HIV Diagnostics and Acute HIV

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2017
Objectives

• Changes in HIV testing algorithms
  – Review the 2006 CDC Testing Recommendations
  – 4th generation HIV tests
  – Changes in confirmatory testing- Geenius

• Acute HIV Infection
  – Test of choice
  – Understanding of the window period
2006 CDC HIV Testing Recommendation

- Routine, voluntary HIV screening for all persons 13-64 in health care setting, **NOT BASED ON RISK**

- Repeat screening with persons of known risk annually

- **OPT out** screening with opportunity to ask questions and option to decline

- No separate consent
HIV Testing Immunology Basics

• Antigen - viral particles or proteins that elicit an immune response.
  – HIV Ag - p24
  – HIV RNA (viral load)
  – Present at the time of infection

• Antibody - immune response that recognizes foreign material
  – IgM
  – IgG
  – Generated by the host-
  – delayed several weeks after infection
<table>
<thead>
<tr>
<th>Generation</th>
<th>Antibody</th>
<th>Antigen</th>
</tr>
</thead>
<tbody>
<tr>
<td>First</td>
<td>IgG</td>
<td></td>
</tr>
<tr>
<td>Second</td>
<td>IgG</td>
<td></td>
</tr>
<tr>
<td>Third</td>
<td>IgM + IgG</td>
<td></td>
</tr>
<tr>
<td>Fourth</td>
<td>IgM+ IgG</td>
<td>p24</td>
</tr>
</tbody>
</table>
2nd Generation

OraQuick Advance

Chembio DPP HIV ½ Assay

Multispot HIV-1/HIV-2

Clearview Complete

MedMira Reveal G3

INSTI

Clearview Stat Pak

Modified from B. Branson CDC
3rd Generation “Sandwich” Immunoassay

Antigen: Recombinant proteins or synthetic peptides

Plasma/serum

HIV antibody

IgG

IgM

enzyme

HIV antigen

Enzyme-detection

Color reagent

Detects HIV IgM or IgG

Courtesy B. Branson CDC
4th Generation: Combined Ag/Ab HIV Assay

Abbott Architect Ag/Ab Combo
2010

Bio-Rad Ag/Ab Combo
2011

Control
Antigen
Antibody

Determine Combo Ag/Ab Rapid Test
2013
4th Generation Combo Immunoassay

Plasma/serum

HIV antibodies

p24 antigen

HIV antigen

p24 antibody

Enzyme-detection

Detects IgM or IgG antibody or p24 antigen

Color reagent

Courtesy B. Branson CDC
<table>
<thead>
<tr>
<th>Detection Range of HIV Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ACUTE SYMPTOMS</strong></td>
</tr>
<tr>
<td><strong>HIV-1 RNA NAAT (2006)</strong></td>
</tr>
<tr>
<td><strong>HIV EIA 4(^{th}) Generation (Ag/Ab)</strong></td>
</tr>
<tr>
<td><strong>HIV EIA 3(^{rd}) Generation</strong></td>
</tr>
<tr>
<td><strong>HIV EIA 1(^{st}) (1985) &amp; 2(^{nd}) Generation</strong></td>
</tr>
<tr>
<td><strong>Western Blot</strong></td>
</tr>
<tr>
<td><strong>Weeks After Infection</strong></td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>3</td>
</tr>
<tr>
<td>4</td>
</tr>
<tr>
<td>5</td>
</tr>
<tr>
<td>6</td>
</tr>
<tr>
<td>7</td>
</tr>
</tbody>
</table>
Confirmatory Testing: Geenius
CDC/APHL Proposed New HIV Testing Algorithm

HIV-1/2 Combination Ag/Ab immunoassay

(+)

(-)

Geenius HIV-1/HIV-2 antibody assay

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

HIV-1 antibodies detected HIV-2 antibodies detected HIV antibodies detected

NAT

NAT (+) NAT (-)

Acute HIV-1 infection Negative for HIV-1
HIV Infection and Laboratory Markers

Primary HIV Infection: Signs & Symptoms

• 40-90% of patients will be symptomatic
• A mononucleosis-like illness of non-specific signs and symptoms
• Signs and symptoms typically begin 1-4 weeks post-exposure
• No specific constellation of signs or symptoms can differentiate acute HIV from other illnesses
• High index of suspicion is critical

# Acute Retroviral Syndrome

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>All Patients n=55*</th>
<th>Acute HIV n=25</th>
<th>Early HIV n=30</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Systemic- no. (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fever</td>
<td>37 (67)</td>
<td>23 (92)</td>
<td>14 (47)</td>
<td>0.000</td>
</tr>
<tr>
<td>Chills</td>
<td>21 (38)</td>
<td>16 (64)</td>
<td>5 (17)</td>
<td>0.000</td>
</tr>
<tr>
<td>Fatigue</td>
<td>26 (47)</td>
<td>17 (68)</td>
<td>9 (30)</td>
<td>0.005</td>
</tr>
<tr>
<td>Rash</td>
<td>19 (35)</td>
<td>10 (40)</td>
<td>9 (30)</td>
<td>0.437</td>
</tr>
<tr>
<td>Lymphadenopathy</td>
<td>25 (45)</td>
<td>13 (52)</td>
<td>12 (40)</td>
<td>0.373</td>
</tr>
<tr>
<td><strong>Respiratory- no. (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sore throat</td>
<td>22 (40)</td>
<td>13 (52)</td>
<td>9 (30)</td>
<td>0.097</td>
</tr>
<tr>
<td>Cough</td>
<td>12 (22)</td>
<td>9 (36)</td>
<td>3 (10)</td>
<td>0.026</td>
</tr>
<tr>
<td><strong>Gastrointestinal- no. (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vomiting</td>
<td>13 (24)</td>
<td>10 (40)</td>
<td>3 (10)</td>
<td>0.012</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>13 (24)</td>
<td>10 (40)</td>
<td>3 (10)</td>
<td>0.012</td>
</tr>
<tr>
<td><strong>CNS- no. (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>17 (31)</td>
<td>12 (48)</td>
<td>5 (17)</td>
<td>0.019</td>
</tr>
<tr>
<td>Dizziness</td>
<td>6 (11)</td>
<td>5 (20)</td>
<td>1 (3)</td>
<td>0.082</td>
</tr>
</tbody>
</table>

*Missing data n = 3
Primary HIV Infection

Rash
Trunk and face > limbs
Small pink macules

Mucosal Lesions
Oral ulcers, thrush
(Kahn, NEJM, 1998)
Oral Ulcers in Acute HIV Infection

Acute Infection: Increased Risk of Sexual Transmission of HIV

Cohen & Pilcher, J Infect Dis. 2005
Ma, J Virol 2009
Routine Testing Insufficient for Diagnosing Acute HIV
Acute HIV Summary

- If you suspect acute HIV, the correct test to order is a viral load or 4\textsuperscript{th} Gen Ag/Ab
- The opportunity for diagnosis is brief
  - Symptoms which prompt healthcare visits
  - Self limited
  - Often unrecognized or attributed to other illnesses
- Acute HIV is highly infectious due to exceedingly high viral loads
- Notify the Health department for rapid partner notification
HIV Diagnostics Summary

• The new testing algorithm no longer recommends western blot or Multi-spot as the confirmatory HIV test.

• The Geenius test, which is a point of care, rapid test is now recommended for confirmation of HIV and replaced Multi-spot for the confirmatory test. Where available, 4th Generation combination Ag/Ab tests are recommend as the first line test.

• **ALL DISCORDANT RESULTS SHOULD REFLEXIVELY RESULT IN HIV VIRAL LOAD TESTING TO RULE OUT ACUTE HIV**
Acknowledgements:
Bernie Branson CDC
James Galbraith
Suzanne McCluskey

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