Performance of the Abbott Architect HIV Ag/Ab Combo assay in the US Army HIV Diagnostic Algorithm

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HIV Diagnostics Conference
Mar 22, 2016
Atlanta, GA
Material has been reviewed by the Walter Reed Army Institute of Research. There is no objection to its presentation and/or publication.

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HIV Diagnosis in US Military

- DODI 6485.01: Human Immunodeficiency Virus (HIV) in Military Service Members
- AR 600-110: Identification, Surveillance, and Administration of Personnel Infected with Human Immunodeficiency Virus, 2014
Rationale

- Protect the blood supply during urgent donation setting from the “walking blood bank”
- Prevent potentially fatal complications from administration of military required live vaccines
- Monitor HIV infected personnel for continuing physical qualification for duty
HIV Diagnostics and Reference Laboratory

- Technical oversight and final authority for HIV diagnosis
  - Army Active Duty, Army Reserve, Army National Guard
  - 1 M HIV serological screening tests annually – contract screening laboratory (enzyme immunoassay only)
  - HIV serological tests for European and Central Commands, Medical Entrance Processing Commands, 51 Medical Treatment Facilities

- Conduct all HIV confirmatory testing and infection status determination for Army personnel

- Provide HIV infection status resolution testing and diagnostic consultation for US Navy/Marines and US Air Force by request
Current HIV Test Requirements

- Medical Entrance Processing Command: Accession into US military service – must screen **Non Reactive**
- Active Duty Surveillance – every 2 years
- USAR/USNG Surveillance – every 2 years
- Overseas assignment – deployment/TDU > 30 days
  - Pre-deployment test within 120 days of deployment
  - Post-deployment test within 30 days return from Area of Operation
HIV Testing Requirements Cont’d

- Suspicious Illness
  - ARS
- STD infection
  - Follow-up at 3, 6, 12 months (if the initial test is NR)
- Sexual partners of HIV-infected individuals
- Injecting Drug Use (IDU)
- Voluntary Screening – per initiated Soldier request
US Army Surveillance HIV Algorithm

HIV Ag/Ab Combo Screening
- Repeat HIV Ag/Ab Combo in Duplicate
  - Non-Reactive
    - Report "HIV Negative"
  - 2 of 3 Tests Reactive
    - HIV 1 Positive
      - HIV 1 Western Blot
        - Positive
          - Report "Positive HIV 1 Ab"
        - Negative or Indeterminate
          - Qualitative RNA PCR (APTIMA)
            - Reactive
              - Report "Acute HIV-1 Infection"
            - Non-Reactive
              - Whole blood specimen Confirmation; Special Cases
      - Request additional specimen

HIV-2 DNA Real Time PCR
- Quantitative HIV-2 RT PCR

Bio-Rad Multispot Rapid Test HIV 1/2
- HIV-2 Positive
  - Request additional specimen

Incident Infection Full or Partial Length Sequencing

All incident infections verified by second independent specimen;
Discordant results resolved by 3rd independent specimen.

WB IND/NEG, Aptima Reactive cases Reflex to HIV-1 viral load, Health care Provider contacted for test request

Proviral HIV-1 DNA Real Time PCR
- Request Test Request from submitting entity/health care provider
The highest percentage of cases coded Physical Examination, followed by Force Test.

<table>
<thead>
<tr>
<th>Test Indication (SOT Code)</th>
<th># Pos</th>
<th>Pos per 100,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical Exam</td>
<td>206</td>
<td>28.2</td>
</tr>
<tr>
<td>Force Testing</td>
<td>4</td>
<td>0.5</td>
</tr>
<tr>
<td>Clinically Indicated</td>
<td>5</td>
<td>0.7</td>
</tr>
<tr>
<td>STI Clinic</td>
<td>1</td>
<td>0.1</td>
</tr>
<tr>
<td>Pre-Deployment</td>
<td>1</td>
<td>0.1</td>
</tr>
<tr>
<td>Requested by Individual</td>
<td>2</td>
<td>0.3</td>
</tr>
<tr>
<td>Post-Deployment</td>
<td>1</td>
<td>0.1</td>
</tr>
<tr>
<td>Redraw (EIA Pos)</td>
<td>1</td>
<td>0.1</td>
</tr>
<tr>
<td>Other</td>
<td>1</td>
<td>0.1</td>
</tr>
<tr>
<td>Not classified</td>
<td>22</td>
<td>3.0</td>
</tr>
<tr>
<td><strong>Total Positive</strong></td>
<td><strong>244</strong></td>
<td><strong>33.5</strong></td>
</tr>
</tbody>
</table>
4<sup>th</sup> Gen Assay Performance

**N = 987,947**

**Algorithm**

- Western Blot: 1,598
- Aptima RNA: 1,107

**Confirmation**

- Revised Algorithm:
  - Bio-Rad Ag/Ab: 1,598
  - Western Blot: 540
  - Aptima RNA: 47

**Pos Neg**

- 1598: Pos 491, Neg 1107
- 16: Pos 16, Neg 1091

(AHI) 68.3%

False Pos
Of 1,058 RR specimens (Architect) and NR by Bio-Rad

- No WB Positive specimens identified
- No Aptima Reactive specimens
- No False Negative specimens
Of 540 specimens RR by both Architect and RR by Bio-Rad
- 491 (90.9%) are confirmed WB Pos

Of 49 WB Neg/IND
- 14 are Aptima R (Acute HIV Infection)
- 33 of 540 (6.1%) are False Positives
1058 specimens RR by both Architect and NR by Bio-Rad

- No MS Positive specimens
- No Aptima Reactive specimens
- No False Negative Specimens
540 RR specimens by both Architect and Bio-Rad Combo
- 466 (86.3%) were MS positive
- 491 (90.9%) were WB Positive

74 Neg or IND MS specimens
- 41 were Aptima R (Acute HIV Infection)
- 33/540 (6.1%) were False Positive
HIV Detection by 4th Gen Ag/Ab Combo

<table>
<thead>
<tr>
<th>Screening Assay</th>
<th>Abbott Ag/Ab Combo</th>
<th>Abbott + BioRad Combo</th>
</tr>
</thead>
<tbody>
<tr>
<td># Screened</td>
<td>987,947</td>
<td>987,947</td>
</tr>
<tr>
<td>EIA RR</td>
<td>1,598</td>
<td>540</td>
</tr>
<tr>
<td>% Initial Pos</td>
<td>0.162%</td>
<td>0.055%</td>
</tr>
<tr>
<td>WB or RNA Confirmed</td>
<td>507</td>
<td>507</td>
</tr>
<tr>
<td>% Pos</td>
<td>0.051%</td>
<td>0.051%</td>
</tr>
</tbody>
</table>

Addition of Bio-Rad Combo as a secondary repeat reactive screen would reduce the number of specimens reflexed to supplemental confirmatory testing
### Sensitivity, Specificity, Positive Predictive Value

<table>
<thead>
<tr>
<th>Resolved HIV Status</th>
<th>+</th>
<th>-</th>
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</thead>
<tbody>
<tr>
<td><strong>Abbott</strong></td>
<td>507</td>
<td>1,091</td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>986,349</td>
</tr>
<tr>
<td></td>
<td>507</td>
<td>987,440</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Resolved HIV Status</th>
<th>+</th>
<th>-</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Abbott + BioRad</strong></td>
<td>507</td>
<td>33</td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>987,407</td>
</tr>
<tr>
<td></td>
<td>507</td>
<td>987,440</td>
</tr>
</tbody>
</table>

**95% CI**

- **Sensitivity** 100% 99.3 - 100% 100% 99.3 - 100%
- **Specificity** 99.9% 99.9 - 99.9% 100% 100%
- **Pos Likelihood Ratio** 905 853 - 960 29,938 21,284 - 421,120
- **Neg Likelihood Ratio** 0 0 0 0
- **Prevalence** 0.05% 0.05 - 0.06% 0.05% 0.05 - 0.06%
- **PPV** 31.8% 29.5 - 34.1% 93.9% 91.5 - 95.8%
- **NPV** 100% 100% 100% 100%
Conclusions

- Transition to Architect Ag/Ab: slight increase in number (3) HIV cases detected
- Increased the number of specimens which required further testing: 67.2% False Positive
- Secondary screen by Bio-Rad Ag/Ab significantly reduced number supplemental confirmatory tests: WB (67.2%); Aptima (95.8%)
- BioRad Ag/Ab repeat reactive secondary screen increased PPV from 31.8% to 93.9%
Acknowledgements

WRAIR - Maryland
- Jennifer Malia
- Brook Danboise
- Annette Mott
- Yvonne Beale
- Linda Jagodzinski

MHRP HJF – Maryland
- Mark Manak
- Jason Ouellette
- Ashley Shutt

Funding Acknowledgement: This work was funded by U.S. Army Medical Command (MEDCOM) of the U.S. Department of Defense (DOD).