Goals of Therapy

- **Primary:**
  - To eliminate the virus

- **Secondary:**
  - To decrease inflammation and cell death in the liver
  - To slow the progression of the disease to cirrhosis
  - To decrease risk of liver cancer
  - To defer or avoid liver transplantation

**Patterns of Response**

- **Nonresponder**
- **Breakthrough (Nonresponder)**
- **Responder**
- **Sustained Responder**
- **Relapser**

**Progress in Hepatitis C Therapy**

- IFN 24 wk: 10%
- IFN 48 wk: 18%
- IFN/RBV: 41%
- Peg-IFN/RBV: 54%
**HEPATITIS C**

**Standard Therapy**

- **Pegylated Interferon**
  - modifies immune system activity
  - antiviral activity

- **Ribavirin**
  - mimics a building block for viral genes
  - interferes with viral replication

**HEPATITIS C**

**The Science of Pegylation**

- Addition of a heavy, inert molecule - polyethylene glycol

- **Advantages:**
  - Longer lasting
  - Better availability to liver
  - Decreased elimination
  - Increased effectiveness
  - More convenient, once a week dosing schedule

**HEPATITIS C**

**Pegylated Interferons**

- **Peg-IFN α-2b**
  - 12 kd molecule
  - Linear chain
  - 30% kidney clearance
  - weight-based dose

- **Peg-IFN α-2a**
  - 40 kd molecule
  - Branched chain
  - ~100% liver clearance
  - single fixed dose

**HEPATITIS C**

**Peg-IFN/RBV Overall Virologic Response**

- Fried et al. NEJM, 2002.
HEPATITIS C
Predicting Response to IFN Therapy

- Virology
  - Genotype 2 or 3
  - Low viral load (<2 million copies/ml)

Adapted from Davis GL et al. Hepatology. 1997;26(suppl 1):123S.

HEPATITIS C
Peg-IFN/RBV
SVR by Genotype

![Graph showing SVR by Genotype and Treatment]

Fried et al. NEJM. 2002.

HEPATITIS C
Peg-IFN α-2a/RBV
SVR Genotype 1 by Viral Load

![Graph showing SVR by Viral Load]


HEPATITIS C
Predicting Response to IFN Therapy

- Virology
  - Low viral load (<2 million copies/ml)
  - Genotype 2 or 3

- Liver biopsy
  - Mild inflammation
  - Absence of scarring
  - Low iron stores in liver

Adapted from Davis GL et al. Hepatology. 1997;26(suppl 1):123S.
**HEPATITIS C**

**Peg-IFN α-2a/RBV SVR Cirrhosis**

- 63% for All patients (n=424)
- 67% for Non-cirrhotics (n=313)
- 50% for Cirrhotics (n=111)

**Predicting Response to IFN Therapy**

- Host factors:
  - younger age
  - shorter duration of disease
  - non-African American race
- Initial response to therapy:
  - 100 times decline in viral load or negative virus by 12 weeks of therapy
- Adherence to therapy:
  - 80% IFN/80% RBV/80% duration


**Response to Therapy: 80/80/80 Adherence**

- ≥80% IFN dose: 41%
- ≥80% RBV dose: 48%
- ≥80% duration of therapy: 15%

**Side-Effects of Pegylated IFN**

- Flu-like symptoms
- Fatigue
- Emotional lability
- Depression
- Sleep difficulties
- Poor appetite/wt loss
- Diarrhea
- Rash
- Injection-site reactions
- Hair loss
- Low white blood count
- Low platelet count
- Thyroid dysfunction
- Visual problems
- Hearing loss
- Nerve damage


### Side-Effects of Ribavirin

- Nausea
- Rash, dry skin, itching
- Chest pain unrelated to heart disease
- Dry cough
- Shortness of breath (out of proportion to anemia)
- Destruction of red blood cells
- Fetal deformities in pregnant women

### Anti-HCV Therapy

#### Indications:
- Scarring on liver biopsy
- Moderate to severe inflammation or cell death
- Symptomatic patients
- Extrahepatic manifestations

#### Duration
- 48 weeks for genotype 1
- 24 weeks for genotype 2 or 3

#### Contraindications:
- Pregnancy
- Liver failure
- Unstable heart disease
- Blood diseases involving red blood cell abnormalities
- Severe bone marrow suppression
- Severe depression

#### Cautious use:
- Anemia or low red blood cell count
- Preexisting psychiatric disorders
- Active substance abuse
- Severe lung disease
- Serious kidney disease
- Autoimmune diseases
Other Management Issues

Dietary Advice

- Alcohol abstinence
- Well-balanced diet
- Exercise

HEPATITIS C

Counseling Issues

- Sexual partner/s should be tested for HCV.
- Practice safe sex if there are multiple sexual partners and during menses.
- Avoid sexual practices that have a high risk for trauma or tear of the genital lining.

HEPATITIS C

Counseling Issues

- No sharing of toothbrushes or razors with other individuals.
- Avoid exposing other people to infected blood during injuries.
- Inform health care personnel (doctors or dentists) about existing hepatitis C infection.
- Support groups are available.
Other Medications

- Be cautious about taking medications that may be harmful to the liver, including natural remedies and herbal medications.
- Vaccination for hepatitis A and B if not yet immune to these viruses.

Conclusions

- Therapy for hepatitis C has come a long way, with sustained viral eradication achievable in about 60% of cases.
- Treatment comes with side-effects, and management of these side-effects is crucial in promoting adherence to therapy.

- Progress is continually being made in the realm of anti-HCV therapy, partly due to advances made in science and medicine but most importantly, due to patients’ participation in clinical trials.