The Latest in HIV Tests: What Do the Results Mean?

Bernard M. Branson MD
Principal Consultant, Scientific Affairs LLC
Atlanta, Georgia
Objectives

At the end of this workshop, participants will be able to:

1. Compare the relative merits of available point-of-care and lab-based HIV tests for different circumstances
2. Describe how recent HIV tests affect the current HIV testing recommendations.
3. Identify the effect that early HIV treatment and PrEP can have on HIV test results
4. State the benefits of Ag/Ab screening for Acute HIV infection
Background and Disclosure of Financial Relationships

• Dr. Branson previously served as Associate Director for Laboratory Diagnostics in CDC’s Division of HIV/AIDS Prevention until October 2014.

• Dr Branson serves as consultant to the Gilead Sciences FOCUS Program and received compensation from Siemens Healthcare for development of a presentation on HIV diagnostics at an educational symposium.
Use of Brand Names

• This presentation will describe general principles of HIV tests, and also refer to individual HIV tests by brand name for the purposes of identification and clarity.

• No endorsement of any specific test is intended.
Outline

- The basics: how tests operate
- Available HIV tests: rapid, lab, & supplemental
- Interpreting results
- How differences between tests relate to accuracy
- Clinical presentation of Acute HIV
- Effect of therapy and PrEP on HIV antibody test results
What is your role with HIV testing?

1. I order HIV lab tests and give results to patients.
2. I perform rapid HIV tests and interpret the results.
3. Patients are referred to me after they have tested HIV-positive.
4. I manage an HIV testing program.
5. I receive HIV test results reported to surveillance.
Which HIV test do you use most?

1. OraQuick oral fluid
2. OraQuick fingerstick blood
3. Clearview Complete/Chembio Sure Check
4. INSTI
5. Determine Combo
6. Uni-Gold Recombigen
7. DPP or Stat-Pak
8. Laboratory-based immunoassay
Evolution of HIV Tests

- 1\textsuperscript{st} generation: whole viral lysate, detects IgG antibody
- 2\textsuperscript{nd} generation: synthetic peptides, detects IgG antibody
- 3\textsuperscript{rd} generation: detect IgM and IgG antibody
- 4\textsuperscript{th} generation: detects IgM, IgG antibodies, p24 antigen
**1st and 2nd Generation EIA**

**Antigen**
1st - Viral lysate
2nd – Recombinant proteins or synthetic peptides

**Plasma/serum**

**IgG HIV antibody**

**Enzyme-detection**

**Color change with HIV IgG**

**Color reagent**
3\textsuperscript{rd} Generation EIA

Antigen: Recombinant proteins or synthetic peptides

Plasma/serum

HIV antibody

IgG

IgM

enzyme

HIV antigen

Enzyme-detection

Color change with HIV IgM or IgG

Color reagent
Rapid HIV Tests

- Designed for results while-you-wait
- CLIA-waived:
  - Use only direct, unprocessed specimens (whole blood, oral fluid)
  - Minimum technical skills required
  - Insignificant likelihood of erroneous test results
  - Fail-safe mechanism to verify test is working (control)
CLIA-waived rapid HIV-antibody tests, 2017

Oraquick Advance

DPP HIV 1/2

Chembio Sure Check

INSTI HIV 1/2

Chembio Stat Pak

Uni-Gold Recombigen
Rapid HIV Tests: Lateral Flow Devices

(immunochromatographic)

Add Sample

Conjugate

1st Test line

Control line

IgG anti-HIV

IgG Antibodies

Colloidal gold conjugated to protein A

HIV antigen

Anti-IgG antibodies
Flow-through devices
(immunoconcentration)

Microparticles immobilized in membrane
form test spots

Control antibody:
-Anti-IgG
-Anti-gold

HIV-1 peptide
(HIV-2 peptide)
INSTI

Reveal G3

Multispot

CLIA: Moderate Complexity
Flow-through devices

Specimen:
- IgG anti-HIV
- IgG antibodies

Control zone
Anti-IgG Antibodies

Test zone
HIV Antigens

Excess antibodies pass through test membrane
Detection agent

Excess detection agent passes through test membrane

Control zone
Anti-IgG Antibodies

Test zone
HIV Antigens

Rinse

Flow-through devices

immunoconcentration
Dual Path Platform

Conjugate

Specimen
DPP HIV

Geenius Supplemental
HIV-1: viral antigens and RNA

- gp120
- gp 41
- p24
- RNA
Which HIV antibodies do rapid tests detect?

1. p24 antibody
2. gp41 antibody
3. gp120 antibody
4. gp41 and gp120 antibody
5. All three: p24, gp41, and gp120
How large a blood specimen?

- Oraquick Advance: 5 µL
- DPP HIV 1/2: 10 µL
- Chembio Sure Check: 3 µL
- INSTI HIV 1/2: 50 µL
- Chembio Stat Pak: 5 µL
- Uni-Gold Recombigen: 50 µL
How long does it take?

- **Oraquick Advance**: 20-40 min
- **DPP HIV 1/2**: 5 + 10-15 (40) min
- **Chembio Sure Check**: 15-20 min
- **INSTI HIV 1/2**: 1 min
- **Chembio Stat Pak**: 15-20 min
- **Uni-Gold Recombigen**: 10-12 min
Determine Combo Ag/Ab rapid test

- CLIA-waived 2014
- Whole blood (50µL)

“4th Generation”

“Ag/Ab Combo”
Rapid HIV tests can be performed only by:

1. A doctor or nurse.
2. A clinical laboratory.
3. An HIV counselor who has received training.
4. Any of the above.
Rapid HIV Test Restrictions

- Sale is restricted to clinical laboratories that:
  - Have an adequate quality assurance program, and
  - Where there is insurance that operators will receive and use instructional materials.

- Test is approved for use only by an agent of a clinical laboratory.

- Test subjects must receive the “Subject Information Notice” prior to specimen collection.
What is Most Frequently Observed CLIA Deficiency?

1. No quality control performed
2. Use of incorrect specimen volume
3. No manufacturer’s instructions available
4. Use of expired test kits
CLIA requirements: Discussion

- Current instructions (package insert) on file
- Quality assurance program
  - Storage and operating temperatures
  - Test result logs
  - Evaluations and proficiency
What’s new in the lab?
HIV-1/2 antigen/antibody immunoassay

(+)

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

(-)

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

HIV-1/HIV-2 antibody differentiation immunoassay

(+)

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

(-)

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

HIV-1 NAT

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

HIV-1 NAT (+)
Acute HIV-1 infection

HIV-1 NAT (-)
Negative for HIV-1

NAT: nucleic acid test

(+): indicates reactive test result
(-): indicates non-reactive test result

(+): indicates reactive test result
(-): indicates non-reactive test result

NAT: nucleic acid test
Abbott Architect Ag/Ab Combo 2010

Bio-Rad Ag/Ab Combo EIA 2011

Siemens Advia Centaur® CHIV 2015
Chemiluminescence Immunoassays

Magnetic Micro-Particles
Coated with Antigens and antibody

- gp41/120 Ag
- gp36 Ag
- HIV1 "O" Ag
- Anti-p24 Monoclonal

Patient Sample

IgM/IgG

LITE Reagent
Antigens and antibodies labeled with AE

- gp41/120 Ag
- gp36 Ag
- HIV1 "O" Ag
- 2 Anti-p24 Monoclonals

WASH

Trigger Solution

Relative light units
On-board Refrigeration of Multiple Different Assays

Random Access Multiplatform analyzers for HIV testing
Random Access Multiplatform analyzers for HIV testing

STAT sample requests without pausing
Results in <60 minutes
Bio-Rad Bioplex HIV Ag/Ab Combo Assay

- Beads conjugated to HIV-1 Group M and O antigens, HIV-2 antigens, and p24 antibody.

- Distinguishes between
  - p24 antigen
  - HIV-1 antibodies
  - HIV-2 antibodies

“Fifth Generation”
Lab Test Challenges: Specimen Handling

- Separate red cells from serum/plasma
- Limited storage/shipment at room temperature:
  - Abbott Architect – 3 days
  - Bioplex – 4 days
  - Bio-Rad HIV Combo Ag/Ab EIA – 2 days
  - Siemens Advia Centaur – 24 hours
26 seroconverters were analyzed with 14 tests
17 seroconverters with Positive WB used for cumulative frequency analysis
Sequence of Test Positivity Relative to WB (plasma)
166 specimens, 17 Seroconverters - 50% Positive Cumulative Frequency

Bangkok Tenofovir Study:
Delayed HIV detection by oral fluid in patients on PrEP

Participants receiving tenofovir (who became HIV-infected) took longer to develop a reactive OraQuick (191.8 days) than participants receiving placebo (16.8 days)


Luo et al, J Clin Virol 2013
Determine can detect infection earlier than IgM/IgG sensitive (antibody-only) immunoassays when used with plasma.

For laboratories in which instrumented antigen/antibody testing is not feasible, Determine can be used with serum/plasma as the first step in the laboratory algorithm. It may not detect infection as early as the instrumented tests.

Laboratories using Determine are advised to acknowledge the limitations of the testing procedure when reporting results.
Determine Combo Ag/Ab with Plasma

- 415 HIV-positive specimens from STOP study of methods to detect acute HIV Infections
  - Architect detected 396 (95%)
  - Determine Combo detected 337 (81.2%)
    - 55 (50%) of 110 Architect reactive, Multispot negative
    - 11 (78.6%) of 14 Architect reactive, Multispot indeterminate
    - 271 (99.6%) of 272 Architect reactive, Multispot positive

- 20 seroconversion panels
  - Determine Combo Ag/Ab detects HIV sooner than rapid antibody tests

Determine Combo Ag/Ab with Whole Blood

- In 4 studies involving >25,000 tests, Determine Combo detected only 1 of 37 acute infections.

- CDC study: seroconversion panels, simulated whole blood:
  - Reactivity significantly higher in plasma (91%) than blood (56%)
  - 8/20 seroconverters showed a median delay of 6 days between Determine Combo reactivity with plasma and reactivity with whole blood

20 Seroconverters: Simulated Whole Blood vs Plasma

- In eight, median delay of 6 days
- No delay
Sequence of Test Positivity Relative to WB (plasma)

166 specimens, 17 Seroconverters - 50 % Positive Cumulative Frequency

Delaney et al, Clin Inf Dis 2017
HIV RNA (plasma)

HIV Ab

HIV p24 Ag

Eclipse Period

Acute Infection

Recent Infection

Longstanding Infection

Days

HIV Infection

Viral Detection

IgM Antibody Detection

IgG Antibody Detection

Positive Western Blot

Seroconversion window
Modeling the Eclipse Period

10,000 Monte Carlo simulations

Delaney et al, Clin Inf Dis 2017
Estimated Window Periods of Available HIV Tests

<table>
<thead>
<tr>
<th>Category (No. of Tests)</th>
<th>Median Days (Interquartile Range)</th>
<th>99th Percentile (Days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibody/antigen laboratory (4)</td>
<td>17.8 (13.0, 23.6)</td>
<td>44.3</td>
</tr>
<tr>
<td>IgG/IgM-sensitive laboratory (3)</td>
<td>23.1 (18.4, 28.8)</td>
<td>49.5</td>
</tr>
<tr>
<td>IgG-sensitive rapid screening (6)</td>
<td>31.1 (26.2, 37.0)</td>
<td>56.7</td>
</tr>
<tr>
<td>IgG-sensitive supplemental (2)</td>
<td>33.4 (28.5, 39.2)</td>
<td>58.2</td>
</tr>
<tr>
<td>Western blot (viral lysate) (1)</td>
<td>36.5 (31.0, 43.2)</td>
<td>64.8</td>
</tr>
</tbody>
</table>

*Delaney et al CID, 2017*
Retesting

- Post exposure, after a negative test, retesting is recommended after at least
  - 45 days with an Ag/Ab test on serum/plasma
  - 90 days using with all other HIV tests

- Offer HIV screening at least annually to all sexually active MSM

- https://www.cdc.gov/hiv/basics/testing.html
- MMWR August 2017
**HIV-1/2 antigen/antibody immunoassay**

(-)  (+)

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

(-)  (+)

HIV-1 antibodies detected

HIV-2 antibodies detected

HIV antibodies detected

**(-) indicates non-reactive test result**

**(+) indicates reactive test result**

NAT: nucleic acid test

**HIV-1 NAT (+)**

Acute HIV-1 infection

**HIV-1 NAT (-)**

Negative for HIV-1

**HIV-1 NAT**

**HIV-1/NAT (+)**

**HIV-1/NAT (-)**

**HIV-1 (-) or indeterminate**

**HIV-2 (-) or indeterminate**

**Negative for HIV-1 and HIV-2 antibodies and p24 Ag**
HIV-1/HIV-2 Differentiation Assays

FDA approved, March 2013

Serum Control
HIV-1 Recombinant gp41

Product Withdrawal
July 29, 2016

HIV-2 Peptide gp36
HIV-1 Peptide gp41
Multispot HIV-1/HIV-2

FDA approved, Oct. 2014

Geenius HIV-1/HIV-2
The Geenius™ HIV-1/2 Lines

HIV-1 & HIV-2 Associated Lines

Control Band

gp36

gp140

gp160

gp41 (group M & O)

p24

p31*

* Inside the nucleocapsid
Add 5 µL serum/plasma
Or
15 µL whole blood
Add 5 drops buffer to Well 2
Insert test cassette in reader for automated interpretation
**Run**

<table>
<thead>
<tr>
<th>Sample ID</th>
<th>74305B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cassette ID</td>
<td>138001210013</td>
</tr>
<tr>
<td>Kit Lot</td>
<td>380012</td>
</tr>
<tr>
<td>Test</td>
<td>Genius HIV-1/2 (1.0-US)</td>
</tr>
</tbody>
</table>

**Band Detection**

- **Automated**

<table>
<thead>
<tr>
<th>Band</th>
<th>Reader detected</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>gp160</td>
</tr>
<tr>
<td>5</td>
<td>p24</td>
</tr>
<tr>
<td>6</td>
<td>gp41</td>
</tr>
<tr>
<td>7</td>
<td>CTR</td>
</tr>
</tbody>
</table>

**Control**

- **Positive Control**
  - Start: 14/08/06 15:20:10
- **Negative Control**
  - Start: 14/08/06 15:20:23

**Preview**

- Barcode: 138001210013
- Sample ID: 74305B

**Interpretation**

- **Conclusion**: HIV-1 POSITIVE

- **Status**: Validated

**Operator**: BioRad_mkt
**Reader**: Connected
**Calibration**: OK
**QC**: Green
**Database size**: OK
# Geenius Results: Interpretations

<table>
<thead>
<tr>
<th>HIV-1 RESULT</th>
<th>HIV-2 RESULT</th>
<th>ASSAY INTERPRETATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative</td>
<td>Negative</td>
<td>HIV NEGATIVE</td>
</tr>
<tr>
<td>Indeterminate</td>
<td>Negative</td>
<td>HIV-1 INDETERMINATE</td>
</tr>
<tr>
<td>Negative</td>
<td>Indeterminate</td>
<td>HIV-2 INDETERMINATE</td>
</tr>
<tr>
<td>Indeterminate</td>
<td>Indeterminate</td>
<td>HIV INDETERMINATE</td>
</tr>
<tr>
<td>Positive</td>
<td>Negative</td>
<td>HIV-1 POSITIVE</td>
</tr>
<tr>
<td>Positive</td>
<td>Indeterminate</td>
<td>HIV-1 POSITIVE</td>
</tr>
<tr>
<td>Negative</td>
<td>Positive</td>
<td>HIV-2 POSITIVE</td>
</tr>
<tr>
<td>Indeterminate</td>
<td>Positive</td>
<td>HIV-2 POSITIVE</td>
</tr>
<tr>
<td>Positive</td>
<td>Positive</td>
<td>HIV-2 POSITIVE with HIV-1 cross-reactivity: Antibody to HIV-2 confirmed in the sample. HIV-1 positivity (with only one HIV-1 envelope band, gp160 or gp41), is due to cross-reactivity and precludes confirmation of HIV-1*. *Note: Differentiation features managed by proprietary algorithm.</td>
</tr>
<tr>
<td>Positive</td>
<td>Positive</td>
<td>HIV POSITIVE Unotypable (undifferentiated): Antibodies to HIV-1 and HIV-2 confirmed in the sample. This may occur in an HIV-2 positive sample with significant cross-reactivity to HIV-1, or may be due to co-infection with both HIV-1 and HIV-2 (rare)*. *Note: Differentiation features managed by proprietary algorithm.</td>
</tr>
</tbody>
</table>

* HIV-1 band(s) detected but did not meet the criteria for HIV-1 Positive
* HIV-2 band(s) detected but did not meet the criteria for HIV-2 Positive
* HIV band(s) detected but did not meet the criteria for HIV-1 Positive or HIV-2 Positive
Geenius results not generated previously

CDC Technical Update August 2016

1. HIV-2 with HIV-1 cross-reactivity
   - Consider HIV-2 Positive
2. HIV-2 Indeterminate
3. HIV Indeterminate
   - Repeat; negative on repeat, report as negative
   - Repeatedly reactive:
     - Conduct HIV-1 NAT
     - Refer for validated HIV-2 antibody or NAT, or
     - Repeat testing in 2-4 weeks
HIV-1/2 antigen/antibody immunoassay

(-)  (+)

(-)  (-)  (+)

HIV-1 antibodies detected  HIV-2 antibodies detected

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

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

HIV-1 RNA viral load

HIV-1 NAT (+)  HIV-1 NAT (-)

Acute HIV-1 infection  Negative for HIV-1

(+), (-) indicates reactive test result, non-reactive test result
NAT: nucleic acid test
HIV Nucleic Acid Test (NAT) for Diagnosis: Qualitative RNA vs Viral Load

- APTIMA HIV-1 qualitative RNA assay is the only NAT FDA-approved for diagnosis

- Under FDA and CLIA regulations, clinicians can order HIV-1 RNA viral load tests, but labs cannot use them as a reflex part of the algorithm
Acute HIV Infection
### HIV Ag/Ab Screening, 8 Emergency Departments

<table>
<thead>
<tr>
<th>City</th>
<th>Chicago</th>
<th>Houston (2)</th>
<th>Los Angeles</th>
<th>Oakland</th>
<th>New Orleans</th>
</tr>
</thead>
<tbody>
<tr>
<td>Annual census</td>
<td>48,000</td>
<td>170,000</td>
<td>170,000</td>
<td>85,000</td>
<td>85,000</td>
</tr>
<tr>
<td>Months screening</td>
<td>39</td>
<td>15,15</td>
<td>31</td>
<td>21</td>
<td>35</td>
</tr>
<tr>
<td>Tests performed</td>
<td>13,170</td>
<td>65,288</td>
<td>55,422</td>
<td>18,876</td>
<td>47,544</td>
</tr>
<tr>
<td>(338/mo)</td>
<td>(4,353/mo)</td>
<td>(1,788/mo)</td>
<td>(899/mo)</td>
<td>(1,358/mo)</td>
<td></td>
</tr>
<tr>
<td>Reactive tests</td>
<td>245 (1.9%)</td>
<td>1,253 (1.09%)</td>
<td>1,019 (1.8%)</td>
<td>119 (0.6%)</td>
<td>405 (0.9%)</td>
</tr>
<tr>
<td>New HIV Dx</td>
<td>96 (39%)</td>
<td>199 (16%)</td>
<td>234 (23%)</td>
<td>58 (49%)</td>
<td>205 (51%)</td>
</tr>
<tr>
<td>Acute HIV</td>
<td>13 (14%)</td>
<td>26 (13%)</td>
<td>24 (10%)</td>
<td>10 (8%)</td>
<td>33 (16%)</td>
</tr>
</tbody>
</table>

(One hospital from Chicago, one from Philadelphia not in table)
## Signs and Symptoms: 122 Patients with Acute HIV

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Patients (Percentage)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>91 (75%)</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>82 (67%)</td>
</tr>
<tr>
<td>Malaise</td>
<td>69 (57%)</td>
</tr>
<tr>
<td>Chills</td>
<td>60 (49%)</td>
</tr>
<tr>
<td>Myalgia</td>
<td>52 (43%)</td>
</tr>
<tr>
<td>No symptoms/signs</td>
<td>8 (7%)</td>
</tr>
<tr>
<td>Headache</td>
<td>47 (39%)</td>
</tr>
<tr>
<td>Pharyngitis</td>
<td>39 (32%)</td>
</tr>
<tr>
<td>Skin rash</td>
<td>16 (13%)</td>
</tr>
<tr>
<td>Sweats</td>
<td>16 (13%)</td>
</tr>
<tr>
<td>Lymphadenopathy</td>
<td>13 (11%)</td>
</tr>
<tr>
<td>Fever &amp; ≥3 others</td>
<td>74 (61%)</td>
</tr>
</tbody>
</table>
Reason for Visit: New HIV Diagnoses in the ED

<table>
<thead>
<tr>
<th>Reason for visit</th>
<th>Acute HIV N = 98</th>
<th>Established HIV N = 507</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viral syndrome</td>
<td>41 (42%)</td>
<td>33 (6%)</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>22 (22%)</td>
<td>90 (18%)</td>
</tr>
<tr>
<td>Fever</td>
<td>12 (14%)</td>
<td>17 (3%)</td>
</tr>
<tr>
<td>Rash</td>
<td>7 (7%)</td>
<td>29 (6%)</td>
</tr>
<tr>
<td>Trauma</td>
<td>1 (1%)</td>
<td>31 (6%)</td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td>1 (1%)</td>
<td>28 (6%)</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>1 (1%)</td>
<td>61 (12%)</td>
</tr>
<tr>
<td>Requested test</td>
<td>0 (0%)</td>
<td>18 (4%)</td>
</tr>
</tbody>
</table>
### New HIV Diagnoses in the ED

<table>
<thead>
<tr>
<th></th>
<th>Acute HIV N = 98</th>
<th>Established HIV N = 507</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viral Load (median)</td>
<td>1,176,913</td>
<td>50,464</td>
</tr>
<tr>
<td>CD4 count (median)</td>
<td>349</td>
<td>213</td>
</tr>
</tbody>
</table>

Linked within:
- 30 days: 54 (55.1) 172 (33.9)
- 90 days: 70 (71.4) 280 (55.2)
- 180 days: 73 (74.5) 294 (58.0)

Viral suppression within:
- 30 days: 3 (3.1) 6 (1.2)
- 90 days: 26 (26.5) 81 (16.0)
- 180 days: 47 (48.0) 162 (32.0)
Identifying Acute HIV Infection

- Screen with Ag/Ab combination assay

- Patients often symptomatic
- High viral load
- Early treatment beneficial
- Opportunity to interrupt transmission

- Empiric and same-day therapy
Cohort of 88 MSM with AHI in Bangkok, Thailand, who initiated ART immediately.

After ART, 48/88 (54.6%) attained HIV RNA <50 copies/ml by week 8, increasing to (89.7%), and (97%) at weeks 24 and 48, respectively.
High Feasibility of Empiric HIV Treatment for Patients With Suspected Acute HIV in an Emergency Department

Kathleen R. Jacobson, MD, Sanjay Arora, MD, Kristin B. Walsh, MD, Meredith Lora, MD, Stephen Merjavy, MD, Shanna Livermore, MPH, and Michael Menchine, MD, MPH

(J Acquir Immune Defic Syndr 2016;72:242–245)

The Effect of Same-Day Observed Initiation of Antiretroviral Therapy on HIV Viral Load and Treatment Outcomes in a US Public Health Setting

Christopher D. Pilcher, MD,* Clarissa Ospina-Norvell, FN-P,* Aditi Dasgupta, BS,† Diane Jones, RN,* Wendy Hartogensis, PhD,* Sandra Torres, MSW,* Fabiola Calderon, MSW,* Erin Demicco, MPH,* Elvin Geng, MD,* Monica Gandhi, MD,* Diane V. Havlir, MD,* and Hiroyu Hatano, MD*

(J Acquir Immune Defic Syndr 2017;74:44–51)
Keating et al. CID, 2016
Initiation of ART During Acute HIV Infection Leads to a High Rate of Nonreactive HIV Serology

De Souza et al. CID, 2016
gp41, p24 antibodies

gp41 antibodies
Follow-up Testing: Persons on PrEP

- Every 3 months:
  - HIV Ag/Ab Combo test
  - STI testing

- Test positivity after infection while on PrEP (resistance or poor adherence) might be delayed or indeterminate

- HIV-1 RNA not always detectable
Quick Case Study

- 25 year old MSM in an HIV-discordant relationship, on PrEP since 12/2015. Perfect adherence by history. Also had 2 other sex partners.

- 4th generation testing repeatedly negative until May 2016:
  - Positive 4\textsuperscript{th} gen, negative Multispot, HIV RNA<20, signal detected

- Repeat 2 and 4 weeks later: same results.
What would you do next?

1. Tell the patient he is not infected
2. Repeat tests in 6 weeks
3. Order a Western blot
4. Order a genotype

2003 study: false-negative Oraquick and waning or absent gp41 titers in patients on early, effective therapy

Bangkok tenofovir study...

Genotype: Multiple drug resistance mutations (including TDF/FTC), virus not related to that of his virally suppressed partner.

- O’Connell et al, J Clin Micro 2003
50 y/o MSM on PrEP for 8 months
Ag/Ab assay reactive; Western blot indeterminate (gp 160 only)
RNA undetectable; DNA undetectable
Viral load became elevated 3 weeks after stopping PrEP
On the Horizon...
“Point-of-Care” Nucleic Acid Tests

- **Xpert HIV-1 viral load**
  - 1 ml plasma
  - Results in 90 minutes
  - LOD 32 copies/mL
  - CE-marked December 2014

*Not available in U.S.*
“Point-of-Care” Nucleic Acid Tests

- 25 µL whole blood specimen
- HIV-1 or HIV-2 viral load in 60 minutes
- CE-marked March 2015

Not available in U.S.
“Point-of-Care” Nucleic Acid Tests

- “Lab in a Tube”
- Influenza A/B – FDA cleared
- Strep A – FDA cleared
  - Results in 15 minutes
  - CLIA-waived May 2015
- HIV under development
Summary

- HIV tests differ in subtle ways that affect different circumstances
- RNA & viral load will play an increasingly important role in HIV diagnosis
- Early treatment and PrEP can lead to non-reactive serology and undetectable RNA
- Only labs can perform HIV tests
  - If you conduct HIV tests, you are a lab
  - Meet requirements to maintain CLIA certificate of waiver