Public Health Impact of Hepatitis C

www.michigan.gov/hepatitis

May 15, 2014

Joe Coyle, MPH
The Virus and the Disease
Hepatitis

- Hepatitis is characterized by inflammation of the liver which is a result of cellular damage.
- Inflammation of the liver can impair liver function.
Causes of Hepatitis

- The most common cause of hepatitis are the hepatitis viruses (hepatitis A, B, C, D, E)

- Non-infectious hepatitis can be caused by:
  - Alcohol consumption
  - Toxins and drugs (acetaminophen)
  - Autoimmune diseases

Table 3. Hepatitis symptoms:

<table>
<thead>
<tr>
<th>Flulike Symptoms</th>
<th>Other Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>Dark urine</td>
</tr>
<tr>
<td>Fatigue</td>
<td>Clay-colored stool</td>
</tr>
<tr>
<td>Nausea</td>
<td>Abdominal pain</td>
</tr>
<tr>
<td>Vomiting</td>
<td>Jaundice</td>
</tr>
<tr>
<td>Loss of appetite</td>
<td></td>
</tr>
<tr>
<td>Joint pain</td>
<td></td>
</tr>
</tbody>
</table>
# Viral Hepatitis

## Table 2. Important characteristics of common hepatitis viral infections

<table>
<thead>
<tr>
<th>Source of Virus</th>
<th>HAV</th>
<th>HBV</th>
<th>HCV</th>
<th>HDV</th>
<th>HEV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Route of Transmission</td>
<td>Feces</td>
<td>Blood / some body fluids</td>
<td>Blood / some body fluids</td>
<td>Blood / some body fluids</td>
<td>Feces</td>
</tr>
<tr>
<td>Chronic Infection</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>Prevention</td>
<td>• Pre / post exposure immunization</td>
<td>• Pre / post exposure immunization</td>
<td>• Risk behavior modification</td>
<td>• Pre / post exposure immunization with HBV vaccine</td>
<td>• Access to clean drinking water</td>
</tr>
<tr>
<td></td>
<td>• Hand hygiene</td>
<td>• HBIG</td>
<td></td>
<td>• Risk behavior modification</td>
<td>• Hand hygiene</td>
</tr>
<tr>
<td></td>
<td>• Total Ig</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vaccine</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

Ig: immunoglobulin; HBIG: hepatitis B immunoglobulin

---

**An Overview of Viral Hepatitis**
Hepatitis C Virus

- Hepatitis C is a disease of the liver caused by the Hepatitis C Virus (HCV)
- Called “non-A non-B hepatitis” until its identification in 1989
- HCV is a blood-borne pathogen meaning it spreads from person-to-person via contaminated blood
There are two stages of Hepatitis C:

- **Acute** – short-term illness presenting 2 weeks to 6 months after exposure to HCV
  - Symptomatic in only 15% of cases
  - Symptoms: fever, fatigue, loss of appetite, nausea, abdominal pain, dark urine, grey-colored stool, and jaundice

- **Chronic** – long-term illness that can last a lifetime
  - Over time chronic HCV infection can lead to liver damage, liver cirrhosis, liver failure and liver cancer

www.cdc.gov/hepatitis/HCV/PDFs/HepCGeneralFactSheet.pdf
HCV Infection

Epidemiology and Health Impact
Global Burden of HCV

- 180 million people are infected with HCV
- 3-4 million new HCV infections each year
- 350,000 attributable deaths each year
HCV in the U.S.

- CDC estimates that 2.7-3.9 million persons in the U.S. have chronic HCV infection (1.3-1.9% of the population)

- HCV plays a role in ~12,000 deaths per year

- US citizens with HCV died 22-23 years earlier than those without HCV

Testing

HEPATITIS C VIRUS IS NEARLY 4 TIMES AS PREVALENT AS HIV AND HEPATITIS B VIRUS IN THE UNITED STATES

Number of Infected Individuals vs Number Aware They Are Infected (Diagnosed)

- HIV
  - 1.1 Million
  - 21% Undiagnosed

- HEPATITIS B
  - ~800,000 to 1.4 Million
  - 65% Undiagnosed

- HEPATITIS C
  - ~2.7 Million to 3.9 Million
  - 75% Undiagnosed

Baby-Boomers (Born 1945-1965)

**Number of Chronic Hepatitis C Cases Reported to MDCH by Birth Year**

- **1945-1965**


- **1988–1994**
- **1999–2002**

August 2012 - CDC recommends all persons born between 1945 and 1965 receive one-time testing for HCV antibody

June 2013 - United States Preventative Services Task Force recommends all persons born between 1945 and 1965 receive one-time testing for HCV antibody

October 2013 - Legislation in NY State requires physicians to offer HCV test to patients born between 1945 and 1965
**Improved Treatments**

**SVR Rates in Patients With HCV**

<table>
<thead>
<tr>
<th>Year</th>
<th>SVR Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1986</td>
<td>6</td>
</tr>
<tr>
<td>1998</td>
<td>16</td>
</tr>
<tr>
<td>2001</td>
<td>34</td>
</tr>
<tr>
<td>2002</td>
<td>42</td>
</tr>
<tr>
<td>2011</td>
<td>39</td>
</tr>
<tr>
<td>2013*</td>
<td>54-56</td>
</tr>
<tr>
<td></td>
<td>68-75</td>
</tr>
<tr>
<td></td>
<td>80-81†</td>
</tr>
<tr>
<td></td>
<td>91†</td>
</tr>
</tbody>
</table>

- **IFN 6 mo**
- **IFN 12 mo**
- **IFN/RBV 6 mo**
- **IFN/RBV 12 mo**
- **PEG-IFN 12 mo**
- **PEG-IFN/RBV 12 mo**
- **PI/PEG-IFN/RBV 6-12 mo**
- **SMV + PEG-IFN/RBV 6-12 mo**
- **SOF/PEG-IFN/RBV 3 mo**

*Year of presentation of QUEST-1, QUEST-2, and NEUTRINO
†SVR12 rate of 80-81% among GT 1 patients in the Phase 3 studies QUEST-1 and QUEST-2 (24-48 weeks of SMV+PEG-IFN+RBV)
‡SVR12 rate of 90% among GT 1 patients in the Phase 3 NEUTRINO trial (12 weeks of SOF+PEG-IFN+RBV)

Treatment Cascade

- 3.2 million of U.S. population with chronic HCV infection
  - 1.6 million (50%) had HCV detected
    - 1.0–1.2 million (32–38%) were referred to care
      - 630,000–750,000 (20–23%) had HCV RNA test
        - 380,000–560,000 (12–18%) underwent liver biopsy
          - 220,000–360,000 (7–11%) were treated
            - 170,000–200,000 (5–6%) were successfully treated

Confirmed Cases of Hepatitis C Infection Michigan, 2004 and 2012

2004*

- No. of Cases reported for year
- Female
- Male

2012†

- No. of Cases reported for year
- Female
- Male

* N = 5,270; excludes 38 cases with missing age or sex information
† N = 7,968; excludes 56 cases with missing age or sex information
Young Adults with HCV Infection

Chronic Hepatitis C Cases among persons aged 18 to 25 reported to MDSS

<table>
<thead>
<tr>
<th>Year</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>2004</td>
<td>165</td>
</tr>
<tr>
<td>2005</td>
<td>228</td>
</tr>
<tr>
<td>2006</td>
<td>310</td>
</tr>
<tr>
<td>2007</td>
<td>272</td>
</tr>
<tr>
<td>2008</td>
<td>408</td>
</tr>
<tr>
<td>2009</td>
<td>449</td>
</tr>
<tr>
<td>2010</td>
<td>515</td>
</tr>
<tr>
<td>2011</td>
<td>717</td>
</tr>
<tr>
<td>2012</td>
<td>784</td>
</tr>
</tbody>
</table>
Funding?

US RESPONSE TO HIV AND VIRAL HEPATITIS EPIDEMICS
Hepatitis C infection is at least five times more prevalent as HIV infection in the United States, yet funding lags far behind.
Hepatitis C Surveillance and Reporting
Clinical HCV Testing

Patient clears HCV infection (~15-25%)

Persistent HCV infection (~75-85%)
Positive Hepatitis C tests are required to be reported:
- HCV Antibody tests
- Qualitative and Quantitative HCV RNA tests
- HCV Genotype tests

HCV cases are classified according to CDC/CSTE case definitions.

<table>
<thead>
<tr>
<th></th>
<th>Unknown</th>
<th>Suspect</th>
<th>Probable</th>
<th>Confirmed</th>
<th>Not a Case</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatitis C, Acute</td>
<td>×</td>
<td>×</td>
<td>×</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Hepatitis C, Past or Present</td>
<td>×</td>
<td>×</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

HCV Labs

- HCV Antibody (Anti-HCV, HCV Ab) – detects the presence of antibodies against the Hepatitis C Virus:
  - With high S/CO Ratio:
  - Without S/CO Ratio:
## Signal to Cutoff Ratios

<table>
<thead>
<tr>
<th>Screening Test Kit Name</th>
<th>Manufacturer</th>
<th>Assay Format</th>
<th>Signal-to-cut–off ratio predictive of a true positive ≥ 95% of the time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ortho HCV Version 3.0 ELISA Test System</td>
<td>Ortho</td>
<td>EIA (Enzyme Immunoassay)</td>
<td>≥ 3.8</td>
</tr>
<tr>
<td>Abbott HCV EIA 2.0</td>
<td>Abbott</td>
<td>EIA (Enzyme Immunoassay)</td>
<td>≥ 3.8</td>
</tr>
<tr>
<td>VITROS Anti-HCV</td>
<td>Ortho</td>
<td>CIA (Chemiluminescent Immunoassay)</td>
<td>≥ 8.0</td>
</tr>
<tr>
<td>AxSYM Anti-HCV</td>
<td>Abbott</td>
<td>MEIA (Microparticle Immunoassay)</td>
<td>≥ 10.0</td>
</tr>
<tr>
<td>Architect Anti-HCV</td>
<td>Abbott</td>
<td>CMIA (Chemiluminescent Microparticle Immunoassay)</td>
<td>≥ 5.0</td>
</tr>
<tr>
<td>Advia Centaur HCV</td>
<td>Bayer</td>
<td>CIA (Chemiluminescent Immunoassay)</td>
<td>≥ 11.0</td>
</tr>
</tbody>
</table>
HCV Nucleic Acid Tests

- An HCV Nucleic Acid Test (NAT) must be conducted to detect the Hepatitis C virus itself:
  - HCV RNA Quantitative PCR:
    
    | Reported Test Name | Result                  |
    |--------------------|-------------------------|
    | HCV RNA SERPL PCR-ACNC/HCV RNA, QUANTITATIVE REAL TIME PCR | 8810 IU/MLIU/MLL |
  
  - HCV RNA Qualitative PCR:

    | Reported Test Name | Result                  |
    |--------------------|-------------------------|
    | Hepatitis C virus RNA/HCV RNA | Detected |
    | Coded Result      | Detected               |
    | Alternate Coded Result | Detected         |
    | Numeric Result    |                         |
    | Abnormal Flags/Susceptibility Results | N |
    | Comments           | Reference Range: Not Detected \ Lower limit of detection is 1,000 IU/ml |
  
  - HCV Genotype:

    | Reported Test Name | Result                  |
    |--------------------|-------------------------|
    | HCV GENTYP SERPL PCR/HCV GENOTYPE, LIPA | GENOTYPE 1b |
    | Alternate Coded Result | GENOTYPE 1b            |
    | Numeric Result    |                         |
HCV Quantitative Tests

- Negative / Not Detected

- Some number IU/mL (e.g. 3,562,822 IU/mL)

- < Some number IU/mL (e.g. <43 IU/mL)
Option 1:
- Discrete onset of acute symptoms (fever, headache, malaise, anorexia, nausea, vomiting, diarrhea, abdominal pain)

AND

- Jaundice OR serum alanine aminotransferase (ALT) > 400IU/L

AND
Hepatitis C, Acute - Confirmed

- One or more of the following:
  - Positive HCV antibody result with a signal-to-cutoff ratio predictive of true positive
  - Positive HCV nucleic acid test (quantitative, qualitative, genotype)

  **AND (if done)**

- Negative Hepatitis A IgM Antibody **AND**
- Negative Hepatitis B core antigen IgM Antibody
Hepatitis C, Acute - Confirmed

- Option 2:
  - One or more of the following:
    - HCV antibody positive result with a signal-to-cutoff ratio predictive of true positive
    - HCV nucleic acid test positive (quantitative, qualitative, genotype)

  AND

  - A negative HCV antibody test in the 6 months preceding the positive result
Omar
Hepatitis C, Past or Present – Confirmed

- Must meet the following criteria:
  - One or more of the following:
    - HCV antibody positive result with a signal-to-cutoff ratio predictive of true positive
    - HCV nucleic acid test positive (quantitative, qualitative, genotype) – this must be true for patients <18 months old

  AND

- Does not meet the definition for Hepatitis C, Acute
Hepatitis C, Past or Present – Probable

- Must meet the following criteria:
  - Positive HCV Antibody test with unknown signal-to-cutoff ratio
  - ALT values above the upper limit of normal
  - Does not meet the case definition for Hepatitis C, Acute
Evidence of acute illness with a discrete onset of any sign or symptom, consistent with acute viral hepatitis (e.g., fever, headache, malaise, anorexia, abdominal discomfort, diarrhea, nausea, vomiting)?

A documented negative HCV antibody laboratory test result followed within 6 months by a positive test result does not require symptoms to meet acute case definition.

Chronic Hepatitis C Track

Anti-HCV positive by EIA?

- NO
  - Nucleic acid test for HCV RNA positive OR Report of HCV Genotype?
    - NO
      - Not a Case
    - YES
      - Confirmed Hep C, Chronic
  - YES
    - Verified by a more specific assay such as nucleic acid testing?
      - NO
        - Anti-HCV screening test positive with a signal to cut-off ratio predictive of a true positive?
          - NO
            - ALT levels above the upper limit of normal? (Only if signal to cut-off ratio unknown for antibody test)
              - NO
                - Not a Case
              - YES
                - Probable Hep C, Chronic
          - YES
            - Confirmed Hep C, Chronic
      - YES
        - Not a Case

Acute Hepatitis C Track

Known to have chronic hepatitis C?

- NO
  - Jaundice OR ALT>400 IU/L?
    - NO
      - Not a Case of Hep C, Acute
    - YES
      - HCV RNA positive OR Anti-HCV positive with a signal to cut-off ratio predictive of a true positive?
        - NO
          - IgM anti-HAV negative AND IgM anti-HBc negative?
            - (ONLY IF BOTH TESTS PERFORMED*)
              - YES
                - Confirmed Hep C, Acute
              - NO
                - Not a Case
        - YES
          - Consider Hep C, Chronic

*IF TESTS NOT PERFORMED OR NOTED, SKIP THIS STEP

Hepatitis C Reporting Flowchart

Michigan Department of Community Health – Revised 04/2013
HEPATITIS C LABORATORY TEST REPORTED

Hepatitis C antibody positive?

YES → Signal to cut-off (S/CO) ratio predictive of true positive?

YES → ALT levels above the upper limit of normal?

YES → Probable, Past or Present Hepatitis C

NO → Confirmed, Past or Present Hepatitis C

UNKNOWN → Confirmed, Acute Hepatitis C

NO → HCV Nucleic Acid Test positive? (RNA Qualitative, RNA Quantitative, Genotype)

YES → Does patient have symptoms of acute hepatitis C?

YES → ALT levels >400 IU/mL or sign of jaundice?

YES → IgM anti-HAV negative and IgM anti-HBc negative?

YES → Not a Case

NO → Not a Case

NOTE:

- A documented negative HCV antibody laboratory test result followed within 6 months by a positive test result does not require symptoms to meet acute case definition.
- Persons less than 18 months of age can only be classified as confirmed, past or present hepatitis C with a positive HCV RNA test.
- Symptoms of acute hepatitis C infection include fever, headache, malaise, anorexia, abdominal discomfort, diarrhea, nausea, and vomiting.
Deduplication

- A person should only be counted once in their lifetime for chronic HCV

- For people with multiple HCV positive labs:
  - Merge the patient and merge the case

- A person can be an acute case and a chronic case if the labs are >6 months apart:
  - Merge the patient, create a new case
Case Follow-up

- For completed cases meeting a CDC/CSTE case definition:

  **Type of Case**
  - Follow-up
  - Active
  - Passive

  **Hepatitis C Case**
  - Acute Cases
  - Young Adults (ages 18-25)
  - Persons Born Before 1945
  - Other Groups
Resources

- CDC/CSTE Case Definitions -

- www.cdc.gov/hepatitis

- www.cdc.gov/knowmorehepatitis

- www.cdc.gov/knowhepatitisb

- www.michigan.gov/hepatitis

- www.michigan.gov/hepatitisb

- www.michigan.gov/cdinfo
Thanks!

Joe Coyle, MPH
CoyleJ@michigan.gov
MDCH-Hepatitis@michigan.gov
www.michigan.gov/hepatitis
517-335-8165