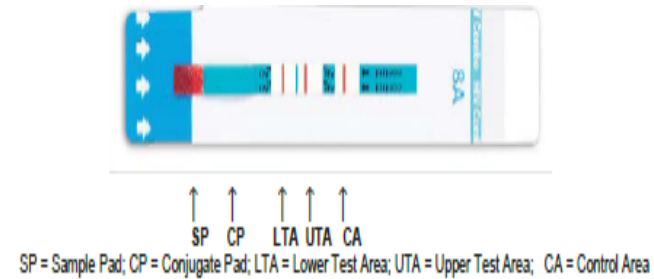
- Sensitivity
  - Early/established infection
    - Whole blood: 84.6% (Stekler, JCV)
    - Serum: 88.9% (Gillis, Dx conference)
  - Established infection
    - Plasma: 99.6%-100% (Delaney, Masciotra, Dx conference)
- Specificity
   - Plasma: 98.9-100% (Delaney, Masciotra); No false positive algorithm results
    - Serum: 98.9% (Wester, NHPC)
   - Whole blood: 98.3%-99.9% (6 sources)

SP = Sample Pad; CP = Conjugate Pad; LTA = Lower Test Area; UTA = Upper Test Area; CA = Control Area

Determine HIV-1/2 Ag/Ab Combo Use in Laboratory

– Data needs

- Sensitivity using whole blood
- Performance data using Determine with plasma as the initial test in the algorithm
  – Specificity of Ag to determine whether to go directly to NAT

SP = Sample Pad; CP = Conjugate Pad; LTA = Lower Test Area; UTA = Upper Test Area; CA = Control Area
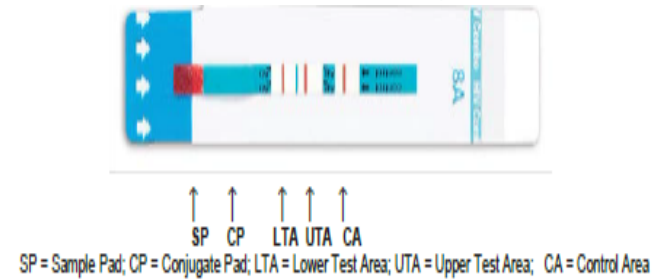
BioPlex 2200 HIV Ag-Ab assay

- Lab-based screening assay for detection and differentiation of HIV-1 Ag, HIV-1 Ab, and HIV-2 Ab in serum or plasma.

  - Early infection detection similar to lab Ag/Ab tests (Masciotra, Delaney)

  - 100% sensitivity, established HIV-1 (Salmona, JCM and Delaney)

  - 100% sensitivity, HIV-2 (package insert)

  - 99.5% specificity (Salmona)

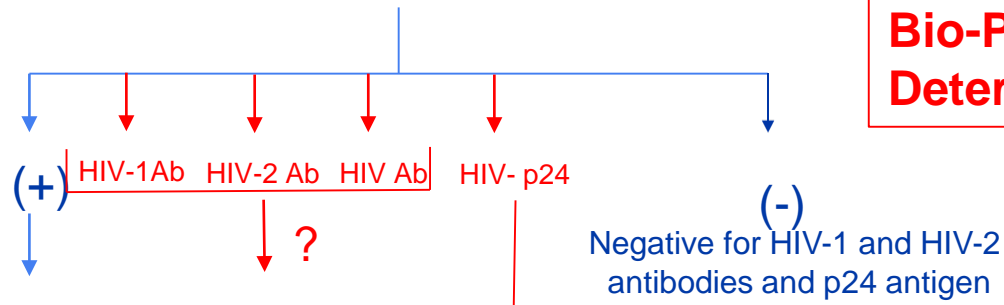 - No false positive algorithm results (Delaney)
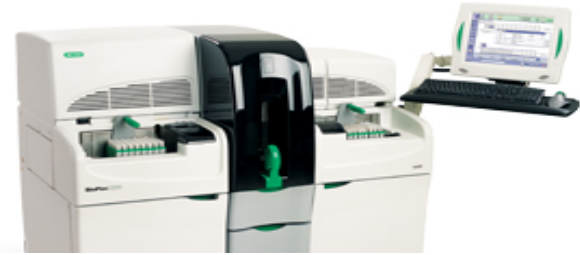
BioPlex 2200 HIV Ag-Ab assay

- Data needs
  - Specificity of Ag reactivity
  - Data on performance of Bioplex with Geenius and NAT
  - If HIV-2 Ab reactive, reflex to an antibody differentiation supplemental test, and if that is HIV-2 negative, an HIV-1 NAT. If HIV-1 NAT negative, conduct another HIV-2 assay.
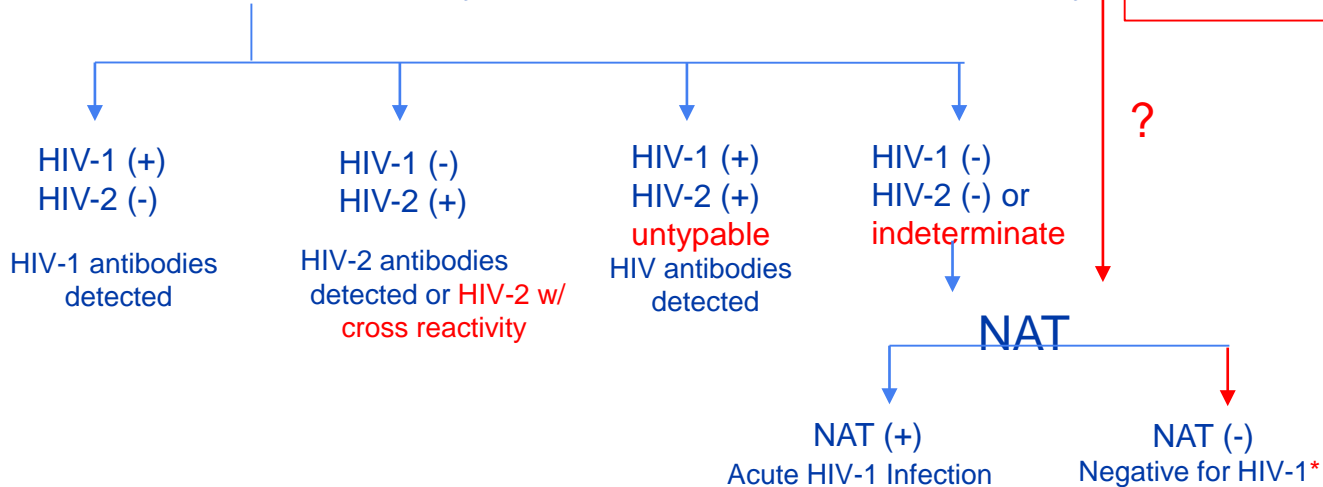
HIV-1/2 antigen/antibody combination immunoassay

Bio-Plex Determine

(+) HIV-1Ab HIV-2 Ab HIV Ab HIV- p24 (-)

?

Negative for HIV-1 and HIV-2 antibodies and p24 antigen

HIV-1/HIV-2 antibody differentiation immunoassay **Geenius**

?

HIV-1 (+)
HIV-2 (-)

HIV-1 antibodies detected

HIV-1 (-)
HIV-2 (+)

HIV-2 antibodies detected or HIV-2 w/ cross reactivity

HIV-1 (+)
HIV-2 (+)
untypable
HIV antibodies detected

HIV-1 (-)
HIV-2 (-) or indeterminate

NAT

NAT (+)
Acute HIV-1 Infection

NAT (-)
Negative for HIV-1*

*Test for HIV-2 if Geenius HIV or HIV-2 IND and HIV-1 NAT NEG OR Bioplex HIV-2 + and Geenius HIV-2 NEG and HIV-1 NAT NEG

Feedback on Geenius

- Is your lab planning to implement Geenius
  - If not, why and what will you use as an alternative?
- Need for alternatives to Geenius in lab algorithm
- Your thoughts on potential modifications to the algorithm due to Geenius

Feedback on Determine Use in Laboratory

- Is there a need to insert Determine in the lab algorithm?

- If Determine was recommended as an alternative first test in the algorithm, would your lab use it?
  - If not, why?

- Your thoughts on potential modifications to the algorithm using Determine

SP = Sample Pad; CP = Conjugate Pad; LTA = Lower Test Area; UTA = Upper Test Area; CA = Control Area

Feedback on Bioplex

- Is your lab using Bioplex?
- Your thoughts on potential modifications to the algorithm based on Bioplex

Feedback Next Conference

- Thoughts on a combined conference on HIV/STD/viral hepatitis and TB testing

- If we can only add STD, viral hepatitis or TB to the next HIV testing conference, which makes the most sense

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348   www.cdc.gov