Overcoming the Challenges and Barriers to Implementing the HIV Diagnostic Testing Algorithm in your Laboratory

2016 HIV Diagnostics Conference
HIV Progression and Immune Response

- Acute syndrome, Virus dissemination
- Clinical Latency
- Opportunistic Infections

- CD4 count
- Virus Load

- Virus RNA (copies/ml)

- Weeks
- Years
- Death
Progression of HIV Viral Markers

- **P24 antigen**
- **HIV RNA**
- **Antibodies**

**Viral and antibody levels**

**Time after infection (days)**

- **Acute**
- **Seroconversion** → **Established**

**IgM**

**IgG**

**Symptoms**
HIV Progression and Detectable Response

Days since infection

HIV Antibody

Infection

1st and 2nd G

3rd G

4th G

Slide courtesy of Bernie Branson
1989: CDC recommended two-test algorithm for HIV diagnosis

T1: HIV-1 EIA

Non-reactive

Report as HIV Neg.

Reactive

T2: Western blot (WB) or immunofluorescence assay (IFA)

Negative

Report as HIV Neg.

Indeterminate

Report as Indeterminate

Positive

Report as HIV-1 Pos.
A HIV-1/HIV-2 Ag/Ab Immunoassay *

A+  
  Repeat A in duplicate †  
  A(- -)  
    Negative for HIV-1 and HIV-2 Ab and HIV-1 p24 ag **
  A1(+- or +-)  

B HIV-1/HIV-2 Ab Differentiation Immunoassay

B  
  HIV-1 (+)  
  HIV-2 (-)  
  Positive for HIV-1 Ab ‡

B  
  HIV-1 (-)  
  HIV-2 (+)  
  Positive for HIV-2 Ab ‡

B  
  HIV-1 (+)  
  HIV-2 (+)  
  Positive for HIV Ab §§

B  
  HIV-1 (-)/HIV-2 (-) or inconclusive

C Individual HIV-1 NAT

C+  
  Positive for HIV-1 RNA ¶¶

C-  
  Negative for HIV-1 RNA #

* A could be an IgM sensitive antibody immunoassay if the Ag/Ab combination immunoassay is not available.
† Repeating A+ is assay dependent.
‡ Refer to care and follow up testing.
§§ HIV positive; further testing required to rule out dual infection
¶¶ Acute HIV-1 infection.
# Consider HIV-2 DNA testing if clinically indicated.
** If early acute infection is suspected, NAT can be performed
4th Generation Ag/Ab Test

- ARCHITECT HIV Ag/Ab Combo (Abbott) Detects HIV-1 p24 Ag, HIV-1 and HIV-2 antibodies
- GS HIV Ag/Ab Combo EIA (Bio-Rad) Detects HIV-1 p24 Ag, HIV-1 and HIV-2 antibodies
- BioPlex 2200 HIV Ag-Ab (BioRad) detects and differentiates HIV-1 Ag, HIV-1 Ab and HIV-2 Ab

- Reactive result:
  - Preliminary positive
  - Supplemental testing required according to current algorithm
Why did we need new HIV testing strategies/algorithms?

• Laboratory algorithm established by CDC and APHL (ASTPHLD) in the late 1980’s
  – Over 20 years later remains largely unchanged
• More is known about the disease
  – HIV-1 and HIV-2
  – Window Period
• Evolving technology
  – Tests recently approved by FDA are not included
  – Availability of rapid tests
  – Increased sensitivity of screening assays
  • Western blot and IFA now less sensitive than some screening assays which they are intended to “confirm”
Continued: Why do we need new HIV testing strategies/algorithms?

- Evolving technology
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  - Increased sensitivity of screening assays
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Relative Sensitivity of Tests

FIGURE 2. Reactivity of FDA-approved assays for HIV-1 compared with Western blot.

From: Branson, JAIDS, 2010, 55 (S2): S102-S105
What were we looking for from these new testing strategies?

• Resolution of indeterminates
• Ability to confirm HIV-2 infections
• Increased detection of acute infection
• Use of assays as screening or confirmatory/supplemental tests and as part of multi-test algorithms
Multispot HIV Ab Test

- Supplemental test
  - used after a reactive 4th Gen EIA
- Replaces WB
  - More sensitive and specific than WB
  - Faster and less expensive than WB
- Will differentiate HIV-1 and HIV-2

BioRad has discontinued this test as of July 2016
BioRad Geenius replaces MultiSpot

- HIV-1/HIV-2 supplemental assay
- Designed to align with the algorithm
Nucleic Acid Amplification Test for HIV-1 RNA

- Supplemental test
  - Used after a reactive EIA and a non-reactive Multispot

- Highly sensitive test which can detect the presence of viral RNA

- HIV-1 RNA/NAAT testing can detect acute HIV-1 infection
<table>
<thead>
<tr>
<th>Year of APHL Survey</th>
<th>Labs Reporting Performing WB</th>
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</thead>
<tbody>
<tr>
<td>2009</td>
<td>78.6% (48/61)</td>
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<tr>
<td>2012</td>
<td>66.2% (43/65)</td>
</tr>
<tr>
<td>2015</td>
<td>13.5% (10/74)</td>
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</table>
## Anti-HIV-1 Western Blot Results by Manufacturer

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Reactive/Positive</th>
<th>Indeterminate</th>
<th>Non-Reactive/Negative</th>
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<tbody>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
<td>No.</td>
</tr>
<tr>
<td>Bio-Rad GS</td>
<td>1</td>
<td>2.3</td>
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<tr>
<td>MP Diagnostics</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Bio-Rad GS</td>
<td>85</td>
<td>98.8</td>
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<td>Calypte/Cambridge Biotech</td>
<td>6</td>
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Questions?

1. What are barriers to adopting the algorithm?
2. If your lab has adopted the new algorithm, what challenges did you face?
3. What reasons can you provide to help labs abandon the western blot?
4. How has your lab overcome obstacles to the new algorithm?
Questions?

5. What recommendations would you make to labs that have not yet adopted the algorithm?

6. From data with MultiSpot, this algorithm is thought to produce fewer indeterminate results, will this hold true with Geenius? In general, does the introduction of Geenius incentivize the adoption of the algorithm or is an additional barrier?
Questions?

7. Does new instrumentation (BioPlex2200) that is able to differentiate with the screening test change your perspective of the algorithm when you consider turnaround time, cost, approved tests, and the need for verification of results?