HEPATITIS C:
A MULTIFACETED DISEASE

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I, Sanjiv Chopra, M.D. serve as Editor-in-Chief for the Hepatology Section of UpToDate and receive royalty income for my services. Some of the references in the bibliography refer to UpToDate.
HCV - Epidemiology

Prevalence

Worldwide 170 million (3%)

United States
- Anti-HCV positive 3.9 million (1.8%)
- HCV RNA positive 2.7 million (1.4%)

Lavanchy D & McMahon B, In: Liang TJ & Hoofnagle JH (eds.)
Hepatitis C Virus

- Nucleic Acid: 9.6 kb ssRNA
- Classification: Flaviviridae, Hepacivirus
- Genotypes: 1 to 6
- Enveloped
- In vitro model: primary hepatocyte and T cell cultures; replicon system
- In vivo replication: in cytoplasm, hepatocyte and lymphocyte; human and other primates
HCV Genotypes and Subtypes

Simmonds P, Journal of Hepatology, 1999
HCV - Epidemiology

Risk Factors for Hepatitis C

- Long-Term Hemodialysis
- Clotting Factor Treatment Prior to 1987
- Blood Transfusion or Organ Transplant Prior to 1992
- Multiple Sexual Partners
- Injection Drug Use
- Mass Injections and Traditional Practices
- Birth from Infected Mother
Epidemics From Parenteral Practices

- Japan: cupping
- Egypt: Schistosomiasis treatment
- Italy: home injections

Kiyosawa K et al., Gastroenterology 1994;106:1596
Frank C et al., Lancet 2000;355:877
Chiaramonte M et al., J Hepatol 1996; 24:129
<table>
<thead>
<tr>
<th>Population Description</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recipients of clotting factors before 1987</td>
<td>75-90%</td>
</tr>
<tr>
<td>Injection drug users</td>
<td>70-85%</td>
</tr>
<tr>
<td>Long term hemodialysis patients</td>
<td>10%</td>
</tr>
<tr>
<td>Individuals with ≥ 50 sexual partners</td>
<td>10%</td>
</tr>
<tr>
<td>Recipients of blood prior to 1990</td>
<td>5%</td>
</tr>
<tr>
<td>Infants born to infected mothers</td>
<td>5%</td>
</tr>
<tr>
<td>Long term sexual partners of HCV positive</td>
<td>1-5%</td>
</tr>
<tr>
<td>Health workers after random needlesticks</td>
<td>1-2%</td>
</tr>
</tbody>
</table>

CDC, MMWR 1998;47(No. RR-19):1
Current Likelihood of Transmission

**Transfusion**
- ~1 in 1,000,000

**Maternal-Infant**
- Mother HIV negative: ~5%
- Mother HIV positive: 15-20%

**Heterosexual partner**
- ~1 in 1,000 per yr

**Needlestick injury**
- HCV positive source: ~5%
- HCV status unknown: ~1%
Previous Screening Guidelines Have Not Been Effective

Baby boomers represent more than 75% of American adults with hepatitis C

2.1 million people

Up to 1.5 million baby boomers are unaware of their infection

One-time testing could identify 800,000 of them

CDC Recommends Screening All Baby Boomers In USA for Chronic Hepatitis C Infection (2012)

- 75% of patients with Chronic Hepatitis C infection in USA were born between 1945-1965 with a prevalence of 3.25%
- Testing this cohort may identify as many as 800,000 additional patients.
Sexual Transmission of HCV

Bisexuality immediately doubles your chance for a date on a Saturday night.

Woody Allen
Sexual Transmission Of HCV

Rare
HCV - Natural History

Outcome Following Hepatitis C Infection

- Acute hepatitis C
  - 55-85% chronic infection
- Chronic hepatitis
  - 70% chronic infection
  - 20% cirrhosis
    - 1-4%/yr HCC
    - 4-5%/yr decompensation

Time (yr)

10 20 30
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; 349:825
<table>
<thead>
<tr>
<th>Alcohol Content</th>
<th>gm/Drink</th>
<th>Drinks/50 gm</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Beer</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12 oz. at 4%</td>
<td>11</td>
<td>4.5</td>
</tr>
<tr>
<td><strong>Wine</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 oz. at 11%</td>
<td>13</td>
<td>3.8</td>
</tr>
<tr>
<td><strong>Martini</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 oz. at 40%</td>
<td>28</td>
<td>1.8</td>
</tr>
</tbody>
</table>
My doctor said you should only have one glass of wine maximum.
### Fibrosis Risk Varies Among Individuals

<table>
<thead>
<tr>
<th></th>
<th>Patient A</th>
<th>Patient B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at infection</td>
<td>25</td>
<td>42</td>
</tr>
<tr>
<td>Alcohol use</td>
<td>Seldom</td>
<td>3-4 drinks/day</td>
</tr>
<tr>
<td>Sex</td>
<td>Female</td>
<td>Male</td>
</tr>
<tr>
<td>Fibrosis stage/yr</td>
<td>0.10</td>
<td>0.25</td>
</tr>
<tr>
<td>Years to cirrhosis</td>
<td>40</td>
<td>16</td>
</tr>
</tbody>
</table>

Source: Poynard T, et al., Lancet 1997; 349:825
Extrahepatic Disorders Associated with Chronic HCV

Hematologic: Essential mixed cryoglobulinemia, Non-Hodgkin’s lymphoma
Renal: Membranoproliferative glomerulonephritis, Membranous nephropathy
Dermatologic: Porphyria cutanea tarda, Leukocytoclastic vasculitis, Lichen planus
Autoimmune: Diabetes mellitus, Idiopathic thrombocytopenic purpura

Gumber SC and Chopra S., Ann Intern Med 1995;126
Cryoglobulinemia

Renal Manifestations

- Most common lesion is membranoproliferative glomerulonephritis (MPGN)

- Clinical features of MPGN include hypertension, microscopic hematuria, proteinuria, nephrotic syndrome and variable degree of renal insufficiency

- Treatment modalities include interferon alfa, immunosuppressive drugs such as corticosteroids or cyclophosphamide and plasmapheresis
