**Chronic hepatitis C:**
Do we have Cure
Do we need liver biopsy

Mumtaz Niazi MD
Assistant Professor of Medicine
Avera Center For Liver Disease
Avera McKennan Hospital& University Health Center
Sioux Falls, South Dakota

---

**HCV History**
- It is a RNA virus
- Used to be known as non-A, non-B hepatitis until it was discovered in 1988\(^1\)
- No vaccine available
- First therapy approved in 1991\(^2\)
- Before 2011, HCV treatment could last as long as a year, with cure (SVR) rates of 40%–50% for the most common genotype in the US\(^3\)
- Since that time, scientific advances have made HCV treatment shorter and more effective

---

**Prevalence**

<table>
<thead>
<tr>
<th>Country</th>
<th>HCV Positive</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Worldwide</td>
<td>170 million</td>
<td>3%</td>
</tr>
<tr>
<td>United States</td>
<td>3.9 million</td>
<td>1.8%</td>
</tr>
<tr>
<td>United States</td>
<td>2.7 million</td>
<td>1.4%</td>
</tr>
</tbody>
</table>

---

**Screening recommendations by CDC**
- Adults born during 1945–1965 should receive one-time testing for HCV without prior ascertainment of HCV risk.
- All HCV infected individuals should receive a brief alcohol screening and intervention as clinically indicated, followed by referral to appropriate care and treatment services for HCV infection and related conditions.

---

**Prevalence of HCV antibody by year of Birth**

- 5X higher
- Prevalence of HCV antibody in adults born between 1945 and 1965 vs adults born in other years

---

1. CDC. MMWR 1998;47(No. RR–19)
2. CDC. Recommendations for the identification of chronic hepatitis C virus infection among persons born during 1945–1965. MMWR 2012;61(No. RR–4)
HCV is underdiagnosed and undertreated

- It is estimated that 3.5 million Americans have chronic hepatitis C and approximately 9% of infected individuals have been successfully treated\(^1\)


CDC, USPSTF, and AASLD recommend the one-time screening of all baby boomers, regardless of risk factors\(^1-3\)

Baby boomers: born between 1945 and 1965

- About 9% successfully treated

CDC, USPSTF, and AASLD


HCV has a mortality rate that exceeds HIV


Anti-HCV Antibody Testing

- ELISA screening tests
- Detect circulating HCV antibodies
- Sensitivity: 97% to 100%
- Positive predictive value
  - 95% with risk factors and elevated ALT
  - 50% without risk factors and normal ALT

\(\text{False Positive More Likely in:} \quad \text{False Negative More Likely in:} \)

<table>
<thead>
<tr>
<th>Patients with low risk of HCV infection</th>
<th>Severely immunosuppressed patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transplantation recipients</td>
<td>Patients with chronic renal failure on dialysis</td>
</tr>
<tr>
<td>HIV-positive patients</td>
<td>HIV-positive patients</td>
</tr>
</tbody>
</table>


AASLD Counseling Guidelines

- Avoid sharing dental or shaving equipment
- Cover bleeding wounds to prevent contact with others
- Discontinue illicit injection drug use; if injection drug use continues:
  - Avoid reusing/sharing needles/syringes
  - Clean injection site with fresh alcohol swab
- Do not donate blood, organs, tissue, or semen
- Due to low sexual transmission rate, barrier protection not needed in monogamous relationships; otherwise, safe sex practices warranted
- No Alcohol
- HAV and HBV vaccinations.
- Hepatitis C does is not spread by kissing, hugging, sneezing, coughing, or sharing food, eating utensils or glasses.

### Outcome Following Hepatitis C Infection

- **Acute hepatitis C**: 55 - 85%
- **Chronic infection**: 70%
- **Chronic hepatitis**: 20%
- **Cirrhosis**: 4 - 5%/yr
- **Decompensation**: 4 - 5%/yr
- **HCC**: 1 - 4%/yr

<table>
<thead>
<tr>
<th>Time (yr)</th>
<th>Chronic infection</th>
<th>Chronic hepatitis</th>
<th>Cirrhosis</th>
<th>Decompensation</th>
<th>HCC</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-10</td>
<td>55 - 85%</td>
<td>20%</td>
<td>1-4%</td>
<td>4-5%</td>
<td></td>
</tr>
<tr>
<td>10-20</td>
<td>55 - 85%</td>
<td>20%</td>
<td>1-4%</td>
<td>4-5%</td>
<td></td>
</tr>
<tr>
<td>20-30</td>
<td>55 - 85%</td>
<td>20%</td>
<td>1-4%</td>
<td>4-5%</td>
<td></td>
</tr>
<tr>
<td>30+</td>
<td>55 - 85%</td>
<td>20%</td>
<td>1-4%</td>
<td>4-5%</td>
<td></td>
</tr>
</tbody>
</table>

**Factors Associated With Fibrosis**

- Duration of infection
- Alcohol > 50 gm per day
- Age > 40 years at infection
- Male gender

Poynard T, et al., Lancet 1997; 349:821

### Alcohol Consumption Increases Risk of Cirrhosis in HCV Patients

- Excessive alcohol intake characterized as > 40 g/day for women and > 60 g/day for men.
- Duration of exposure defined as either first blood transfusion before 1990 or from the year of initial intravenous drug use.


### HCV–Infected US Population: 2009-2028

- Assuming no changes in standard of care

Total number of patients with advanced liver disease in 20 yrs projected to be > 4-fold higher than today.


### HCV Viremia Was Associated With Increased Mortality in a Prospective Taiwanese Cohort Study

- Anti-HCV+, HCV RNA detectable
- Anti-HCV+, HCV RNA undetectable
- Anti-HCV–

**Hepatocellular carcinoma**

- Liver transplantation
- Decompensated cirrhosis

### Increasing Health Care Costs Associated With Progressive Liver Disease in the Aging HCV-infected Population

While the prevalence of HCV infection is declining from its peak, the incidence of advanced liver disease and associated health care costs continue to rise.

Hepatitis C Virus Genotypes in the USA

- **Type 1**: 72% (1a: 79%, 1b: 21%)
- **Type 2**: 17%
- **Type 3**: 10%
- **All others**: 1%


Goals of Hepatitis C Treatment

**Primary**
- Eradicate the virus

**Secondary**
- Prevent progression to cirrhosis
- Reduce incidence of HCC
- Reduce need for transplantation
- Enhance survival

HCV treatment advances through the years

- **1991**: Standard Interferon
- **1998**: Peginterferon/Ribavirin
- **2001**: Interferon + Ribavirin
- **2011-Present**: Direct acting antiviral Agents

Cure Rate is 90 to 100% depending on genotype

Hypertension
Diabetes
HCV

Unlike Some Chronic Conditions, HCV Can Be Cured

**MANAGEABLE**

**Diabetes**

**CURABLE**

**Hypertension**

**HCV**

SVR Equivalent to Viral Cure

Nearly 100% of patients who achieve SVR remain undetectable during long-term follow-up[1-4]

<table>
<thead>
<tr>
<th>Duration of Follow-up</th>
<th>Patients with SVR (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.2 yrs (mean)</td>
<td>99%</td>
</tr>
<tr>
<td>3.4 yrs (median)</td>
<td>99%</td>
</tr>
<tr>
<td>3.3 yrs (median)</td>
<td>100%</td>
</tr>
<tr>
<td>3.4 yrs (median)</td>
<td>100%</td>
</tr>
</tbody>
</table>

SVR Reduced Risk of All-Cause Mortality in a Retrospective VA Study

- Genotype 1 (n=12,166)
  - SVR rate: 35%
- Genotype 2 (n=2904)
  - SVR rate: 72%
- Genotype 3 (n=1794)
  - SVR rate: 62%


SVR Was Associated With Reduced Long-Term Risk of All-Cause Mortality in an International, Multicenter Study

- Cumulative Mortality (%)
  - Genotype 1
  - Genotype 2
  - Genotype 3

International, multicenter, long-term follow-up study from 5 large tertiary care hospitals in Europe and Canada. Patients with chronic HCV infection started an interferon-based treatment regimen between 1990 and 2003 (n=530).


SVR Reduced HCC and Liver-Related Complications in Patients With Bridging Fibrosis or Cirrhosis

- HCC (n=307)
- Liver-Related Complications (n=307)


SVR Was Associated With Reduced Long-Term Risk of All-Cause Mortality

- SVR
- Non-SVR

Cumulative Mortality (%)


SVR Associated With Improved Outcome

- Durable
- Leads to improved histology
- Leads to clinical benefits
  - Decreases decompensation
  - Prevents de novo esophageal varices
  - Decreases risk of hepatocellular carcinoma
  - Decreases mortality


SVR Associated With Improved Outcome

FibroScan
Noninvasive Liver Stiffness Testing

Assess mechanical properties of liver tissue

FibroScan Noninvasive Liver Stiffness Testing

Mechanical Shear Wave Induction

Shear Wave Speed Correlates to Stiffness

Low speed = Low Stiffness
High speed = High Stiffness

FibroScan Noninvasive Liver Stiffness Testing
Primary FibroScan Applications

- Assess urgency of need for care
- Longitudinal testing
  - Therapeutic response
  - Disease progression

VCTE Accuracy Validation

<table>
<thead>
<tr>
<th># Studies</th>
<th># Patients</th>
<th>ETIOLOGY</th>
<th>Diagnosis of significant fibrosis AUROC F2F3</th>
<th>Diagnosis of cirrhosis AUROC F4</th>
<th>REFERENCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>546</td>
<td>HCV</td>
<td>0.83</td>
<td>0.95</td>
<td>[1]</td>
</tr>
<tr>
<td>9</td>
<td>2063</td>
<td>Multiple</td>
<td>0.87</td>
<td>0.96</td>
<td>[2]</td>
</tr>
<tr>
<td>38</td>
<td>8433</td>
<td>Multiple</td>
<td>0.84</td>
<td>0.94</td>
<td>[3]</td>
</tr>
</tbody>
</table>

FibroScan Cutoff Value Reference

<table>
<thead>
<tr>
<th>Disease</th>
<th>F0-F1</th>
<th>F2</th>
<th>F3</th>
<th>F4</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBV</td>
<td>≤ 6.0</td>
<td>&gt; 6.0</td>
<td>≥ 9.0</td>
<td>≥ 12.0</td>
</tr>
<tr>
<td>HCV</td>
<td>≤ 7.0</td>
<td>&gt; 7.0</td>
<td>≥ 9.5</td>
<td>≥ 12.0</td>
</tr>
<tr>
<td>HCV-HIV</td>
<td>≤ 7.0</td>
<td>≤ 10.0</td>
<td>≥ 11.0</td>
<td>≥ 14.0</td>
</tr>
<tr>
<td>Cholestatic</td>
<td>≤ 7.0</td>
<td>≥ 7.5</td>
<td>≥ 10.0</td>
<td>≥ 17.0</td>
</tr>
<tr>
<td>NAFLD/NASH</td>
<td>≤ 7.0</td>
<td>≥ 7.5</td>
<td>&lt; 10.0</td>
<td>≥ 14.0</td>
</tr>
</tbody>
</table>

Utilization of FibroScan in Clinical Practice; Current Gastroenterology Reports; Bonder & Altaf; 2014; 16:372.
Conclusions

- Chronic Hepatitis C is a major liver disease worldwide and in the US
- It is under diagnosed, undertreated and is curable
- Adults born during 1945–1965 should receive one-time testing for HCV without prior ascertainment of HCV risk.
- Treatment for hepatitis C is very effective with cure rate 95-100%
- HCC screening is recommended for all cirrhotics and hepatitis B infected non-cirrhotics
- Therapy success has definite great impact on patients' survival
- FibroScan is alternative tool to assess the fibrosis