Challenges in the Serodiagnosis of Infectious Diseases

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Abbott Laboratories
Distinguished Scientist, Volwiler Society

AGENDA

- HIV Diversity
- Abbott HIV Global Surveillance Program
- Challenges for early detection of HIV Infection
- New CDC recommendations for HIV testing
- Hepatitis B surface antigen escape mutants
- New CDC recommendations for laboratory testing to diagnosis HCV infection

LEADING CAUSES OF INFECTIOUS DISEASE DEATHS WORLDWIDE (2000)

<table>
<thead>
<tr>
<th>Disease</th>
<th>Est. Deaths per Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lower respiratory tract infections</td>
<td>~3.5 million</td>
</tr>
<tr>
<td>HIV/AIDS</td>
<td>~3.0 million</td>
</tr>
<tr>
<td>Diarrheal diseases</td>
<td>~2.2 million</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>~2.0 million</td>
</tr>
<tr>
<td>Malaria</td>
<td>~1.3 million</td>
</tr>
<tr>
<td>Measles</td>
<td>~888,000</td>
</tr>
<tr>
<td>Hepatitis B Virus</td>
<td>~620,000</td>
</tr>
<tr>
<td>Hepatitis C Virus</td>
<td>~366,000</td>
</tr>
<tr>
<td>Hepatitis E</td>
<td>~330,000</td>
</tr>
<tr>
<td>Pertussis</td>
<td>~355,000</td>
</tr>
<tr>
<td>Neonatal tetanus</td>
<td>~300,000</td>
</tr>
<tr>
<td>Intestinal Parasites</td>
<td>~135,000</td>
</tr>
</tbody>
</table>

HIV Diversity

Put science on your side.

**IMPACT OF HIV**

**WORLDWIDE:**
- Living with HIV: 34 million
- Newly infected in 2011: 2.5 million
- Unaware: 1 in 5
- Diagnosed too late: 36%
- Healthcare costs: $12.6 billion

**UNITED STATES:**
- Newly infected annually: 50,000
- Someone is infected every 9 ½ minutes
- Living with HIV in 2011: 1.1 million

Hall et al., JAMA 2008; 300:520-529; Hernandez A, et al. MMWR, June 2012

**Estimated Percentage of HIV infections by Transmission Category, 2009**

- Male to male sexual contact and injection drug use, 3%
- Male to male sexual contact, 57%
- Heterosexual contact, 31%
- Injection drug use, 9%

N=41845

*Some states and 5 dependent areas
**EXCEPTIONAL DIVERSITY OF HIV-1: INFLUENZA COMPARISON**

Adapted from Korber et al., Brit Med Bull, 2001; 58:19-42

**SOURCES OF HIV-1 GENETIC DIVERSITY**

- Cross-species transmission
  - HIV-1: SIVcpz (chimpanzee; P.t. troglodytes)
    SIVgor (gorilla; G.g. gorilla)
  - HIV-2: SIVsm (sooty mangabey)
- Error-prone RT enzyme
  - High mutation rate
  - High replication rate
- Cross-species transmission
  - Recombination - leap in evolution
  - In vivo selective pressure

**ORIGINS OF HIV-1**

Each group arose from an independent transmission

- Group M: SIVcpz in southeast Cameroon
- Group N: SIVcpz in south central Cameroon
- Group O: SIVgor in south central Cameroon
- Group P: SIVgor in southwest & south central Cameroon

D'Arc, et al CROI 2014
**DISCOVERY OF HIV STRAINS:**

1983 - HIV-1 Group M:
- AIDS patients in France and USA

1986 - HIV-2:
- West African AIDS patients
- HIV-1 EIA nonreactive, absence of env bands on HIV-1 WB

1990 - HIV-1 Group O:
- Cameroon AIDS patients in Belgium
  - HIV-1 EIA/IFA low reactive, absence of env bands on HIV-1 WB

1998 - HIV-1 Group N:
- Cameroon: epidemiological survey
  - HIV-1 seropositive, V3 FIAA negative for M and O, positive for SIVcpz gab

2009 - HIV-1 Group P:
- Cameroonian in Paris
  - HIV-1 seropositive, undetectable viral load by group M specific assays, high viral load by M and O specific assays

**EXTENSIVE VARIATION AMONG HIV**

Like other viruses, HIV mutates at a very high rate creating different virus types and many subtypes

<table>
<thead>
<tr>
<th>Virus Type</th>
<th>Subtypes</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV-1 Group M</td>
<td>A, B, C, D, E, F, G, H, J</td>
</tr>
<tr>
<td>HIV-1 Group O</td>
<td>Evidence of 5 subtypes</td>
</tr>
<tr>
<td>HIV-2**</td>
<td>A, B, C, D, E, F, G, H</td>
</tr>
<tr>
<td></td>
<td>(8 subtypes)**</td>
</tr>
</tbody>
</table>
| HIV-1 Recombinants | B/F, A/E, G/A, B/D, F/B, D/A, A/E (CRF) |**

*Yamaguchi et al, Evaluation of HIV Type 1 Group O Isolates: Identification of Five Phylogenetic Clusters. AIDS Research and Human Retroviruses, 18: 269-282, 2002 (Published by Abbott's Retroviral Discovery Group)

It is very important to select an assay which detects all of these subtypes to ensure all infections are detected

**IMPACT OF HIV DIVERSITY**

Genetic diversity of HIV-1 has the potential to impact:
- Blood screening assays
- Diagnostics assays
- Therapeutic monitoring assays
  - Viral load testing
  - Resistance genotyping
- Resistance to antiretroviral agents
- Vaccine development
- Pathogenesis
Meeting The Challenge: The Abbott HIV Global Surveillance Program

- Monitor HIV global diversity and emergence of new viral strains
- Establish well-characterized specimen panels representing global strain diversity
  - All types, groups and subtypes, as well as recombinants
- Scientific foundation for reagent and assay development
- Global specimen panel to evaluate assay performance
  - Design assays to detect infections due to diverse strains
  - Demonstrate reliable assay performance regardless of viral strain and geographical location


GLOBAL SURVEILLANCE PROGRAM: STUDY SITES

GLOBAL SURVEILLANCE PROGRAM: STUDY SITES

- Brazil
- England
- USA
- Spain
- Argentina
- Thailand
- E. Guinea
- Cameroon
- Brazil
- Argentina
- S. Africa
- Spain
- Ghana
- Israel
- Senegal
- Saudi Arabia
- Russia

CAMEROON: IDENTIFICATION AND CHARACTERIZATION OF RARE STRAINS

- Identified >200 Group O infections
  - 1-2% prevalence
- Identified 9 Group N infections
  - Only 13 reported to date
  - < 0.1% prevalence
  - Husband/wife* pair confirms horizontal transmission
- Identified 1 Group P infection
  - Only 2 reported to date
  - < 0.001% prevalence
ABBOTT HIV GLOBAL SURVEILLANCE PROGRAM: IDENTIFICATION OF THE 2ND GROUP P STRAIN

GLOBAL HIV PANEL: GENETIC & GEOGRAPHIC DIVERSITY

12 Countries
- Cameroon
- E. Guinea
- Ghana
- Uganda
- South Africa
- Thailand
- Brazil
- Argentina
- Saudi Arabia
- Spain
- UK
- USA

Groups, Subtypes, CRFs, URFs

- A
- B
- C
- D
- F
- G
- CRF01_AE
- CRF02_AG
- CRF03_cpx
- CRF04_cpx
- CRF06_cpx
- CRF09_cpx
- CRF11_cpx
- CRF13_cpx
- CRF22_01A1
- CRF25_cpx
- CRF36_cpx
- CRF37_cpx
- CRF43_GG
- URF

- Group O
- Group N

>1500 Specimens

ARCHITECT HIV COMBO: BEST OVERALL AG SENSITIVITY

- ARCHITECT HIV Combo assay performance is not impacted by HIV-1 strain diversity
- In contrast other CE marked Ag/Ab Combination assays are impacted
Acute HIV Infection

WHY IS DETECTION OF AHI IMPORTANT?

- AHI makes a significant contribution to the ongoing epidemic
  - May account for 15-50% of new infections
  - Quebec study: 10% AHI accounted for 49% of transmissions
- During the acute phase, the risk of transmission is ~26-fold higher compared to asymptomatic chronic phase
  - Period of high viremia
  - Virus appears to be more infectious
- Individual unaware of infection status
  - Often test negative

Detection of acute HIV infection has important implications for HIV prevention strategies

SEROLOGIC DIAGNOSIS OF HIV INFECTION
ARCHITECT 4th Gen Combo

Put science on your side.

ARCHITECT 4th GEN HIV AG/AB COMBO ASSAY

- Detects all known HIV groups/subtypes:
  - HIV-1 Group M, Group O
  - HIV-2
- Intended Use:
  - Detects HIV infections including Acute HIV Infection (AHI)
  - Pediatric subjects as young as 2 years old
  - Pregnant Females
- p24 antigen sensitivity:
  - As low as 18 pg/ml of p24
  - As low as 15,000 RNA copies/ml
- Increased Specificity:
  - 99.77%
- Excellent Workflow:
  - Fully automated
  - Random-access
  - 29 minutes to first result
  - ~160 tests per hour

HIV AG/AB COMBO ASSAY SCHEMATIC

Adapted from ARCHITECT HIV Ag/Ab Combo Package Insert
ACUTE HIV INFECTION STUDIES

- Basic testing strategy:
  - Specimens screened with an HIV antibody test
  - All negative specimens tested by HIV NAT

- Define acute HIV infection:
  - Specimens detected utilizing HIV NAT i.e. Ab-, RNA+

- Stored specimens blinded and sent to Abbott for Combo testing
  - Included HIV antibody positive, Western blot confirmed specimens and HIV negative specimens
  - Used ARCHITECT HIV Ag/Ab Combo (CE marked version; 4J27)

CDC ACUTE STUDY

PATEL P, ET AL, ARCH INTERN MED 2010; 170:66-74

- Study designed to evaluate yield of HIV NAT after screening with a 3rd generation HIV EIA; previously evaluated NAT after 1st generation EIA
  - 2006-2008
  - Los Angeles: 14 county STD clinics, 1 gay community STD clinic
  - New York City: 3 municipal STD clinics
  - Florida: 80 public health clinics

- Retrospectively expanded study to include ARCHITECT HIV Combo
  - Tested subset of specimens

CDC ACUTE STUDY RESULTS

- Population demographics:
  - Heterosexual: 69%
  - Female: 53%
  - Black, non-Hispanic: 38%
  - Median age: 26 years

- Screened 102,334 specimens:
  - HIV infected N=1215 (1.2%) [Ab+ plus NAT+]
  - Classified as acute HIV infection N=57 (4.7%) ARCHITECT HIV Combo: tested 38 of 57 AHI
    - Detected 34 of 38 (89%) 4 not detected were Ab negative, <21,500 RNA copies/mL
ARCHITECT HIV COMBO DETECTS ACUTE HIV INFECTIONS

<table>
<thead>
<tr>
<th>Site</th>
<th># AHI Combo tested</th>
<th># AHI Combo detected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seattle (Stekler, CID 2009; 49:444-453)</td>
<td>16</td>
<td>15 (94%)</td>
</tr>
<tr>
<td>San Francisco (Pandori, JCM 2009; 47:2639-2642)</td>
<td>64</td>
<td>57 (89%)</td>
</tr>
<tr>
<td>EXPLORE (Eshleman, JAIDS 2009; 52:121-124)</td>
<td>21</td>
<td>13 (62%)*</td>
</tr>
<tr>
<td>CDC AHI Study (Patel, Arch Int Med 2010; 170:66-74)</td>
<td>38</td>
<td>34 (89%)</td>
</tr>
<tr>
<td>CDC Rapid Study (Delaney, CROI 2009, poster 997)</td>
<td>17</td>
<td>13 (76%)*</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>156</strong></td>
<td><strong>132 (85%)</strong></td>
</tr>
</tbody>
</table>

*Site used individual NAT instead of pooled NAT

Combo assay detected 85% of acute HIV infections

ACUTE HIV INFECTED HUMAN SPECIMENS (RNA+, AB-)

![Graph showing acute HIV infected human specimens](image)

Combo assay detected 97% of AHIs with >30,700 RNA copies/mL and 98.5% with >58,000 copies/mL. (Brennan et al, J Clin Viral 57:169-172)

EVOLUTION OF TEST REACTIVITY: BASED ON SEROCONVERSION PANELS

![Graph showing evolution of test reactivity](image)

Days before Western blot positive. (Adapted from Owen et al, J Clin Micro 2008; 46:1568; Masciotra et al, J Clin Virol 2011; 50:271; Brennan S, CROI 2012 Session 2611A)
NEW HIV DIAGNOSTIC TESTING ALGORITHM

Published on June 27, 2014

Key Changes:
- Initial test is an HIV Ag/Ab combination assay
- Use of Western blot and IFA as confirmatory tests eliminated

Key Advantages:
- More accurate diagnosis of acute and early HIV-1 infection
- Equally accurate diagnosis of established HIV-1 infection
- More accurate diagnosis of HIV-2 infection
- Fewer indeterminate results
- Faster turn around time for most results

CDC NEW HIV DIAGNOSTIC TESTING ALGORITHM

Laboratory Testing for the Diagnosis of HIV Infections: Updated Recommendations
http://stacks.cdc.gov/view/cdc/23447

NEW HIV DIAGNOSTIC TESTING ALGORITHM

Box 1. Recommended Laboratory HIV Testing Algorithms for Serum or Plasma Specimens

1. Laboratories must conduct initial testing for HIV-1 using a rapid HIV test and ELISA or alternate rapid test that can be reactive for HIV-1, HIV-2, antibodies to p24, and antibodies to HIV-1 core antigen to resolve indeterminate results. No further testing is required for specimens that are reactive on the initial diagnosis.
Impact of Missing One Case of AHI: North Carolina

Dr. Peter Leone MD
Professor of Medicine, University of North Carolina
Medical Director, North Carolina HIV/STD Prevention and Care

Difference in Clinical Sensitivity of Combo Tests

17 ACUTE HIV CASES DETECTED BY SAN DIEGO PHL

<table>
<thead>
<tr>
<th>Test Description</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV Combo detected</td>
<td>17 Acute HIV Patients</td>
</tr>
<tr>
<td>HIV Combo 4th GEN NON-REACTIVE</td>
<td>14,238</td>
</tr>
<tr>
<td>HIV COMBO 4th GEN REPEAT REACTIVE</td>
<td>279</td>
</tr>
<tr>
<td>HIV COMBO 4th GEN REPEAT REACTIVE &amp; IFA POSITIVE</td>
<td>240</td>
</tr>
<tr>
<td>HIV COMBO 4th GEN REPEAT REACTIVE &amp; IFA NEGATIVE</td>
<td>36**</td>
</tr>
<tr>
<td>HIV COMBO 4th GEN REPEAT REACTIVE &amp; RNA POSITIVE</td>
<td>17</td>
</tr>
<tr>
<td>HIV COMBO 4th GEN REPEAT REACTIVE &amp; RNA NEGATIVE</td>
<td>13</td>
</tr>
<tr>
<td>HIV COMBO 4th GEN REPEAT REACTIVE &amp; STATE LAB POSITIVE</td>
<td>16</td>
</tr>
<tr>
<td>HIV COMBO 4th GEN REPEAT REACTIVE &amp; STATE LAB NEGATIVE</td>
<td>12</td>
</tr>
<tr>
<td>HIV COMBO 4th GEN REPEAT REACTIVE &amp; STATE LAB INCONCLUSIVE</td>
<td>3</td>
</tr>
</tbody>
</table>

March 2011 to November 15, 2012
TOTAL SAMPLES: 14,559
MOVING HIV DIAGNOSTICS FORWARD: HIV TESTING IS A KEY COMPONENT OF PREVENTION

Implementation of the new CDC HIV testing guidelines impacts patient care and prevents new transmissions:

- More Testing
  - Everyone should know their HIV status
- Maximize benefit of testing by using the most sensitive test
- Earlier Diagnosis
  - Linkage to health care
  - Prevent further transmissions
- Simplified testing algorithm
  - Requires only 3 assays
  - Priority on sensitivity
  - Reduces time to report positive result
  - Increases accuracy of result

SUMMARY

- Genetic diversity of HIV can impact the performance of diagnostic and blood screening assays
- Abbott’s HIV assays have been designed to detect all available viral variants and mutants
  - Global surveillance studies will continue to monitor the changing diversity of these viruses and to make adjustments to assays to ensure continued detection
- The CDC has issued recommendations for HIV testing practices:
  - For HIV, fourth generation HIV combination ag/ab tests are recommended

HBsAg Detection

Put science on your side.
HBV GLOBAL PREVALENCE

Globally 350 million persons are chronically infected
With ~1 million deaths per yr

http://www.who.int/csr/disease/hepatitis/HepatitisB_whocdscsrlyo2002_2.pdf

Abbott Hepatitis Milestones:
40th anniversary of HBsAg screening in 2012

BLOOD SCREENING TESTS HAVE MINIMIZED THE RISK OF POST-TRANSFUSION HEPATITIS

Adapted from CDC data.
**HBV PREVALENCE AND PREDOMINATE GENOTYPE**

- High (≥ 8%)
- Intermediate (2% to 8%)
- Low (< 2%)

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**HBSAG A-DETERMINANT**

- G145R the most prevalent mutant

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**ARCHITECT HBsAg : Mutant Detection**

- Most HbsAg assays have monoclonal antibodies against epitopes in the amino acid region 139–147
- Antibody does not bind to HBsAg
- Produces False Negative Result

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P. Martin, University of Miami
HBSAg MUTANTS – NEW THREAT

HBsAg carriers with variants showing escape mutant characteristics have been found in:

- renal dialysis patients
- pregnant women
- blood and plasma donors

HBV SURVEILLANCE PROGRAM

Primary Goals:

- Establish well characterized specimen panels representing:
  - Native HBV sAg mutants
  - HBV sAg genotype/subtypes
  - HBsAg global specimen panel for assay development and to evaluate assay performance

- HBsAg is key marker for acute and chronic HBV infection
- HBsAg mutants are prevalent worldwide
  - Mutations in the HBsAg "a" determinant arise naturally in chronic carriers
    - Immune escape
    - Vaccine escape
  - HBsAg mutations can lead to altered antibody recognition sites and impact diagnostic assays
    - Knock out detection
    - Reduced analytical sensitivity
  - Historically used recombinant HBsAg mutants to demonstrate assay performance but conflicting data driving trend to "real" mutants i.e. occur in human population:
- Surveillance program will focus on finding naturally occurring HBsAg mutants to supplement recombinant HBsAg mutants
HBSAG MUTANTS:
REPORTS TO FDA WEB SITE

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>Report Date</th>
<th>Report No.</th>
<th>Adverse Event</th>
</tr>
</thead>
</table>
| Ortho Antibody to HBsAg ELISA Test System 3 | 26 June, 2003 (Aware Date: 02 April, 2002) | 2250051-2003-00828         | Customer identified a sample that was negative in Ortho HBsAg System 3 ELISA,
|                     |                              |                         | but positive on the Murex HBsAg ELISA. Sample was later determined to be an HBsAg mutant |
| Ortho Antibody to HBsAg ELISA Test System 3 | 26 June, 2003 (Aware Date: 19 May, 2003) | 2250051-2003-00829        | Customer identified a sample that was negative in Ortho HBsAg System 3 ELISA,
|                     |                              |                         | but positive on the Abbott PRISM HBsAg CHLIA and Abbott AxSYM HBsAg CHLIA. Sample was later determined to be an HBsAg mutant |

HBsAg: Mutant Detection

<table>
<thead>
<tr>
<th>Assay</th>
<th>Sensitivity (S/CO)</th>
<th>Regev (S/CO)</th>
<th>Regen (S/CO)</th>
<th>Ortho* (S/CO)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive-Control</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Sample 1</td>
<td>0.22</td>
<td>0.22</td>
<td>0.22</td>
<td>-</td>
</tr>
<tr>
<td>Sample 2</td>
<td>0.22</td>
<td>0.22</td>
<td>0.22</td>
<td>-</td>
</tr>
<tr>
<td>Sample 3</td>
<td>0.22</td>
<td>0.22</td>
<td>0.22</td>
<td>-</td>
</tr>
<tr>
<td>Sample 4</td>
<td>0.22</td>
<td>0.22</td>
<td>0.22</td>
<td>-</td>
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<tr>
<td>Sample 5</td>
<td>0.22</td>
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<td>0.22</td>
<td>-</td>
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<tr>
<td>Sample 6</td>
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<tr>
<td>Sample 7</td>
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<td>0.22</td>
<td>0.22</td>
<td>-</td>
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<tr>
<td>Sample 8</td>
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<td>0.22</td>
<td>0.22</td>
<td>-</td>
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<tr>
<td>Sample 9</td>
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<td>0.22</td>
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<td>-</td>
</tr>
<tr>
<td>Sample 10</td>
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<td>0.22</td>
<td>0.22</td>
<td>-</td>
</tr>
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<td>Sample 11</td>
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<td>Sample 12</td>
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<td>-</td>
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<td>Sample 13</td>
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<td>-</td>
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<td>Sample 14</td>
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<td>Sample 15</td>
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<td>Sample 16</td>
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<td>Sample 17</td>
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<td>Sample 18</td>
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<td>Sample 19</td>
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<tr>
<td>Sample 20</td>
<td>0.22</td>
<td>0.22</td>
<td>0.22</td>
<td>-</td>
</tr>
</tbody>
</table>

*AxSYM HBsAg Assay was tested in each participating lab, i.e. three estimates

Note: S/CO values 1.0 are reactive for each assay, negative results are shaded

Table 2: Detection of HBsAg mutants by different HBsAg assays


PAKISTAN BLOOD DONORS

- Identified 39 mutants (39/1769; 2.2%)
- PCR and sequencing confirmed mutations
  - 121-124 loop: Q30K, T123S, N131K
  - 139-147 loop: S143L
  - 139-147 loop: L26L/R, S143L, T189T/I,
  - 139-147 loop: C76C/Y, G145G/R, V177V/A
  - 139-147 loop: L104L/W, S143S/L
  - 139-147 loop: N40S, S143L
  - 139-147 loop: L109M, M133I, D144A, G145R
  - both loops: T118T/A, T123T/I, S143S/L, E164E/D, L175L/S
  - between loops: T127P/L, Q139Q/H

- Many mutants have vaccine escape mutations
- All are genotype D, subtype ayw2
- Genotype A and C also present in population at low frequency

SUMMARY

- HBsAg mutants can impact the performance of diagnostic and blood screening assays
- Abbott’s HBV assays have been designed to detect all available mutants
- global surveillance studies will continue to monitor the changing diversity of these viruses and to make adjustments to assays to ensure continued detection
Despite falling incidence, a substantial burden of disease exists in the US due to the propensity of HCV establish chronic infections.
ADVANCES IN ANTIVIRAL THERAPY

NEWLY APPROVED ANTIVIRAL - SOFOBUVIR (SOF) (GS-7977)

NS5B nucleotide polymerase inhibitor

- Once daily, well-tolerated regimen

- 12 weeks of SOF+PEG+RBV achieved 90% SVR in treatment naïve patients with GT 1, 4, 5, or 6

- 90% of patients had HCV RNA < LLOQ by treatment week 4 and all virologic failures were due to relapse

Prevalence of HCV among Persons Born 1945-1965

- 74% of 2.7-3.9 M HCV infected

- Prevalence 5-5 times higher than other ages (3.29% vs 0.55%) ²

- 73% of all HCV-associated mortality ³

HEPATITIS C TESTING RECOMMENDATIONS

Testing Recommendations for Chronic Hepatitis C Virus Infection
In August 2012, CDC published Recommendations for the Identification of Chronic Hepatitis C Virus Infection Among Persons Born During 1945–1965 (MMWR 2012;61(RR04);1-18).

Person who should be tested once for hepatitis C virus (HCV) infection without prior ascertainment of HCV risk factors include: Adults born during 1945 through 1965

http://www.cdc.gov/mmwr/preview/mmwrhtml/rr6104a1.htm

Laboratory Diagnosis of HCV Infection

Two clinical outcomes from acute HCV infection (serologic patterns):

1. Acute HCV Infection with Recovery
   - Time after Exposure: 01 2 3 4 5 6 12 3 4
   - Titer: Normal
   - HCV-RNA: Negative
   - HCV Core Ag: Negative
   - Symptoms: +/−

2. Acute HCV Infection with Progression to Chronic Infection
   - Time after Exposure: 0 1 2 3 4
   - Titer: Normal
   - HCV-RNA: Positive
   - HCV Core Ag: Positive
   - Symptoms: +/−

New CDC Guidelines for HCV Testing

Proprietary and confidential — do not distribute
SUMMARY

- HIV and Hepatitis B are major global health problems.
- Genetic diversity of HIV and HBV can impact the performance of diagnostic and blood screening assays
- Abbott's HIV and HBV assays have been designed to detect all available viral variants and mutants
  - Global surveillance studies will continue to monitor the changing diversity of these viruses and to make adjustments to assays to ensure continued detection
- The CDC has issued recommendations for HIV and HCV testing practices:
  - For HIV, fourth-generation HIV combination ag/ab tests are recommended
  - For HCV, the CDC has recommended that HCV RNA testing should be the test of choice for determining the status of HCV seropositive individuals
  - The CDC has recommended that all individuals born between 1945 and 1965 be tested for HCV