The Natural History
and Epidemiology
of Hepatitis C in US Veterans

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San Francisco VA Medical Center
Prevalence of HCV Infection in the VA

- General US population: 1.8% or 3.8 million
- US veteran population treated by the VA
  - Point prevalence of 8%-10% as of 3/17/99
  - Estimated that 280,000-350,000 veterans are HCV seropositive
  - Wide geographical variation in prevalence
Prevalence of HCV Infection in the VA

- General perception by VA clinicians that hepatitis C is a common problem
- Seroprevalence:
  - 20% at the Washington, DC VA in admitted patients
  - 10% at the San Francisco VA in inpatients who were sources of needle stick injury
- HCV infection ± alcohol is the leading indication for liver transplantation in the VA
Race/Ethnicity of HCV Seropositive Veterans

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>Tested Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hispanic/White</td>
<td>10%</td>
</tr>
<tr>
<td>Hispanic/Black</td>
<td>50%</td>
</tr>
<tr>
<td>Native-American</td>
<td>20%</td>
</tr>
<tr>
<td>African-American</td>
<td>30%</td>
</tr>
<tr>
<td>Asian-American</td>
<td>40%</td>
</tr>
<tr>
<td>Caucasian</td>
<td>10%</td>
</tr>
<tr>
<td>Unknown</td>
<td>50%</td>
</tr>
</tbody>
</table>

Age Distribution of HCV Seropositive Veterans

48.5 ± 9.1 years
(Mean ± SD)

Military Service of HCV Seropositive Veterans


% of Total Who Tested Positive

- WW II
- Korea
- Vietnam
- Post-Vietnam
- Desert Shield
- Other
- None
HCV Infection In Different VA Programs

- Methadone clinic = 100%
- Homeless veterans program = 47%
- PTSD clinic = 43%

Estimated seroprevalence = 18%
Estimated incidence = 3.3% (4/122 who were initially seronegative)

Risk Factors for HCV Infection

- Injection drug use = 54%
- Transfusion = 24%
- Tattooing = 45%
- Excessive alcohol consumption = 45%
- Independent risk factors for HCV infection are under analysis

Briggs M, MPH, 1999. SFVAMC Seroprevalence Study
Distribution of Liver Disease in Seropositive Veterans

HCV Cirrhosis: Survival With and Without Decompensation

HCV Cirrhosis: Risk of Developing Decompensation


- Ascites (48%)
- Variceal bleed (22%)
- Encephalopathy (8%)
- Jaundice (6%)
- Multiple complications (16%)

Years After Diagnosis

Risk of Complications (%)
Probability of HCC Occurrence

Tentative Conclusions

- HCV is highest in veterans who are 45-60 years old (~60% of those who are seropositive)
- HCV is most common in Vietnam-era veterans
- HCV is strongly associated with "traditional" risk factors (IVDU, crack cocaine)
- HCV is less strongly associated with transfusion
- The role of nontraditional risk factors is under evaluation
- Alcohol use is common
- Veterans with risk behaviors should be tested and positive ELISAs confirmed if indicated
- Concern that there is a cohort effect which will result in increased incidence of ESLD and/or HCC in the future
Case Study #1

- 48-year-old Vietnam-era veteran
- Followed in liver clinic for HCV cirrhosis
- Initially counseled
  - Discussion regarding transmission of HCV
  - Assessment of risk factors
    - Denied:
      - IVDU
      - Transfusions
      - Body piercing
      - Cocaine use
    - Only possible exposure
      - Manicuring without gloves
- Married without children
- Worked as a carpenter

- Combat blood exposure
- Excessive alcohol consumption
- Needlestick
- Dialysis
Case Study #1 (cont’d)

- Initial complaint: mild fatigue
- Liver biopsy revealed cirrhosis with preserved synthetic function
- Adequate platelet and WBC counts
- Initial treatment:
  - Interferon monotherapy (3 MU, t.i.w.)
  - Treatment discontinued after 3 months due to:
    - Persistent viremia
    - Elevated serum ALT
Case Study #1 (cont’d)

- Disease course over the next 2 years:
  - Progressive deterioration of hepatic synthetic function
    - Reduction in serum albumin to 2.6 g/dL
    - Increase in prothrombin time to 15 s (control 13 s)
  - Referred to Portland VA for consideration of transplantation
    - During evaluation, he developed ascites that became difficult to control
**Case Study #1 (cont’d)**

- He was accepted for liver transplantation and placed on a waiting list.
- During the subsequent year, he:
  - Became increasingly fatigued.
  - Began to loss muscle mass.
  - Continued to have compromised synthetic function.
Case Study #1 (cont’d)

• After 1 year:
  – He underwent successful liver transplantation
    • Uncomplicated postoperative course
    • Received standard immunosuppressive therapy
      – Imuran
      – Prednisone
      – Cyclosporine
Case Study #1 (cont’d)

- Six months posttransplantation, he had:
  - Transaminitis
    - AST – 110 IU/L
    - ALT – 150 IU/L
  - Liver biopsy consistent with recurrent HCV
  - HCV RNA level – 10.2 MEq/mL
  - HCV infection with genotype 3
Case Study #1 (cont’d)

- Posttransplantation treatment
  - Experimental protocol
    - Interferon 3 MU, t.i.w.
    - Ribavirin 1,000 mg/d
  - He rapidly developed anemia
    - Ribavirin dose was reduced to 400 mg/d and then increased to 600 mg/d
  - After 6 months of treatment, his:
    - Liver enzymes normalized
    - HCV RNA <0.2 MEq/mL
  - He is currently being followed to determine whether he achieves a sustained response to therapy
Case Study #1: Points for Discussion

- Natural history of HCV cirrhosis
- Indications for liver transplantation
- Recurrent HCV disease following liver transplantation
Case Study #2

- 56-year-old Vietnam-era veteran
- Presented to liver clinic with HCV cirrhosis
- Counseled about:
  - Transmission of HCV
  - Natural history of HCV
- Assessed for treatment
  - Not considered a candidate due to:
    - Cytopenia
      - Platelet count – 45,000
      - WBC count – 2,200
    - Initial AFP – 7 ng/mL
    - Ultrasound did not detect focal mass lesions
Case Study #2 (cont’d)

- One-year follow-up, he developed:
  - Progressive decline in hepatic synthetic function
  - Uncontrolled ascites (despite spironolactone and furosemide)
  - AFP – 75 ng/mL
  - CT scan showed:
    - No focal mass lesions
    - Irregular contour of the liver consistent with cirrhosis
Case Study #2 (cont’d)

• Repeat follow-up 6 months later:
  – AFP – 3,200 ng/mL
  – CT scan revealed a possible focal lesion in the dome of the liver that was not detected by FNA
  – Evaluation by surgeons did not find him to be a candidate for resection due to:
    • Impaired hepatic synthetic function
    • Massive ascites
  – The patient continues to be followed in the liver clinic
    1 month after this assessment
Case Study #2: Points for Discussion

- Risk of developing hepatocellular carcinoma
- Screening strategies
Hepatitis C: Standards for Evaluation, Screening, and Testing

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Screening Criteria for HCV

One or more of the following (past or present):
- Vietnam-era veteran
- Illicit injection drug use
- Blood/blood product exposure prior to 1992
- Unequivocal blood exposure
- Multiple sexual partners
- Hemodialysis
- Tattoo/repeated body piercing
- Intranasal cocaine use
- Unexplained elevated ALT or liver disease
- Intemperate alcohol use
- Requested by patient
Diagnosis of Hepatitis C:
Indications for Screening

- Risk factors:
  - In patients with risk factors, perform liver enzyme and serologic tests
  - In patients without risk factors, consider ALT as part of routine screening
  - Many infected patients deny risk factors
- Individuals with letters from the Red Cross or insurance companies regarding positive ELISAs
Diagnosis of HCV Infection in Patients With Risk Factors

- A single normal ALT test does not rule out chronic HCV.
- Patients who test positive for anti-HCV but have normal ALT levels should have serial determinations of ALT levels.
- ALT levels may be intermittently normal in a significant number of patients with chronic HCV.
- Direct viral assessment is currently necessary.
Enzyme-Linked Immunosorbent Assay (ELISA)

- An HCV antibody test
- First HCV antibody test performed
- Cannot distinguish between:
  - Acute and chronic infection
  - Resolved and current HCV infection
- Sensitivity: 92%-97%
- Positive test results
  - Suggests viremia until proven otherwise
  - Usually diagnostic in patients with elevated ALT and presence of risk factors
ELISA: False Test Results

- Development of antibodies adequate for detection requires an average of 12 weeks after infection (window period)

- False Negatives
  - Patients screened for anti-HCV during “window period”
  - Immunosuppressed patients
  - Chronic dialysis patients

- False Positives
  - Autoimmune hepatitis
  - Hypergammaglobulinemia
Recombinant Immunoblot Assay (RIBA)

- Confirmatory assay for HCV
- Consider RIBA for:
  - Patients with positive ELISA but not fitting high-risk profile
  - Suspected autoimmune hepatitis
  - Hypergammaglobulinemia
Available HCV RNA Tests

• Polymerase chain reaction (PCR)
  – Qualitative and quantitative types
  – Qualitative tests are most sensitive and specific in detecting HCV viremia
  – Quantitative tests are used to measure actual viral load

• Branched DNA amplification (bDNA)
  – Quantitative, but less sensitive than PCR methods
  – Diminished sensitivity limits usefulness
  – Concentrations <2 x 10⁶ Eq/mL are undetectable
  – Easier to perform, less variability in results
Genotyping

- Six major HCV genotypes
- ≥ 90 subtypes
- Determination of genotype and subtype assists in deciding the duration of treatment and the potential response to therapy
- Performing a PCR is necessary in determining HCV genotype
Liver Biopsy

- Gold standard in the assessment of patients with chronic hepatitis
- Recommended before treatment to assess grade and stage of disease or complications
- Not recommended for follow-up testing (except in research situations)
Summary

- Screening and counseling for HCV is necessary in patients with risk factors
- Diagnostic testing for HCV has improved with each generation of ELISA
- Quantitative PCR and genotyping should be performed prior to initiation of treatment
Case Study

- 52-year-old Vietnam veteran
- 10-year history of chronic fatigue
- Dull right upper quadrant pain for the past 3 months
- **PMH:** IVDU in Vietnam 25 years ago
  - Alcohol consumption >80g/d for 20 years
  - Abstinent for 2 years
- **PE:** Liver 1 fb below RCM
  Tender to deep palpation
- **LAB:**
  - Hgb - 15 ALT - 40 (nl <50) HCV Ab - (+)
  - Hct - 45 AST - 42 (nl <50) PT - nl
  - Plts - 140,000 (nl >150,000) Alb - nl
- **Ultrasound:** Liver appearance - nl
Case Study: Questions

• Should this patient undergo treatment?

• What, if any, additional lab tests are needed?

• If treatment is being considered, is HCV genotyping necessary prior to the initiation of therapy?
Treatment of Chronic Hepatitis C in the VA: A New Approach Using Interferon/Ribavirin Combination Therapy

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Associate Professor of Medicine
University of Minnesota
Staff Physician in Gastroenterology
Veterans Affairs Medical Center
Minneapolis, Minnesota
Available Treatments for Hepatitis C

- **Interferon (IFN) monotherapy**
  - alfa-2b (Intron A)
  - alfa-2a (Roferon A)
  - alfacon-1 (Infergen)
- **Combination therapy**
  - IFN alfa-2b + ribavirin (Rebetron)
Interferon Alfa-2b Alone or in Combination With Ribavirin in Treatment-Naive Patients With Chronic HCV: Patient Characteristics and Experimental Design

- Patients:
  - 44 US sites
  - n = 912 treatment-naive patients
    - Mean age 44 years old; 66% male
  - Increased ALT ≥6 months
  - Positive HCV RNA
  - No patients with:
    - Anemia, decompensation, CAD

Interferon Alfa-2b Alone or in Combination With Ribavirin in Treatment-Naive Patients With Chronic HCV: Patient Characteristics and Experimental Design

- Stratified by:
  - Genotype
    - 72% genotype 1
    - 16% genotype 2
    - 10% genotype 3
  - Pretreatment HCV level
    - >2 x 10^6 copies/mL (70%)
  - ± Cirrhosis
    - 4%-7% cirrhosis
    - Mean HAI score = 7.4

Interferon Alfa-2b Alone or in Combination With Ribavirin in Treatment-Naive Patients With Chronic HCV: Patient Characteristics and Experimental Design

• Design:
  – IFN Alfa-2b + Placebo x 24 wks
  – IFN + Placebo x 48 wks
  – IFN + Ribavirin x 24 wks
  – IFN + Ribavirin x 48 wks
  • f/u + biopsy 24 wks post rx

Interferon Alfa-2b Alone or in Combination With Ribavirin in Treatment-Naive Patients With Chronic HCV: Patient Characteristics and Experimental Design

• Dose:
  – <75 kg 1000 mg/d ribavirin
  – >75 kg 1200 mg/d
  – IFN 3 MU t.i.w.

• Endpoints:
  – HCV viral level
  – Histology
  – ALT levels

Interferon Alfa-2b Alone or in Combination With Ribavirin in Treatment-Naive Patients With Chronic HCV: Sustained Virologic Response 24 Weeks Posttherapy

<table>
<thead>
<tr>
<th>Treatment</th>
<th>% HCV RNA Negative</th>
<th>n</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IFN 24 wk</td>
<td>6%</td>
<td>231</td>
<td>0.001</td>
</tr>
<tr>
<td>IFN 48 wk</td>
<td>13%</td>
<td>225</td>
<td>0.001</td>
</tr>
<tr>
<td>IFN/R 24 wk</td>
<td>31%</td>
<td>228</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>IFN/R 48 wk</td>
<td>38%</td>
<td>228</td>
<td>&lt;0.05</td>
</tr>
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</table>

Interferon Alfa-2b Alone or in Combination With Ribavirin in Treatment-Naive Patients With Chronic HCV: Sustained Virologic Response in Subgroups

<table>
<thead>
<tr>
<th>Genotype</th>
<th>n</th>
<th>I/P 24 wk</th>
<th>I/P 48 wk</th>
<th>I/R 24 wk</th>
<th>IFN/Ribavirin 48 wk</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>659</td>
<td>2</td>
<td>7</td>
<td>16</td>
<td>28</td>
</tr>
<tr>
<td>non-1</td>
<td>253</td>
<td>16</td>
<td>29</td>
<td>69</td>
<td>66</td>
</tr>
</tbody>
</table>

HCV RNA

<table>
<thead>
<tr>
<th>HCV RNA</th>
<th>n</th>
<th>I/P 24 wk</th>
<th>I/P 48 wk</th>
<th>I/R 24 wk</th>
<th>IFN/Ribavirin 48 wk</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;2x10^6</td>
<td>637</td>
<td>4</td>
<td>7</td>
<td>27</td>
<td>36</td>
</tr>
<tr>
<td>&lt;2x10^6</td>
<td>275</td>
<td>9</td>
<td>29</td>
<td>42</td>
<td>43</td>
</tr>
</tbody>
</table>

### Interferon alfa-2b Alone or in Combination With Ribavirin in Treatment-Naive Patients With Chronic HCV: Sustained Virologic Response in Subgroups

<table>
<thead>
<tr>
<th>Fibrosis</th>
<th>I/P n 24 wk</th>
<th>I/P n 48 wk</th>
<th>I/R n 24 wk</th>
<th>IFN/Ribavirin n 48 wk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 3-4</td>
<td>250</td>
<td>5</td>
<td>13</td>
<td>29</td>
</tr>
<tr>
<td>Stage 1-2</td>
<td>608</td>
<td>5</td>
<td>13</td>
<td>32</td>
</tr>
<tr>
<td>DC of rx (any reason)</td>
<td>9</td>
<td>14</td>
<td>8</td>
<td>21</td>
</tr>
</tbody>
</table>

Interferon Alfa-2b Alone or in Combination With Ribavirin in Treatment-Naive Patients With Chronic HCV: Histologic Response

Interferon Alfa-2b/Ribavirin Combination Therapy or Interferon/Placebo for 48 Weeks or 24 Weeks in Relapsers With Chronic HCV: Patient Characteristics and Experimental Design

- Patients:
  - Male = 66%
  - Mean age = 43 years
  - Stratified by:
    - Cirrhosis
      - Mean METAVIR fibrosis score = 1.3
      - Activity score = 2.0

Interferon Alfa-2b/Ribavirin Combination Therapy or Interferon/Placebo for 48 Weeks or 24 Weeks in Relapsers With Chronic HCV: Patient Characteristics and Experimental Design

- Pretreatment serum HCV RNA concentration >2 x 10^6 copies/mL (66%)

- Pretreatment HCV Genotype
  - 66% genotype 1
  - 13% genotype 2
  - 18% genotype 3
  - 3% genotype non 1-3

Interferon Alfa-2b/Ribavirin Combination Therapy or Interferon/Placebo for 48 Weeks or 24 Weeks in Relapsers With Chronic HCV: Patient Characteristics and Experimental Design

- Design:
  - 3 arms randomized
  - Primary endpoint:
    - Sustained response — loss of HCV RNA 24 wks post rx
    - All patients receiving ≥1 dose were analyzed

Interferon Alfa-2b/Ribavirin Combination Therapy or Interferon/Placebo for 48 Weeks or 24 Weeks in Relapsers With Chronic HCV: Patient Characteristics and Experimental Design

Interferon Alfa-2b/Ribavirin Combination Therapy or Interferon/Placebo for 48 weeks or 24 Weeks in Relapsers With Chronic HCV: Sustained Loss of HCV RNA 24 Weeks Posttreatment

Interferon Alfa-2b/Ribavirin Combination Therapy or Interferon/Placebo for 48 Weeks or 24 Weeks in Relapsers With Chronic HCV: Predictors of Sustained Response (Logistic Regression Analysis)

- Genotype 2 or 3
- Viral level <3.5 x 10^6 copies/mL
- No portal fibrosis
- Age <40 years old
- Female gender

Interferon Alfa-2b/Ribavirin Combination Therapy or Interferon/Placebo for 48 Weeks or 24 Weeks in Relapsers With Chronic HCV: Sustained Response and Risk Factors

Interferon Alfa-2b Alone or in Combination With Ribavirin for the Treatment of Relapsers With Chronic HCV: Baseline patient characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Interferon n (%)</th>
<th>Interferon+ Ribavirin n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex</td>
<td>112 (65)</td>
<td>112 (65)</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>42</td>
<td>44</td>
</tr>
<tr>
<td>White race</td>
<td>158 (92)</td>
<td>165 (95)</td>
</tr>
<tr>
<td>Estimated duration of infection (y)</td>
<td>16±8</td>
<td>15±8</td>
</tr>
<tr>
<td>Source of infection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transfusion</td>
<td>52 (30)</td>
<td>42 (24)</td>
</tr>
<tr>
<td>IVDU</td>
<td>68 (40)</td>
<td>70 (40)</td>
</tr>
<tr>
<td>Unknown</td>
<td>52 (30)</td>
<td>61 (35)</td>
</tr>
</tbody>
</table>

Interferon Alfa-2b Alone or in Combination With Ribavirin for the Treatment of Relapsers With Chronic HCV: Baseline patient characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Interferon n (%)</th>
<th>Interferon+ Ribavirin n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genotype</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>94 (55)</td>
<td>98 (57)</td>
</tr>
<tr>
<td>Non-1</td>
<td>78 (45)</td>
<td>75 (43)</td>
</tr>
<tr>
<td>Viral level</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;2 million copies/mL</td>
<td>131 (76)</td>
<td>128 (74)</td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>6 (3)</td>
<td>3 (2)</td>
</tr>
</tbody>
</table>

### Interferon Alfa-2b Alone or in Combination With Ribavirin for the Treatment of Relapsers With Chronic HCV: Rates of Sustained Response to Treatment

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Interferon</th>
<th>Interferon+Ribavirin*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genotype 1</td>
<td>3/94 (3)</td>
<td>29/98 (30)</td>
</tr>
<tr>
<td>Genotype non-1</td>
<td>5/78 (6)</td>
<td>55/75 (73)</td>
</tr>
<tr>
<td>&gt;2 million copies/mL</td>
<td>2/131 (2)</td>
<td>54/128 (42)</td>
</tr>
<tr>
<td>≤2 million copies/mL</td>
<td>6/41 (15)</td>
<td>30/45 (67)</td>
</tr>
<tr>
<td>Fibrosis/cirrhosis</td>
<td>1/35 (3)</td>
<td>12/26 (46)</td>
</tr>
<tr>
<td>Minimal to no fibrosis</td>
<td>6/134 (4)</td>
<td>70/142 (49)</td>
</tr>
</tbody>
</table>

*P<.001 for comparison with interferon for each characteristic

Impact of Interferon Alfa-2b and Ribavirin on Liver Fibrosis Progression in Patients With Chronic HCV: Results

- n = 1,972 patients from randomized trials with paired biopsies
- Treatment with IFN and IFN/R reduced fibrosis progression compared with:
  - Pretreatment biopsies
  - Controls
- Among SR with initial septal fibrosis, the fibrosis disappeared in:
  - 62% of IFN/R
  - 47% of IFN
  - 9% of controls (P<.001)

Impact of Interferon Alfa-2b and Ribavirin on Liver Fibrosis Progression in Patients With Chronic HCV: Results

- Among the non-SR the fibrosis did not progress in:
  - 82% of IFN/R
  - 81% of IFN
  - 41% of controls ($P<.001$)

- Among 133 with extensive fibrosis, progression to cirrhosis occurred in:
  - 6% of SR
  - 36% of non-SR
  - 60% of controls ($P<.01$)

Contraindications to and Adverse Effects of HCV Therapy

Contraindications

- Recent or ongoing illicit drug use or alcohol use
  - Patients must be alcohol and illicit drug-free for ≥6 months
- Moderate or severe psychiatric disease
  - Uncontrolled depression
  - Suicide ideation
- Inadequate social support
- Noncompliance
Contraindications to and Adverse Effects of HCV Therapy

Contraindications

- Life-limiting nonhepatic disease
- Pregnancy or inability to use birth control
- Clinically decompensated cirrhosis
- Uncontrolled clinical conditions
  - Autoimmune disorder
  - Other medical illness
Contraindications to and Adverse Effects of HCV Therapy

Adverse Effects

- IFN alfa-2a; alfa-2b; alfacon-1
  - Flu-like symptoms and headache
  - Cytopenia
    - Thrombocytopenia
    - Leukopenia
  - Neuropsychiatric symptoms
  - Autoimmune disorders
    - Hypothyroidism
    - Hyperthyroidism
  - Retinopathy
  - Uncommon syndromes
    - Seizures
    - Acute cardiac and renal failure
    - Interstitial fibrosis
Contraindications to and Adverse Effects of HCV Therapy

- Ribavirin
  - Hemolytic anemia
  - Teratogenic effects
  - Rash
  - Dyspnea
  - Pharyngitis
  - Nausea
  - Insomnia
  - Anorexia
Summary: Current Treatment Recommendations for HCV

- Treatment-naive patients
  - IFN alfa-2b 3 MU t.i.w. + ribavirin 1000-1200 mg/d
    - Genotype 1: treat for up to 48 weeks
    - Genotypes non-1: treat for 24 weeks
  - Treatment-naive patients with contraindication for ribavirin:
    - IFN alfa-2a, alfa-2b, or alfacon-1 for 48 weeks
    - If no initial response and HCV RNA remains positive at 3 months, then DC therapy
Summary: Current Treatment Recommendations for HCV

- Relapsing patient after IFN monotherapy
  - IFN alfa-2b 3MU t.i.w. + ribavirin 1000-1200 mg/d for 24 weeks
Summary: Current Treatment Recommendations for HCV

- Nonresponder to IFN monotherapy or nonresponder or relaper after combination therapy
  - Retreat nonresponders to IFN monotherapy using combination therapy
  - Treatment goal shifts from viral eradication to delaying disease progression and preventing the need for liver transplantation and the development of cirrhosis, decompensation, or HCC
Summary: Current Treatment Recommendations for HCV

- Decide whether to continue or stop treatment
- If treatment is to continue, individualize regimen based on histologic and other patient factors
  - Continue treatment within the confines of a clinical trial whenever possible
  - Consider adjunctive and alternative therapies
  - Switch to a different form of interferon
Case Study

- 53-year-old male with:
  - A heavy smoking habit
  - Chronic HCV contracted from:
    - Cocaine use
    - “Jailhouse tattoos” received 25 years ago
    - History of blood transfusion
  - Cryoglobulinemia
Case Study (cont’d)

- 53-year-old male with:
  - Vasculitic skin rash
    - Present on trunk and extremities despite treatment with prednisone (60 mg/d)
  - Severe pain in extremities that requires a wheelchair and is treated daily with morphine
  - Past medical history includes:
    - Alcohol abuse (sober for 6 months)
    - Clinical depression requiring antidepressants
    - Appendectomy
    - Invasive squamous cell cancer of the larynx treated with radiation
Case Study (cont’d)

• Current medications include:
  – Morphine sulfate (MS contin)
  – Lorazepam (Ativan)
  – Oxycodone HCL with acetaminophen (Percocet)
  – Prednisone
  – Lansoprazole (Prevacid)
  – Inhalers
Physical Exam revealed the following:
- Cushingoid male
- Multiple erythematous papules on arms, legs, and trunk
- Ulceration on left forearm and bilateral ankles
- Tattoos on both arms

HEENT showed:
- Normal fundi
- No neck mass
Case Study (cont’d)

• Lung exam revealed:
  – Bilateral inspiratory and expiratory rhonchi
  – Heart sounds: normal

• Abdominal exam found:
  – Midline scar
  – Moderate obesity
  – No hepatosplenomegaly

• Neurological exam: symmetrical diffuse weakness
Case Study (cont’d)

• Laboratory exam findings:
  – WBC – 19.8
  – Hgb – 13.2
  – Plts – 277
  – Electrolytes – normal
  – AST – 12
  – ALT – 27
  – Alk Phos – 98
  – T. Bili – 0.4
  – PT – 13.5
  – Albumin – 3.4
Case Study (cont’d)

- Cryoglobulin – 23.75 (nl – 0 to 1.8)
- CD4 – low
- Total Complement – normal
- C3 FANA – negative
- HBsAg – negative
- TSH – 3.65
- HCV PCR titer – 274,651 copies/mL
- HCV Genotype – 3

• EKG – normal
• Liver Biopsy – stage 1, grade 2 chronic HCV
Case Study: Question

• How would you manage this patient with:
  – Chronic HCV
  – Cryoglobulinemia
  – Severe vasculitis
  – Multiple psychiatric problems
  – Various concomitant medical conditions
Case Study: Answer

- The patient was started on interferon alfa-2b and ribavirin combination therapy at the usual dose.
- Within one week:
  - Significant improvement of vasculitis
  - Prednisone dose was tapered and discontinued after one month.
Case Study: Answer

- The patient suffered numerous complications due to therapy including:
  - Anemia requiring:
    - Ribavirin dose reduction
    - One blood transfusion
  - Two episodes of pneumonia
    - One requiring inpatient treatment
  - Exacerbation of depression
    - Treated with sertraline
    - Monitored closely by psychiatric follow-up
Case Study: Answer

• After completing 6 months of therapy the patient has:
  – Negative HCV PCR
  – Healing of all vasculitic ulcers
  – Continuing requirement of morphine for pain control