Hepatitis C

- Hepatitis C (HCV) is a flavivirus related to Yellow Fever and West Nile Virus
- Most common chronic bloodborne infection in the US
- Contagious liver disease causing mild illness to serious, lifelong illness or death
The Virus

- Single stranded, positive sense, RNA
- Falviviridae family
- Spherical, enveloped
- ~ 50 nm
- Discovered in 1989

Choo, Science 1989;244:359-62
HCV - Genetics

- Six genotypes, 1 through 6
- Multiple subtypes, a, b, c, etc.
  - Further divided into quasispecies, varying in RNA sequence by 1-9%
- RNA sequence may vary by 35% between genotype
- Great genetic diversity

Farci, Semin Liver Dis 2000;20:103-26
HCV – Natural History

Acute HCV-100 patients

Resolved - 25

Chronic - 75

Stable - 45-55

Cirrhosis - 20-30

Stable - 15-25

 Decompensation – 5-8

HCC – 1-3 per year

20 – 30 years

Accelerated by:

alcohol

HIV
Hep C Transmission

• Spread by blood to blood contact:
  – IV drug use
  – Mother to child transmission
  – Can be sexually transmitted but less common
  – Since 1992, screening has limited spread through transfusions and transplants

• For most, acute infection leads to chronic infection

• There is no vaccine for Hepatitis C
Primary Causes of Chronic Liver Disease*

- Hepatitis C Virus (26%)
- Alcohol (24%)
- Hepatitis B Virus (11%)
- Hepatitis C Virus and Alcohol (14%)
- Unknown (17%)
- Other (5%)

*Jefferson County, Alabama, USA
Strategies for Hep C Treatment

• Monitoring early stages of Hep C rather than treatment acceptable and occurs in free world

• Treatment based on progression:
  – Liver function tests
  – Liver biopsy
  – Other factors: age, co-infection with HIV, etc.

• Monitor patients with earlier stages of fibrosis & sentences under 5 years & coordinate with community providers for potential treatment
Goals of Treatment

- Eradicate HCV replication
- Delay fibrosis
- Prevent liver failure
- Prevent hepatocellular carcinoma
- Prevent death
- Enhance quality of life

## HCV - Treatment

### Indications for treatment

<table>
<thead>
<tr>
<th>Recommended</th>
<th>Not recommended</th>
<th>Unclear</th>
</tr>
</thead>
<tbody>
<tr>
<td>Detectable HCV RNA</td>
<td>Persistently normal ALT</td>
<td>• Compensated cirrhosis</td>
</tr>
<tr>
<td>• Persistently elevated ALT</td>
<td>• Advanced or decompensated cirrhosis</td>
<td>• Elevated ALT</td>
</tr>
<tr>
<td>• Abnormal liver biopsy showing portal or bridging fibrosis, or at least moderate inflammation</td>
<td>• Excessive alcohol use</td>
<td>• Elevated ALT but normal liver histology</td>
</tr>
</tbody>
</table>

- Excessive alcohol use
- Active drug use
- Contraindications to treatment
Current Hepatitis C Treatment

• PEG-Interferon
  – Increases expression of proteins that interfere with Hep C viral replication

• Ribavirin
  – Enhances the antiviral effect of interferon
  – Precise mechanism of action uncertain

• Treatment lasts for one year; if successful, induces cure
HCV – Pretreatment Workup

- History and Physical Exam
- Psychiatric history/evaluation
- Blood counts
- Chemistry panel
- Liver panel, including PT
- TFTs
- HCV genotype
- HCV RNA
- AFP; ?liver imaging
- Liver biopsy
# HCV - Treatment

Drugs approved for the treatment of HCV infection

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Trade name (manufacturer)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Interferon alfa-2b</td>
<td>• Intron A (Schering-Plough)</td>
</tr>
<tr>
<td>• Interferon alfa-2a</td>
<td>• Roferon (Roche)</td>
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<tr>
<td>• Interferon alfacon-1</td>
<td>• Infergen (?Amgen)</td>
</tr>
<tr>
<td>• Interferon alfa-2b plus Ribavirin</td>
<td>• Rebetron (Schering-Plough)</td>
</tr>
<tr>
<td>• Pegylated Interferon alfa-2a</td>
<td>• Pegasys (Roche)</td>
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<tr>
<td>• Pegylated Interferon alfa-2b</td>
<td>• PEG-Intron (Schering-Plough)</td>
</tr>
</tbody>
</table>
HCV – Treatment (non-HIV Patients)

Sustained Virologic Response Rates

- IFN 24 wks: 6
- IFN 48 wks: 16
- IFN/RBV 24 wks: 24
- IFN/RBV 48 wks: 41
- PEG-IFN: 39
- PEG/RBV: 54
HCV - Treatment

Predictors of a Favorable Response

- Genotype 2 or 3
- Low HCV Viral Load (<2 million)
- No or only portal fibrosis
- Female gender
- Age ≤ 40 years

Role of gender not an independent factor if controlled for body weight
Side Effects Current Hep C Treatment

- **INTERFERON** - Hematologic complications (i.e., neutropenia, thrombocytopenia), neuropsychiatric complications (i.e., memory and concentration disturbances, visual disturbances, headaches, depression, irritability), flulike symptoms, metabolic complications (i.e., hypothyroidism, hyperthyroidism, low-grade fever), gastrointestinal complications (i.e., nausea, vomiting, weight loss), dermatologic complications (i.e., alopecia), and pulmonary complications (i.e., interstitial fibrosis)

- **RIBAVIRIN** - Hematologic complications (i.e., hemolytic anemia), reproductive complications (i.e., birth defects), and metabolic complications (i.e., gout)