HCV Epidemiology, Screening, and Natural History

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Hepatitis C In the U.S.

Why Should You Care?

5.1 million estimated true prevalence

3.9 million CDC estimate

25% Diagnosed

Large reservoir of infected patients who are undiagnosed

And Untreated

Chak E, et al. Liv Int 2011;31:1090-1101
Natural History of HCV

- **Acute Infection**: Most have minimal symptoms
- **Chronic Infection**: 75%-85%
- **Cirrhosis**: 10%-20% over 20 years
  - Cirrhosis: 1%-4% per year
  - Decompensated Cirrhosis: 5-yr survival rate 50%

**Most Americans infected >35 y**
- Additional impact of:
  - Alcohol
  - Obesity
  - Older age

Consequences of Under-Diagnosis of HCV Infection

- 33% of undiagnosed Americans have advanced fibrosis/cirrhosis

**Now**

- **Decompensated Cirrhosis**
- **Hepatocellular Carcinoma (HCC)**

HCV is a Systemic Disease

- **Acute Infection**
  - 75%-85%

- **Chronic Infection**
  - 10%-20% over 20 years

- **Cirrhosis**
  - 10%-20% over 20 years

- **HCC**
  - 1%-4% per year

- ** Decompensated Cirrhosis**
  - 5-yr survival rate 50%

**Extra hepatic Manifestations**

- Mixed cryoglobulinemia
- Sjögren (sicca) syndrome
- Lymphoproliferative disorders
- Porphyria cutanea tarda
- Neuropathy
- Membranoproliferative glomerulonephritis
- Cryoglobulinemic vasculitis

**Strongly associated**

- Corneal ulcers (Mooren ulcers)
- Thyroid disease
- Lichen planus
- Pulmonary fibrosis
- Type 2 diabetes
- Systemic vasculitis (polyarteritis nodosa, microscopic polyangiitis)
- Arthralgias, myalgias, inflammatory polyarthritis
- Autoimmune thrombocytopenia

**Possibly associated**

HCV Infection Increases Risk of Chronic Kidney Disease – REVEAL-HCV Study

N=23,785; 1,313 seropositive for HCV

Lai TS, et al. AASLD 2014, Abstract #172

HCV Infection is Associated with Increased All Cause Mortality “Reveal-C”

Increasing Healthcare Costs Associated with the Aging HCV Population


Expensive to have end stage liver disease

We Can Make A Difference!

SVR Improves Long-Term Liver Outcomes

Cumulative Incidence of Any Liver-Related Outcome Among Patients With Bridging Fibrosis or Cirrhosis

- SVR (n=180)
- Nonresponders* (n=309)

<table>
<thead>
<tr>
<th>Percent</th>
<th>0</th>
<th>5</th>
<th>10</th>
<th>15</th>
<th>20</th>
<th>25</th>
<th>30</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.5 Years</td>
<td>0.23</td>
<td>2.35</td>
<td>1.11</td>
<td>11.35</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>5 Years</td>
<td></td>
<td>2.65</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>7.5 Years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>27.16</td>
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</tbody>
</table>


Outcome After SVR in Advanced Fibrosis (HALT-C)

Liver-related Death or Liver Transplantation

- E

- P value for 3-way comparison: 0.005
- P values for 2-way comparison
  - BT/R vs. NR: 0.11
  - SVR vs. BT/R: 0.13
  - SVR vs. NR: 0.003

NR = non response; BT/R= Breakthrough/relapse; SVR = Sustained response

How Do You Get Hepatitis C?

1998 CDC Risk Based HCV Screening Recommendations

- Ever injected illegal drugs
- Received blood, organs, or clotting factors prior to 1992
- Have ever been on hemodialysis
- Have elevated ALT
- Born to HCV-infected mothers
- Have HIV infection
- Percutaneous or mucosal exposure to HCV positive blood

Risk-Based Screening Does Not Work

- Primary care setting, U.S. – 2005-2010
- 17,464 tested for HCV
  - 6.4% positive
- Odds ratios for positive anti-HCV
  - IVDU: 6.3
  - 1945-1965 birth cohort: 4.4
  - Elevated ALT: 4.8
- Risk based screening missed 4 out of 5 HCV positive adults

Yartel AK, et al. AASLD 2013; abstract #24

HCV in the US – 2001-2010

Milliman Study: Based on NHANES and Claim Forms

82% aged 44-63 years

HCV in the U.S.

8,810 Americans with hepatitis C infection
Danville PA, Detroit MI, Portland OR, Honolulu HI

Distribution by Birth Year

- 1935-1944: 7.40%
- 1945-1954: 42%
- 1955-1964: 33.30%
- 1965-1974: 9.20%
- 1975-1984: 4.60%
- 1985-1990: 1.40%

75% born between 1945-1964

Moorman AC, et al. CID 2013;56:40-50

Baby Boomer Epidemic

Anti-HCV Prevalence by Birth Year, NHANES 1999-2008

1945-1965: 3.6%
Others: 0.8%

Smith BD, et al. AASLD 2011, abstract 241
Birth Year 1945 – 1965
Baby Boomers

Woodstock Festival 1969
"Share Love and Hep C"

Not Only the Boomer’s Fault...

- Hepatitis C was not on the radar
- Blood supply was contaminated
- No universal precautions in healthcare settings
- No way to screen organs or blood products
2012 CDC Recommendations for Birth Cohort Screening (1945 - 1965)

Recommendation #1
- Adults born from 1945-1965 should receive one-time testing for HCV.

Recommendation #2
- HCV (+) individuals
  - Brief alcohol screening and intervention
  - Referral to appropriate care for HCV


2013 USPSTF HCV Screening Recommendations

1. Those at high risk for HCV infection
2. Those born from 1945 to 1965
   - Grade B recommendation – high certainty that the net benefit is moderate to substantial

The Affordable Care Act
- Requires insurance plans to provide Grade A or B recommendations without cost sharing

USPSTF = United States Preventive Services Task Force

Moyer VA - on behalf of the USPSTF. Ann Intern Med 2013;159:349-357
Baby Boomers in the VA Population

VA Screening program; 5.5 million eligible for screen

<table>
<thead>
<tr>
<th>Birth Year</th>
<th>% screened</th>
<th>Anti-HCV (+)</th>
<th>HCV-RNA (+)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1945</td>
<td>42%</td>
<td>2.9%</td>
<td>1.7%</td>
</tr>
<tr>
<td>1945-1965</td>
<td>64%</td>
<td>13.1%</td>
<td>9.9%</td>
</tr>
<tr>
<td>&gt;1965</td>
<td>58%</td>
<td>1.9%</td>
<td>1.1%</td>
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Backus L, et al. AASLD 2013; Abstract #21

Is it Effective?

3 Randomized Controlled Trials

Compared to “standard of care”
- Testing for HCV in persons born 1945-1965 with no prior testing
- Was 5 times more effective in identifying persons with current or prior infection

Smith BD, et al. AASLD 2014, Abstract #194
For “Non-Baby Boomers”

Risk based screening
- IVDU – single or multiple
- Intranasal cocaine use
- Getting an unregulated tattoo and other percutaneous exposures
- Blood or blood product transfusion before 1992
- Born to an HCV-infected mother
- Incarceration

Transmission of HCV

<table>
<thead>
<tr>
<th>Route</th>
<th>Hepatitis C</th>
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</thead>
<tbody>
<tr>
<td>IV drug use</td>
<td><img src="image" alt="Common" /></td>
</tr>
<tr>
<td>Transfusion</td>
<td><img src="image" alt="Common" /></td>
</tr>
<tr>
<td>Hemodialysis</td>
<td><img src="image" alt="Common" /></td>
</tr>
<tr>
<td>Intra-institutional</td>
<td><img src="image" alt="Common" /></td>
</tr>
<tr>
<td>Sexual</td>
<td><img src="image" alt="Common" /></td>
</tr>
<tr>
<td>Household</td>
<td><img src="image" alt="Infrequent" /></td>
</tr>
<tr>
<td>Mother-to-newborn</td>
<td><img src="image" alt="Infrequent" /></td>
</tr>
<tr>
<td>Oral-oral contact</td>
<td><img src="image" alt="Never" /></td>
</tr>
<tr>
<td>Food-borne</td>
<td><img src="image" alt="Never" /></td>
</tr>
<tr>
<td>Fecal (oral)</td>
<td><img src="image" alt="Never" /></td>
</tr>
<tr>
<td>Water-borne</td>
<td><img src="image" alt="Never" /></td>
</tr>
<tr>
<td>Raw shellfish</td>
<td><img src="image" alt="Never" /></td>
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Generates Questions in my Clinic
HCV Is Not Going Away!

You Want Your Doctor to Avoid These Mistakes

“Liver tests are normal, not much can be going on.”
“Hepatitis C does not damage the liver unless alcohol is involved.”
“I discussed vaccinating patient vs. HCV & patient declined.”
“There is nothing to do about treating hepatitis C.”
“Treatment of hepatitis C is worse than the disease.”
Reported number of acute hepatitis C cases — United States, 2000 – 2012


Source: National Notifiable Diseases Surveillance System (NNDSS)
Not All anti-HCV (+) Patients Are Infected!

- **Acute Infection**: 75%-85%
- **Clearance of HCV RNA**: 15%-25%
- **Chronic Infection**: 15%-25%
- **Cirrhosis**: 10%-20% over 20 years
- **HCC**: 1%-4% per year
- ** Decompensated Cirrhosis**: 5-yr survival rate 50%

**HISTOLOGIC STAGING**

- **Stage 0**: No Fibrosis
- **Stage 1**: Portal Fibrosis
- **Stage 2**: Few Septa
- **Stage 3**: Numerous Septa
- **Stage 4**: Cirrhosis

STOP Before Here
Importance of Confirming Viremia

- Anti-HCV Antibody Positive
- HCV RNA Positive
- HCV Genotype
  - Consider Liver Biopsy
  - Vaccinate for HAV / HBV*

- Anti-HCV Antibody Negative
- HCV RNA Negative
- No Further Testing
- No Active Disease

Benefits of Diagnosis

**PREVENT TRANSMISSION**
- Avoid sharing objects with blood
- Stop illicit drugs or sharing needles
- Discuss risk of sexual transmission with “unsafe sex”

**OTHER RECOMMENDATIONS**
- Avoid alcohol consumption
- Discuss available treatments
- Vaccinate for hepatitis A and B
- Test for HBV, HIV
- Consider family member screening
HCV Epidemiology, Screening and Natural History - Summary

1. Most HCV patients remain undiagnosed
2. 75% of them were born from 1945-1965
3. 33% of them have advanced fibrosis
   - “ticking time bombs” waiting to explode (bleed) on a Friday at midnight when you are on call
4. Therapy is more effective and safer
5. It’s time to incorporate screening into your practice!