Disclosure Information

- Scientific advisory board member: Gilead Sciences, Inc, Monogram Biosciences, GlobeImmune, Inc
- Grant support: Boehringer Ingelheim, Bristol-Myers Squibb
- Scientific collaborator: MBio Diagnostics
- Consultant: Santaris Pharma A/S, Merck & Co, Inc
- Stockholder: GlobeImmune, Inc
Laboratory Diagnostics in HCV Infection

- Diagnosis of HCV infection
- Communicating the results to the patient
- Linkage to care
Diagnosis of HCV Infection
Recommended Testing Sequence for Identifying Current HCV infection

HCV ANTIBODY
Serologic Diagnosis of Current HCV Infection

**Primary screening test**

<table>
<thead>
<tr>
<th></th>
<th>Core</th>
<th>NS3</th>
<th>NS4a</th>
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</tr>
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<tbody>
<tr>
<td>EIA 1.0</td>
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<td></td>
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<td>EIA 2.0</td>
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<td>EIA/CIA 3.0</td>
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</tbody>
</table>

EIA = enzyme immunoassay  
CIA = chemiluminescence assay

MMWR 1998 and MMWR 2003; Adapted from Kamili et al, Clin Infect Dis, 2012, S1
### Serologic Diagnosis of Current HCV Infection

#### Primary screening test

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#### Confirmatory test*

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RIBA = recombinant immunoblot assay

*MMWR 1998 and MMWR 2003; Adapted from Kamili et al, Clin Infect Dis, 2012, S1
Serologic Diagnosis of Current HCV Infection

### Primary screening test

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### Confirmatory test

*Not required in 2013 revision*

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MMWR 1998 and MMWR 2003; Adapted from Kamili et al, Clin Infect Dis, 2012, S1
## Confirmatory Test Substitution by Sample-to-Cutoff (S/Co) Ratio

<table>
<thead>
<tr>
<th>Assay</th>
<th>Manufacturer</th>
<th>S/Co for &gt;95% specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abbott HCV EIA 2.0</td>
<td>Abbott</td>
<td>≥3.8</td>
</tr>
<tr>
<td>AxSYM Anti-HCV</td>
<td>Abbott</td>
<td>≥10.0</td>
</tr>
<tr>
<td>Architect Anti-HCV</td>
<td>Abbott</td>
<td>≥5.0</td>
</tr>
<tr>
<td>Ortho EIA 3.0</td>
<td>Ortho</td>
<td>≥3.8</td>
</tr>
<tr>
<td>Vitros Anti-HCV</td>
<td>Ortho</td>
<td>≥8.0</td>
</tr>
<tr>
<td>Advia Centaur HCV</td>
<td>Siemens</td>
<td>≥11.0</td>
</tr>
</tbody>
</table>

MMWR, 2003; Adapted from Kamili et al, Clin Infect Dis 2012, S1
Recommended Testing Sequence for Identifying Current HCV infection

- **HCV ANTIBODY**
  - **NON-REACTIVE**
    - **STOP***
Recommended Testing Sequence for Identifying Current HCV infection

- **HCV ANTIBODY**
  - **NON-REACTIVE**
    - **STOP**
      - *Repeat HCV Ab testing if HCV exposure within past 6 months*

CDC Division of Viral Hepatitis, 2013
Recommended Testing Sequence for Identifying Current HCV infection

CDC Division of Viral Hepatitis, 2013

- **HCV ANTIBODY**
  - NON-REACTIVE
    - STOP*
  - REACTIVE
    - *Repeat HCV Ab testing if HCV exposure within past 6 months
Acute HCV Infection: Viral Clearance or Chronic Infection

Spontaneously Clearing Acute HCV Infection
15% – 35%

Acute ➔ Chronic HCV Infection
65% – 85%
Recommended Testing Sequence for Identifying Current HCV infection

**HCV ANTIBODY**

- **NON-REACTIVE**
  - STOP*

- **REACTIVE**
  - *Repeat HCV Ab testing if HCV exposure within past 6 months

* CDC Division of Viral Hepatitis, 2013
Recommended Testing Sequence for Identifying Current HCV Infection

**HCV ANTIBODY**
- **NON-REACTIVE**
  - **STOP***
  - *Repeat HCV Ab testing if HCV exposure within past 6 months*
- **REACTIVE**
  - **HCV RNA**
    - **DETECTED**
    - **CURRENT HCV INFECTION**
    - **NOT DETECTED**
    - **NO CURRENT HCV INFECTION**
Recommended Testing Sequence for Identifying Current HCV infection

CDC Division of Viral Hepatitis, 2013

**Repeat HCV RNA testing if HCV exposure within past 6 months or recent HCV infection or has clinical evidence of HCV disease**

* Repeat HCV Ab testing if HCV exposure within past 6 months
### Serologic Diagnosis of Chronic HCV Infection

#### Primary screening test

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Nucleic Acid (RNA) Test

MMWR 1998 and MMWR 2003; Adapted from Kamili et al, Clin Infect Dis, 2012, S1
Serologic Diagnosis of Chronic HCV Infection

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Nucleic Acid (RNA) Test

MMWR 1998 and MMWR 2003; Adapted from Kamili et al, Clin Infect Dis, 2012, S1
# Commercially Available Qualitative HCV RNA Assays

<table>
<thead>
<tr>
<th>Assay</th>
<th>Manufacturer</th>
<th>Lower Limit of Detection (LLD), IU/mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Versant HCV RNA</td>
<td>Gen-Probe</td>
<td>10</td>
</tr>
<tr>
<td>Procleix HIV/HCV*</td>
<td>Gen-Probe</td>
<td>&lt;50</td>
</tr>
<tr>
<td>UltraQual HCV RT-PCR</td>
<td>National Genetics</td>
<td>10</td>
</tr>
<tr>
<td>Amplicor HCV v2.0</td>
<td>Roche</td>
<td>50</td>
</tr>
<tr>
<td>COBAS Amplicor HCV v2.0</td>
<td>Roche</td>
<td>50</td>
</tr>
<tr>
<td>AmpliScreen*</td>
<td>Roche</td>
<td>&lt;50</td>
</tr>
</tbody>
</table>

* Blood screening only

Adapted from Kamili, et. al, Clin Infect Dis 2012, S1
# Commercially Available Quantitative HCV RNA Assays

<table>
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<th>Assay</th>
<th>Manufacturer</th>
<th>LLD, (Dynamic Range) IU/mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>LCx HCV RNA Quantitative*</td>
<td>Abbott</td>
<td>25 (25-2,630,000)</td>
</tr>
<tr>
<td>RealTime HCV/m2000sp/m200ort</td>
<td>Abbott</td>
<td>12 (12 – 100,000,000)</td>
</tr>
<tr>
<td>HCV SuperQuant</td>
<td>National Genetics</td>
<td>20 (20 – 1,000,000)</td>
</tr>
<tr>
<td>Amplicor HCV Monitor</td>
<td>Roche</td>
<td>50 (600 - 700,000)</td>
</tr>
<tr>
<td>COBAS Amplicor HCV Monitor v2.0</td>
<td>Roche</td>
<td>50 (600 - 700,000)</td>
</tr>
<tr>
<td>COBAS Ampliprep/TaqMan</td>
<td>Roche</td>
<td>18 (43-69,000,000)</td>
</tr>
<tr>
<td>Versant HCV RNA 3.0</td>
<td>Siemens</td>
<td>615 (615 – 7,700,000)</td>
</tr>
</tbody>
</table>

* Blood screening only

Adapted from Kamili, et. al, Clin Infect Dis 2012, S1
Communicating the Results to the Patient
Implications of a Negative Anti-HCV Antibody Test and a Negative HCV RNA Test

- Your patient is not currently infected with HCV or is in the early “window period” between infection and the appearance of anti-HCV antibodies or RNA.
Implications of a Positive Anti-HCV Antibody Test and a Negative HCV RNA Test

- Your patient is not currently infected with HCV
  - Message for the patient:
    - You previously had an HCV infection that was cleared
      - Spontaneous clearance during acute HCV infection
        - More common in patients with the IL28B CC genotype and those not also infected with HIV
      - Clearance as the result of successful HCV treatment
    - If you engaged in activities that put you at risk for HCV infection in the past 6 months, you should be tested again for HCV RNA at least 6 months after your last potential exposure
    - You can be reinfected with HCV if you engage in risk behaviors that are associated with HCV transmission; if you are engaging in these behaviors, HCV RNA testing should be repeated at regulars intervals. You will continue to have HCV antibodies for a prolonged period of time and repeat antibody testing will not be of benefit to you
Implications of a Positive Anti-HCV Antibody Test and a Positive HCV RNA Test

- Your patient is currently infected with HCV
  - **Message for the patient:**
    - You are currently infected with HCV
    - You need to be evaluated to understand the severity of your liver disease and to be counseled about how not to accelerate the damage the virus may be doing to your liver
    - You should be tested for other infections like HBV and HIV that may be transmitted in the same ways as HCV
    - You may benefit from certain vaccinations such as those for HBV and HAV
    - You can transmit the virus to other people
    - HCV can be successfully treated with HCV medications
      - With successful treatment, your viral infection will be cured
      - Your liver disease will stop progressing although you may need to be followed for certain complications of HCV infection
Implications of a Negative Anti-HCV Antibody Test and a Positive HCV RNA Test

**Possibilities**

- Your patient is in the “window period” in the first 6–12 weeks of HCV infection. HCV RNA appears in the blood before HCV antibodies develop
  - If acute HCV infection is suspected, an urgent referral to a practitioner with expertise in treating HCV infection is appropriate because the virus is particularly responsive to therapy within the first 6 months of infection

- Your patient is immunocompromised and is not making detectable antibodies to HCV despite an active HCV infection
  - This is much less common with second and third generation anti-HCV antibody tests but it can occasionally occur in immunocompromised patients, including those with advanced HIV infection or those on dialysis
Linkage to Care
Recommended Testing Sequence for Identifying Current HCV infection

CDC Division of Viral Hepatitis, 2013

**Repeat HCV RNA testing if HCV exposure within past 6 months or recent HCV infection or has clinical evidence of HCV disease**

**Repeat HCV Ab testing if HCV exposure within past 6 months**
Recommended Testing Sequence for Identifying Current HCV infection

Flowchart:
- **HCV ANTIBODY**
  - **NON-REACTIVE**
    - STOP*
  - **REACTIVE**
    - **HCV RNA**
      - **DETECTED**
        - CURRENT HCV INFECTION
      - **NOT DETECTED**
        - NO CURRENT HCV INFECTION
- Link to Care

*Repeat HCV Ab testing if HCV exposure within past 6 months

**Repeat HCV RNA testing if HCV exposure within past 6 months or recent HCV infection or has clinical evidence of HCV disease**
Linkage to Care

The primary reason to offer testing for HCV infection is to identify those who are candidates for anti-HCV therapy.

Newer anti-HCV regimens (and those in development) are:
- Associated with substantially higher treatment success rates
- Much better tolerated
- Increasingly all-oral and interferon-free
- Usually shorter in duration
Contemporary diagnosis and management of HCV infection requires an understanding of the proper use of serological and molecular tools for the detection of HCV infection and for monitoring the response to therapy.

HCV antibody tests are useful for the diagnosis of a prior or current HCV infection.

HCV RNA assays are useful in the diagnosis of current infection and in monitoring the success of HCV therapy.

Detection of HCV infection and linkage of those who are infected to medical care has the potential to substantially improve quality and quantity of life, and to reduce the risk that HCV will be transmitted to others.
End

This presentation is brought to you by the International Antiviral Society-USA (IAS-USA) in collaboration with Hepatitis Web Study & the Hepatitis C Online Course

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