HIV/Hepatitis Testing Update: Death of the Western Blot

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Disclaimer: The findings and conclusions in this presentation are those of the author and do not necessarily represent the views of the Centers for Disease Control and Prevention

Disclosure: No relevant financial relationships
Learning Objectives

- Describe updated diagnostic recommendations for HIV and HCV infection
- Apply updated guidelines to common clinical situations
Overview

- Routine Hepatitis C Testing
- Routine HIV Testing
- Home HIV Testing
- Acute HIV Infection
- Novel HIV Tests - A look into the future
HCV Testing Case 1:

- A 61-year-old man with past medical history of diabetes type 2 and hypercholesterolemia presents to your office.
- At a health fair he was screened for Hepatitis C and had a reactive rapid HCV test result.
- He denies any history of injection drug use, blood transfusion, and he had a negative HIV test 5 years ago.
- He has no signs or symptoms of liver disease on exam and his laboratories are normal.
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Projected Increase in Burden of Hepatitis C-Related Morbidity and Mortality in the United States

Of 2.7 M HCV-infected persons in primary care
- 1.47 M will develop cirrhosis
- 350,000 will develop liver cancer
- 897,000 will die from HCV-related complications

(Rein D et al. Dig Liver Dis 2010)
Limited Effectiveness of Risk-based HCV Testing Strategies

• CDC recommendations include testing persons who
  – inject recreational drugs
  – had blood transfusion before 1992 and other blood exposures
  – have HIV infection

BUT

• Many clinicians are not aware of HCV testing guidelines
• Clinicians may be reluctant to ask about risks
• Patients may be reluctant to disclose or not recall risks
• 45-85% are unaware of their HCV infection

Heavy Burden of HCV Morbidity and Mortality Among Persons Born 1945-1965

- HCV prevalence 5.3 times > other age-groups (3.29% vs 0.55%) \(^1,2\)
- Represents 81% of all U.S. adults with chronic HCV infection \(^3\)
- Represents 73% of all HCV-associated mortality \(^4\)

New CDC Recommendation (2012)

Recommendations for the Identification of Chronic Hepatitis C Virus Infection Among Persons Born During 1945–1965
Previous CDC algorithm for testing for HCV infection

*RIBA= Strip Immunoblot Assay 3.0 (Chiron/Novartis)

MMWR 2003;52( No. RR-3)
Changes in availability of HCVAb testing technologies

**OraQuick HCV Assay**
- **Non reactive**
- **Reactive**

**RIBA**
- Representative RIBA reaction patterns

**CLIA-waiver***
- granted by FDA, May 2011

*facilitates widespread testing, e.g., in:
- Physician offices
- Hospital emergency departments
- Health department clinics
- Other freestanding counseling and testing sites

**Discontinued by Novartis, March 2013**
Current CDC algorithm for HCV testing defaulted
Current algorithm for HCV testing

HCV ANTIBODY

NON-REACTIVE

STOP

REACTIVE

HCV RNA

DETECTED

CURRENT HCV INFECTION

LINK TO CARE

NOT DETECTED

NO CURRENT HCV INFECTION

Additional testing as appropriate

Current algorithm for HCV testing

(MMWR 2013; 62: 362-365)
HIV SCREENING RECOMMENDATIONS
Which of these people should get an HIV test?
Which of these people should get an HIV test?

All of them

HIV testing can save your life.

Take control. Ask your provider for the test.
Repeat HIV Screening

1. Treatment for an sexually transmitted infection (STI)
   • Test at every STI-related visit regardless of other risk

2. Patients at high risk for HIV
   • Assess for pre-exposure prophylaxis (PrEP); if not indicated then at least annual
   • Offer

3. Initiating new sexual relationship
   • Test regardless of other risk

4. Clinical judgment
   • Test at or before treatment initiation

5. Tuberculosis treatment

Branson BM et al. MMWR Recomm Rep. 2006 Sep 22;55(RR-14):1-17
Pre-exposure Prophylaxis (PrEP) for Prevention of HIV Infection

INDICATIONS FOR PrEP USE BY MSM
• Male sex partners in past 6 months
• Not in a monogamous partnership with HIV-negative man (recent test)

AND at least one of the following:
• Any anal sex without condoms in past 6 months
• Any STI diagnosed or reported in past 6 months
• Ongoing sexual relationship with HIV-positive partner

HIV Testing Case 1

A 32-year-old previously healthy man presents to your office interested in Truvada.

He states that nothing is bothering him but he does mention that his throat has been a little sore for 24 hours. On further review he reports receiving an influenza vaccination one week ago and having unprotected anal sex with a new male partner approximately three weeks ago.

On exam he has a temperature of 39.3°C, a non-exudative pharyngitis, and a mild morbilliform rash on his back. An HIV test is sent with his initial lab panel.
Case Study

- A preliminary lab report returns later that day and indicates that an Architect HIV Ag/Ab Combo assay was repeatedly reactive.

- HIV-1 Western blot test result is pending.

- Two days later, the Western blot result is reported as negative (no bands).
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### Terminology

<table>
<thead>
<tr>
<th>Immunoassay Generation</th>
<th>Detects</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>1&lt;sup&gt;st&lt;/sup&gt;</td>
<td>Antibody (IgG)</td>
<td>Western Blot</td>
</tr>
<tr>
<td>2&lt;sup&gt;nd&lt;/sup&gt;</td>
<td>Antibody (IgG)</td>
<td>Avioq Rapid tests</td>
</tr>
<tr>
<td>3&lt;sup&gt;rd&lt;/sup&gt;</td>
<td>Antibody (IgG and IgM)</td>
<td>Vitros, Advia, BioRad</td>
</tr>
<tr>
<td>4&lt;sup&gt;th&lt;/sup&gt;</td>
<td>Antibody (IgG and IgM) and p24 Antigen</td>
<td>Architect BioRad Combo</td>
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</tbody>
</table>
What is Acute HIV infection (AHI)?

- Absence of HIV antibodies
- Rapid rise with plasma viremia
- Acute viral syndrome: fever, rash, diarrhea, fatigue, headache
- Detect AHI by NAT or p24 antigen

Sequence of Test Positivity Relative to WB (plasma)

166 specimens, 17 Seroconverters - 50% Positive Cumulative Frequency


Luo et al, J Clin Virol 2013
Testing for the Diagnosis of HIV Infection

- 1989 Diagnostic Algorithm (HIV type 1)

Antibody-based Immunoassay → Western Blot (WB) or Immunofluorescent Assay (IFA)

Screening → “Confirmation”
Laboratory Testing for the Diagnosis of HIV Infection
Updated Recommendations

Published June 27, 2014

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1. Laboratories should conduct initial testing for HIV with an FDA-approved antigen/antibody combination (4th generation) immunoassay (IA)* that detects HIV-1 and HIV-2 antibodies and HIV-1 p24 antigen to screen for established infection with HIV-1 or HIV-2 and for acute HIV-1 infection.

*Exception: Determine Ag/Ab – insufficient data
2. Specimens with a reactive 4\textsuperscript{th} gen IA result (or repeatedly reactive, if repeat testing is recommended by the manufacturer) should be tested with an FDA-approved antibody IA that differentiates HIV-1 antibodies from HIV-2 antibodies.

\begin{itemize}
  \item Multispot HIV1/HIV2 Rapid Test
  \item Geenius HIV 1/2 Supplemental Assay
\end{itemize}
Initiate medical care
HIV-1/HIV-2 antibody differentiation
Immunoassays (IA)

Geenius™ HIV 1/2 Confirmatory System

Multispot™ HIV-1/HIV-2 Rapid Test

~ 20-30 mins
WB is no longer the “gold standard”

Western Blot
SUPPORT
GROUP
3. Specimens that are reactive on the initial assay and non-reactive (negative) or indeterminate on the HIV-1/HIV-2 antibody differentiation IA should be tested with an FDA-approved HIV-1 nucleic acid test (NAT).

GenProbe APTIMA HIV-1 RNA Qualitative assay
Or HIV-1 Viral load ordered by doctor
Technology

Hologic Aptima HIV-1 Qualitative NAAT

Roche COBAS® AmpliPrep/COBAS® TaqMan® HIV-1*

Abbott RealTime m2000*

All require ~ 6 hours
Abbott and Roche platforms- multiple pathogens

* Not FDA approved for diagnosis
A reactive HIV-1 NAT result and nonreactive HIV-1/HIV-2 antibody differentiation immunoassay result indicates laboratory evidence for **acute HIV-1 infection**.

Under these circumstances, a reactive NAT result indicates the presence of acute HIV-1 infection.
A negative HIV-1 NAT result and nonreactive or indeterminate HIV-1/HIV-2 antibody differentiation assay result indicates a false-positive result on the initial immunoassay.†

A negative result indicates the absence of HIV-1 infection, either a false-positive result on the initial IA or possibly, recent HIV-2 infection.
Alternatives

1. Initial step: 3rd generation IA instead of 4th generation IA

2. Second step: Alternative FDA-approved supplemental antibody test (e.g., HIV-1 WB or IFA) instead of an HIV-1/HIV-2 antibody differentiation IA

A 35 y/o man presents to your office after being told he had a reactive rapid test at a community testing event.

He reports no symptoms.

Sexual history:
- Three male sex partners in past 12 months
- Unprotected anal sex with a new male partner approximately three months ago
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4. Laboratories should use this same testing algorithm, beginning with an antigen/antibody combination immunoassay, with serum or plasma specimens submitted for testing after a reactive (preliminary positive) result from any rapid HIV test.

**Preliminary positive rapid test**
What about HIV Point of Care (POC) Testing

- Locations/populations that lab testing is difficult or not feasible
  - Better to use POC than no test

- POC assays continue to improve but...
  - Be aware of assay limitations
    - Provide informed counseling messages
  - Oral Fluid assays will miss acute infections and some early infections

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\(^1\) Stekler et al, JCV 2013, \(^2\) Luo et al JCV 2013
Increased Diagnostic Yield with the Addition of Assays that Detect Acute HIV Infection – The STOP Study, September 2011 – October 2013

**HIV Diagnostic Strategy**

- **Rapid HIV testing only**
  - 1155 patients diagnosed

- **Additional Architect HIV Ag/Ab Combo Assay testing**
  - 134 additional reactive
  - 34 additional HIV-1 RNA detectable
  - 11.6% increase

- **Additional pooled HIV-1 RNA testing**
  - 34 additional reactive
  - 2.6% increase

**Patients Diagnosed with HIV Infection**

0 200 400 600 800 1000 1200 1400
A look into the future: New FDA-approved tests and Tests in the pipeline
Technology

Bio-Rad GS HIV Combo Ag/Ab  
Abbott Architect Ag/Ab Combo Assay  
Alere Determine™ HIV-1/2 Ag/Ab*

~ 3-4 hours  
~ 3-4 hours  
~30 mins  
~25 mins

BioPlex® 2200 HIV Ag-Ab **  
ADVIA Centaur® HIV Ag/Ab Combo**

~ 1 hour  
~ 1 hour

- Need HIV algorithm data  
- Not yet FDA approved -HIV  
- Automated platforms – multiple pathogens
Point of Care Nucleic Acid Test (Viral Load)
0 Could resolve discordant test results on site
0 Could decrease time from diagnosis to treatment
0 Potential use for monitoring
0 Currently being developed for PEPFAR
0 Potential to be introduced in US market (2-4 years out)

Liat™ Analyzer          Alere Q          Gene Xpert®
Laboratory Tests

In this section we provide resources for all FDA-approved diagnostic HIV tests for use in moderate and high complexity laboratories.

Laboratory Testing Guidance


Resources

- M53-A Criteria for Laboratory Testing and Diagnosis of Human Immunodeficiency Virus Infection; Approved Guideline from the Clinical and Laboratory Standards Institute (CLSI)

- HIV Diagnostic Conference

List of all FDA Approved HIV Tests

- Advantages and Disadvantages of Different Types of HIV tests
- List of non-clinical tests (CLIA-Waived)  
- List of HIV-CLIA waived tests that are US FDA-approved
- FDA-approved Moderate Rapid HIV Tests for laboratory use
- FDA-Approved Moderate and High Complexity HIV tests for laboratory use
- Alere Determine™ HIV-1/2 Ag/Ab Combo Information Sheet for Testing Programs
HIV Diagnostics Conference  
www.hivtestingconference.org

- Proposed date for next conference: Spring 2016
- We bring together in one room for 2.5 days all US HIV test manufacturers, FDA, CDC, CMS, other regulatory agencies, CAP, DOD, HIV program managers, HIV test researchers, and laboratorians who specialize in HIV testing.
HIV-1/2 antigen/antibody combination immunoassay

(+)

(-)
Negative for HIV-1 and HIV-2 antibodies and p24 Ag

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

1-4 hours
30 mins
6 hours

(+) indicates reactive test result
(-) indicates non-reactive test result
NAT: nucleic acid test
HIV Screening. Standard Care.™

- A program developed to help physicians establish HIV screening as a routine part of medical care

ACTHIV 2015: A State-of-the-Science Conference for Frontline Health Professionals

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