HIV & HCV Testing in 2016:
- What’s New?
- What’s Next?

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Disclosures

Dr Branson has served as a consultant to

- Gilead Sciences, Inc.
- Caldwell-Everson
- Daktari Diagnostics
- Siemens Healthcare
Objectives

- Compare the relative merits of different FDA-approved HIV tests for different circumstances.
- Describe how new HIV and HCV tests fit in with current testing recommendations
- Recognize the increasing role that RNA tests play in HIV & HCV diagnosis
Outline

- The basics
- New tests: rapid, lab, & supplemental
- How differences between tests relate to accuracy
- On the horizon
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 work in a lab and perform all kinds of tests, including HIV.
Epidemiologic Notes and Reports

Kaposi’s Sarcoma and *Pneumocystis* Pneumonia Among Homosexual Men — New York City and California

During the past 30 months, Kaposi’s sarcoma (KS), an uncommonly reported malignancy in the United States, has been diagnosed in 26 homosexual men (20 in New York City [NYC]; 6 in California). The 26 patients range in age from 26-51 years (mean 39 years). Eight of these patients died (7 in NYC, 1 in California) — all 8 within 24 months after KS was diagnosed. The diagnoses in all 26 cases were based on histopathological examination of skin lesions, lymph nodes, or tumor in other organs. Twenty-five of the 26 patients were white, 1 was black. Presenting complaints from 20 of these patients are shown in Table 1.
Do you remember a time before AIDS?

1. I was born before 1945.
2. I was born between 1945 and 1965.
3. I was born between 1965 and 1980.
4. I was born in 1981 or later.
1983 Almanac

- “Evil Empire” speech
- Mortgage rate: 12%
- “Year of the Bible”
- U.S. invades Granada
HIV Infection and Laboratory Markers

HIV RNA (plasma)

HIV p24 Ag

IgM

IgG

HIV Antibody

Days

Infection

Lab Ag/Ab tests

Lab Ab tests

Most Rapid tests

HIV-1 antigens and RNA

- gp120
- gp 41
- p24
- RNA
We are a testing culture: we test our urine for drugs; we test our sweat for lies. It is not surprising that we should also test our blood for the acquired immunodeficiency syndrome (AIDS). But before we screen low-risk groups for antibody to the human immunodeficiency virus (HIV), we should consider what the results will mean.
Use of Two Tests in Sequence

- After a **positive** screening test, conduct a second test on persons who test positive.
- Decision rule: Must be positive on - both tests - either test

- Positive on **both** tests = reduces false positives
  - Increases specificity, but reduces sensitivity
The Public Health Service recommends that no positive test results be given to clients/patients until a screening test has been repeatedly reactive (i.e., greater than or equal to two tests) on the same specimen and a supplemental, more specific test such as the Western blot has been used to validate those results.
1989: State of the Art

EIA

Western blot
1989 Almanac

- Berlin Wall dismantled
- Tiananmen Square
- Exxon Valdez oil spill
- U.S. invades Panama
Treatment Era

- 1989 – PCP prophylaxis
- 1993 – PCP and MAC prophylaxis
- 1996 – Potent ART with protease inhibitors
CLIA-waived rapid HIV-antibody tests

- Oraquick Advance
- DPP HIV 1/2
- Chembio Sure Check
- INSTI HIV 1/2
- Chembio Stat Pak
- Uni-Gold Recombigen
The Roll-out of Rapid HIV Testing in The United States
CLIA-waived

The Roll-out of Rapid HIV Testing in The United States
2003 Almanac

- Department of Homeland Security Established
- Euro adopted by the EU
- Enron collapses
- U.S. invades Iraq
Which 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 specimen?

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

- **Oraquick Advance**: 20-40 min
- **DPP HIV 1/2**: 5 + 10-15 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
What’s new?

Chembio SureCheck

DPP HIV 1/2

INSTI HIV 1/2

Determine HIV-1/2 Ag/Ab Combo
Product name change:
Clearview Complete is now Sure Check
DPP HIV-1/2

- Finger-stick, oral fluid
- Swab gums 4 times (15 seconds) or 10 μL whole blood
- Read time 10-25 min blood 40 min oral fluid
Dual Path Platform Technology
INSTI HIV-1/2

- CLIA-waived for whole blood, finger-stick
- 50 µL specimen volume
- Results <1 minute
- Detects IgM antibodies

Moshgabadi et al, J Clin Virol 2015
What’s new in the lab?
Abbott Architect Ag/Ab Combo 2010

Bio-Rad Ag/Ab Combo 2011

Siemens Advia Centaur® CHIV 2015

“4th Generation”

“Ag/Ab Combo”
Chemiluminescence Immunoassays

Magnetic Micro-Particles
Coated with Antigens and antibody

Patient Sample

IgM/IgG

LITE Reagent
Antigens and antibodies labeled with AE

gp41/120 Ag

gp36 Ag

HIV1 “O” Ag

Anti- p24 Monoclonal

gp41/120 Ag

gp36 Ag

HIV1 “O” Ag

2 Anti- p24 Monoclonals

WASH

g41/120 Ag

Chemiluminescence

Relative light units

Trigger Solution
Random Access Multiplatform analyzers for HIV testing

On-board Refrigeration of Multiple Different Assays
Random Access Multiplatform analyzers for HIV testing

STAT sample requests without pausing
Results in <60 minutes
“5th generation” HIV Ag/Ab Combo Assay

- Beads conjugated to HIV-1 Group M (gp160) and O antigens, HIV-2 gp36 antigen, and p24 antibody

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

BioPlex 2200 HIV Ag-Ab
July 2015
Bioplex assay principle

1. Microspheres are aligned in single file and passed through 2 lasers.

2. 1st laser excites molecular tags. Data output as mean fluorescent intensity (MFI).

3. 2nd laser excites microsphere and identifies dye signature (identifies analyte).
Abbott Architect Ag/Ab Combo
2010 p24 Antigen
Control

Antibody gp41, gp120

Determine Combo Ag/Ab Rapid Test 2013

Siemens Advia Centaur® CHIV 2015

“4th Generation”

- CLIA-waived
- Whole blood (50µL)
Which factor is least important for the accuracy of a rapid HIV antibody test?

1. The type of specimen (serum, whole blood, oral fluid).
2. The volume of specimen the test requires.
3. The way the test is designed.
4. The time it takes to run the test.
5. The prevalence of HIV in the population tested.
Accuracy: Performance Characteristics

- **Sensitivity**
  - The ability of the test to identify correctly those who have the disease
    - HIV: ≥99.8%

- **Specificity**
  - The ability of the test to identify correctly those who do not have the disease
    - HIV: ≥99.8%
What is the Window Period?

1. The period after infection when HIV is undetectable.
2. The interval when HIV RNA is detectable but antibodies have not yet developed.
3. The time after infection before antibodies appear.
4. The time you must wait before reading rapid test results.
Evolution of HIV Tests: Four Generations
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
26 seroconverters were analyzed with 14 tests
17 seroconverters with WB positive used for cumulative frequency analysis
Sequence of Test Positivity Relative to WB (plasma)

166 specimens, 17 Seroconverters - 50% Positive Cumulative Frequency

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)


Limitations of the 1989 HIV Algorithm

- Antibody tests do not detect infection in ~10% of infected persons at highest risk of transmission

- Western blot confirmation is less sensitive during early infection than many widely used screening tests

- Delays inherent with centralized screening reduce the “effective sensitivity” because infected persons do not learn their test results
Hepatitis C Virus (HCV) Genome
Evolution of HCV Tests (IgG antibodies)

- **EIA 1.0:** NS4a antigen
  - Sensitivity: 80%. Window period 15 weeks
- **EIA 2.0:** Core, NS3, NS4a antigen
  - Sensitivity 98% - Window period 10 weeks
- **EIA/CIA 3.0:** Core, NS3, NS4a, NS5b antigens
  - Sensitivity 99% - Window period 10 weeks
Evolution of HCV Tests:
Four Generations

NS4

Core, NS3, NS4

Core, NS3, NS4, NS5

Ag/Ab combo?
Testing for HCV Infection: An Update of Guidance for Clinicians and Laboratorians
2013 Almanac

- U.S. Government shutdown
- Pope Benedict resigns
- Kim Jung Un threatens the US (after a bad haircut)
- U.S. doesn’t invade anyone
Laboratory Diagnosis of HCV infection

- HCV ANTIBODY
  - NON-REACTIVE: No HCV infection
  - REACTIVE: HCV RNA
    - POSITIVE: Current HCV Infection
    - NEGATIVE: No current HCV Infection

Additional testing as appropriate
HCV Test Results

- Antibody positive - RNA positive:
  - Current, active HCV infection

- Antibody positive – RNA negative
  - Resolved HCV infection, or
  - False-positive antibody test
    - Consider different antibody test to resolve
Laboratory Testing for the Diagnosis of HIV Infection

Updated Recommendations

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Centers for Disease Control and Prevention
National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention
**4th generation HIV-1/2 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 (-)
  - RNA
  - RNA (+) → Acute HIV-1 infection
  - RNA (-) → Negative for HIV-1
In 6 studies involving >26,000 persons, Determine Combo failed to detect p24 antigen in whole blood from any of the 26 acute infections.

CDC study: Nine seroconverters showed a median delay of 6 days between DC reactivity with plasma and reactivity with whole blood.

- 2016 CDC HIV Diagnostics Conference: http://hivtestingconference.org
FDA-approved HIV-1/HIV-2 Antibody Differentiation Assay
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 4th 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
HIV-1/HIV-2 Differentiation Assays

**FDA approved, March 2013**

- Serum Control
- HIV-1 Recombinant gp41
- HIV-2 Peptide gp36
- HIV-1 Peptide gp41

**Product Withdrawal**

**July 29, 2016**

**Multispot HIV-1/HIV-2**

**FDA approved, Oct. 2014**

- Geenius HIV-/HIV-2
Where’s My Western Blot?
What HIV Specialists Need to Know about
Updated HIV Testing Recommendations
Geenius™ HIV-1/2 Lines

HIV-1 & HIV-2 Associated Lines

Control Band

gp36

gp140

gp41 (group M & O)

p31*

p24

gp160

HIV-2

HIV-1

* inside the nucleocapsid
Dual Path Platform:
Add
5 µL serum/plasma
Or
15 µL whole blood
to specimen well
Add 5 drops buffer To buffer well.
Wait min 15-20 min (max 30 min) for results
Insert test cassette in reader for automated interpretation
# Geenius Results: New 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&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Negative</td>
<td>Indeterminate</td>
<td>HIV-2 INDETERMINATE&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Indeterminate</td>
<td>Indeterminate</td>
<td>HIV INDETERMINATE&lt;sup&gt;c&lt;/sup&gt;</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>
</tbody>
</table>

### Notes:

<sup>a</sup> HIV-1 band(s) detected but did not meet the criteria for HIV-1 Positive

<sup>b</sup> HIV-2 band(s) detected but did not meet the criteria for HIV-2 Positive

<sup>c</sup> HIV band(s) detected but did not meet the criteria for HIV-1 Positive or HIV-2 Positive

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<sup>Note</sup>: Differentiation features managed by proprietary algorithm.

### Additional Information:

- 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.<br>
  *Note: Differentiation features managed by proprietary algorithm.*

- HIV POSITIVE Un typable (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).<br>
  *Note: Differentiation features managed by proprietary algorithm.*
Arizona Experience 3/16 - 9/16

- 179 specimens submitted for Geenius testing
  - 111 (62%) HIV-1 positive
  - 56 (31%) HIV-negative
  - 7 (4%) HIV-1 indeterminate
  - 2 (1%) HIV-2 indeterminate
  - 1 (0.5%) HIV-2 positive
HIV-2 Infection

- Remains uncommon in U.S., but
  - Does not respond to NNRTIs, some PIs (first line therapy)
  - Undetectable by HIV-1 viral load tests

- Misclassification by HIV-1 Western blot:
  - 54/58 (93%) HIV-2 patients tested had positive HIV-1 WB (NYC)¹
  - 97/163 (60%) HIV-2 cases reported had positive HIV-1 WB (CDC)²

- HIV-2 often diagnosed after immunologic deterioration in patient with negative viral load

¹ Torian et al, Clinical Infectious Disease 2010
² MMWR July 2011
HCV in the Context of HIV in the US

HIV 1.1 million

HCV 3.2 million
Burden of Disease
Persons with HIV and Awareness of HIV Status, United States - 2012

Number HIV infected 1,201,100

Number unaware of their HIV infection 168,300 (14 %)

Estimated new infections annually 47,500

CDC HIV Surveillance Supplemental Report, 2014
Burden of HCV Infection and Disease

- **United States**
  - ~ 3.2 M (2.7-3.9) persons living with HCV
  - 29,700 new cases (2013)
  - 19,300 deaths

- *CDC. Hepatitis Surveillance 2013*
The Future Burden of Hepatitis C in the United States

- Of 2.7 million HCV-infected persons in primary care
  - 1.47 million will develop decompensated cirrhosis (DCC)
  - 350,000 will develop hepatocellular carcinoma (HCC)
  - 897,000 will die from HCV-related complications

HIV and HCV Co-infection

- Prevalence of co-infection varies by region
  - 25% of HIV infected persons in US

- HIV hastens progression of HCV related liver disease

- Liver disease is second leading cause of death for persons with HIV

Mortality associated With Hepatitis B, Hepatitis C, and HIV, United States, 1999 – 2008

HCV Prevalence by Year of Birth
Revised Recommendations for HIV Testing of Adults, Adolescents, and Pregnant Women in Health-Care Settings
HIV Screening Recommendations: Adults and Adolescents

- Routine, voluntary HIV screening for all persons 13-64 in health care settings, not based on risk

- All patients with TB or seeking treatment for STDs should be screened for HIV

- Repeat HIV screening of persons with known risk at least annually
Recommendations for the Identification of Chronic Hepatitis C Virus Infection Among Persons Born During 1945–1965
Revised CDC recommendations for HCV Screening

- One-time testing of all adults born 1945-1965 without prior ascertainment of risk

- Adults of any age with risks for HCV:
  - Injection drug use
  - Blood transfusion before 1992 and other blood exposures
US Preventive Services Task Force

2013 Recommendation for HIV screening:
- All pregnant women - Grade A
- Persons at increased risk for HIV – Grade A
- Adolescents and adults ages 15 to 65 years – Grade A

2013 Recommendation for HCV screening
- Persons at increased risk: Grade B
- Persons born between 1945-1965: Grade B
Why USPSTF Grades Matter

Health Care Reform:

**SEC. 2713. COVERAGE OF PREVENTIVE HEALTH SERVICES.**

(a) IN GENERAL.—A group health plan and a health insurance issuer offering group or individual health insurance coverage shall, at a minimum, provide coverage for and shall not impose any cost sharing requirements for—

(1) evidence-based items or services that have in effect a rating of ‘A’ or ‘B’ in the current recommendations of the United States Preventive Services Task Force;
1. The Medical Rationale for screening

- **Treatment for HIV is Effective.**
  - Treatment is recommended for all patients with HIV, regardless of CD4 count
    - *(March 2012 – DHHS Treatment Guidelines)*

- **Treatment can cure HCV**
  - Treatment is recommended for all patients with chronic HCV infection
    - *(2015 AASLD and IDSA HCV Guidance)*
HIV Antiretroviral Therapy Improves Survival

Mortality and HAART Use Over Time
HIV Outpatient Study, CDC, 1994-2003
HCV Therapy Can Eliminate HCV Infection and Reduce Morbidity/Mortality Risks

- Therapy can cure HCV infection - sustained virologic response (SVR)

- SVR is associated with
  - 70% reduction in Hepatocellular carcinoma
  - 50% reduction in all-cause mortality

Clinicians should treat HCV-infected patients with the goal of achieving an SVR, preferably early in the course of their chronic HCV infection before the development of severe liver disease and other complications.

Recent reports suggest that initiating therapy in patients with lower stage fibrosis may extend the benefits of SVR and improve survival rates.

IDSA/AASLD  http://hcvguidelines.org/
Advances in HCV Therapy

- 1991: 6% IFN 6 m
- 1999: 16% IFN 12 m, 34% IFN/RBV 6 m
- 2001: 42% IFN/RBV 12 m
- 2002: 39% Peg-IFN 12 m
- 2011: 54% - 56% Peg/RBV 12 m
- 2014: 67-72% Peg/RBV DAA 6 m
- >90% All oral DAA 12 wk

Adapted from Strader DB, et al. Hepatology. 2004
SOF/LDV in Treatment Naïve HCV, GT1

Afdhal, NEJM 2014
SOF/LDV in HIV/HCV

SVR12

Overall: 96%, 321/335
Naïve: 95%, 142/150
Experienced: 97%, 179/185
No Cirrhosis: 96%, 258/268
Cirrhosis: 94%, 63/67

Naggie, CROI 2015; Abs LB 152
How Much Does Screening Cost?

It Depends.

<table>
<thead>
<tr>
<th></th>
<th>Submitted Charges</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV Antibody</td>
<td>$127</td>
</tr>
<tr>
<td>HCV Antibody</td>
<td>$150</td>
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</tbody>
</table>
How Much Does Screening Cost?

It Depends.

<table>
<thead>
<tr>
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<th>Plan Allowance</th>
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<tbody>
<tr>
<td>HIV Antibody</td>
<td>$127</td>
<td>$11.02</td>
</tr>
<tr>
<td>HCV Antibody</td>
<td>$150</td>
<td>$19.42</td>
</tr>
</tbody>
</table>
Billing Practices for Routine HIV & HCV Tests

Sites Reporting Consistent Coding, Charge Capture, & Billing

<table>
<thead>
<tr>
<th>Setting</th>
<th>Consistent Coding, Charge Capture, &amp; Billing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inpatient</td>
<td>100%</td>
</tr>
<tr>
<td>ED</td>
<td>50%</td>
</tr>
<tr>
<td>Ambulatory Care</td>
<td>83%</td>
</tr>
</tbody>
</table>

Reimbursement Findings

- All setting types received bundled payments for clinical services
- Ambulatory care settings reported potential for fee-for-service reimbursement
- Remittance for point-of-care HIV tests often “covered under capitation”
- Sites reported fewer denials and less departmental expenditures for laboratory-based tests

- Penrose et al, June 2015 Summit on HIV/HCV
2. Potential Effects on Transmission
BREAKTHROUGH
OF THE YEAR
HIV Treatment as Prevention
HPTN 052: HIV Transmissions

1,763 sero-discordant couples (97% heterosexual)
HIV infected partners: 890 men, 873 women

39 HIV transmissions

28 linked HIV transmissions
11 unlinked transmissions

Immediate ART: 1 transmission
Deferred ART: 27 transmissions

96% reduction with ART

- Cohen M et al, NEJM 2011
ANOTHER BLUE PILL FOR SEX
**PrEP: PrEP works... if you take it**

**iPrEx Open Label Extension Study (MSM)**

<table>
<thead>
<tr>
<th>Adherence by Drug Concentration</th>
<th>HIV Incidence per 100 PY</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 pills/week</td>
<td>4.7</td>
</tr>
<tr>
<td>&lt;2 pills/week</td>
<td>2.3</td>
</tr>
<tr>
<td>2-3 pills/week</td>
<td>0.6</td>
</tr>
<tr>
<td>≥4 pills/week</td>
<td>0.0</td>
</tr>
</tbody>
</table>
Women might need to be more adherent than MSM

Percent of Women Achieving Effective Drug Concentrations in CD4+ Cells
Pharmacokinetics in 49 healthy female volunteers

Rectal Tissue

2-7 doses/week (28% adherence) protects colorectal tissue

Female Genital Tract Tissue

6-7 doses/week (85% adherence) to protect female genital tract tissue
# Results of HCV Screening Programs

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HCV Antibody tests</strong></td>
<td><strong>334,611</strong></td>
<td></td>
</tr>
<tr>
<td>Antibody-positive</td>
<td>22,815 (6.8%)</td>
<td>Range: 4.5% - 20%</td>
</tr>
<tr>
<td>RNA tests done</td>
<td>20,175 (77%)</td>
<td>Range: 34% - 87%</td>
</tr>
<tr>
<td>HCV RNA-positive</td>
<td>13,108 (65%)</td>
<td>Range: 61% - 100%</td>
</tr>
</tbody>
</table>

*Source: Gilead FOCUS Program*
Compare with HIV Screening Programs

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Number</th>
<th>Positivity (%)</th>
<th>Range</th>
</tr>
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<td>334,611</td>
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</tr>
<tr>
<td>HCV RNA-positive</td>
<td></td>
<td>4%</td>
<td></td>
</tr>
<tr>
<td><strong>HIV Antibody tests</strong></td>
<td>2,218,461</td>
<td>16,890 (0.7%)</td>
<td></td>
</tr>
<tr>
<td>Antibody positive</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
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Source: Gilead FOCUS Program
On the Horizon...
4th generation HIV-1/2 immunoassay

HIV-1/HIV-2 antibody differentiation immunoassay

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

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

HIV-1 RNA viral load

RNA (+) RNA (-)

Acute HIV-1 infection Negative for HIV-1

June 27, 2014
HIV Nucleic Acid Test (NAT) for Diagnosis: Qualitative 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
# Qualitative HCV RNA Tests

<table>
<thead>
<tr>
<th>Test Name</th>
<th>Manufacturer</th>
<th>Intended Use</th>
<th>LOD/LLOQ</th>
<th>Specimen Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>VERSANT HCV RNA Qualitative Assay/ APTIMA HCV RNA Qualitative Assay</td>
<td>Gen-Probe</td>
<td>Diagnostic</td>
<td>7.5 IU/mL (genotype 1) 9.6 IU/mL overall</td>
<td>Serum or plasma (EDTA, sodium heparin, sodium citrate, and ACD)</td>
</tr>
<tr>
<td>COBAS Amplicor HCV Test, v2.0 and COBAS AmpliPrep/COBAS Amplicor HCV Test, v2.0</td>
<td>Roche</td>
<td>Diagnostic</td>
<td>100 IU/mL</td>
<td>Serum or plasma (EDTA)</td>
</tr>
<tr>
<td>AMPLICOR HCV Test, v2.0</td>
<td>Roche</td>
<td>Diagnostic</td>
<td>50 IU/mL</td>
<td>Serum or plasma (EDTA)</td>
</tr>
</tbody>
</table>

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**COBAS® AmpliPrep/COBAS® TaqMan® HCV Test, v2.0**

**INTENDED USE**

The test is intended for use as an aid in the diagnosis of HCV infection.

The test is intended for use as an aid in the management of HCV-infected patients.
How about...

4th generation HIV-1/2 immunoassay

(+)

HIV-1 RNA viral load

(-)

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

VL detectable
HIV-1 infection

Useful clinical information

VL (-)

HIV-1/HIV-2 antibody differentiation assay

HIV-1+
(Viral suppression)

HIV-2+
HIV-2 infection

Negative
“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

GeneXpert

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

- Xpert HCV viral load
  - 1 mL serum or plasma
  - Genotypes 1-6
  - Range 10 – 100,000,000 IU/mL
  - Results in 105 minutes
  - CE-marked April 2015

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
What’s Next: 2017 Almanac?
Summary

- HIV and HCV tests keep getting better
- RNA viral load will play an increasingly important role in HIV and HCV diagnosis
- You never know what’s next.