Feedback Session: New Technology and its Impact on the CDC/APHL Laboratory Testing Algorithm

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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
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)
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
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

- (+) 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

- 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 (+)
  - HIV antibodies detected
  - HIV-1 Ab
  - HIV-2 Ab
  - HIV Ab
  - HIV- p24
  - HIV-1Ab  HIV-2 Ab  HIV Ab  HIV- p24
  - (-) Negative for HIV-1 and HIV-2 antibodies and p24 antigen
- HIV-1 (-)  HIV-2 (-) or indeterminate
- HIV-1 (-)  HIV-2 (-) or indeterminate

Bio-Plex
Determine

Geenius

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
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
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.