Pediatric Hepatitis C: Who is at risk and What do you do?

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Human Hepatitis Viruses

- **Non-enveloped (enterically-transmitted)**
  - HAV: RNA, 27 nm
  - HEV: RNA, 32 nm

- **Enveloped (bloodborne pathogens)**
  - HBV: DNA, 42 nm
  - HDV: DNA, 36 nm
  - HCV: RNA, 55 nm
  - HGV: DNA, ?
HCV in the United States

- 2.7 million infected, ++
- 30,000 infections/year
- Lifetime risk of death from HCV: 10-20%
- 10,000 deaths/year
- Leading cause for liver transplantation
HCV-Current Management Approaches

Screening for infection

- Assays (how)
- Populations at risk (who, when)
  - Pregnant women
  - Infants and Children
  - High-risk exposures
Monitoring Liver Disease
- Clinical tools (laboratory, radiologic)
- Liver biopsy
- Monitoring for cancer

Indications for treatment
- Variables to consider
- Treatments
Screening - How

1) EIA/RIBA testing for HCV-antibodies
   a) Sensitivity ~ 99%, Specificity~99%
      (sensitivity 50-60% in low risk patients)
   a) Acute Infection (>8 weeks)

2) HCV RNA
   a) Verify infection when anti-HCV+
   b) Acute infection (>2 weeks)
   c) Conditions with diminished Antibody production
Screening - How

2) HCV RNA (con’t)

- Qualitative: Positive/Negative;
  PCR/TMA 9.6-50 IU/mL

- Quantitative: Level of HCV RNA;
  PCR/branched DNA signal amplification
  variable dynamic ranges (25-7,7000,000 IU/L)

3) HCV Genotype
Screening for HCV – Who

- Children of (+) Mothers (6%)
- History of Blood products pre 1992 (10%)
- History of IVDA/INDA (90%)
- History of hemodialysis (15-50%)
- Hemophilia prior to 1987 (90%)
- Sexual partners of HCV+ person (2-5%)
- Needle stick exposure (2-5%)

Adapted from AASLD Practice Guidelines on HCV, 2004, Hepatology
HCV Screening in Pregnancy

1-4.3% Pregnant Women Infected
25-30% Aware of infection

Compared:
  a) No screening (current SOC)
  b) Screening and Rx
  c) Screening, elective C-section, Rx

Evaluated: Costs and Quality-adjusted life years for mother and child.

*Screening asymptomatic pregnant women for HCV is not cost-effective*

Infants born to HCV+ Mothers

- 5% Perinatal transmission
- **Prevention:**
  - Avoid fetal scalp electrode monitors
  - ROM < 6 hours
- **Screening:**
  - Anti-HCV when > 12-18 months, or
  - HCV RNA > 1 month
Population at Risk for HCV

- 0.2 – 0.4% of children
- 1.8% of adults
- 80% of new IVDU become infected within 12 months of use
- 10 – 83% of inmates at adult correctional facilities

Preventative Medicine 1999; 28
police.fife.net/leftlinks/advice/drugsidentification.shtml
## HCV in High Risk Youth

### Echo Glen Children’s Center

<table>
<thead>
<tr>
<th>Percentage</th>
<th>Description</th>
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<tbody>
<tr>
<td>305 (74%)/406</td>
<td>Children screened (mean age 14 yrs)</td>
</tr>
<tr>
<td>70%</td>
<td>Sexual activity (mean age of onset 12 yrs)</td>
</tr>
<tr>
<td>18%</td>
<td>history of STDs</td>
</tr>
<tr>
<td>35%</td>
<td>&gt; 5 partners</td>
</tr>
<tr>
<td>6%</td>
<td>IVDA</td>
</tr>
<tr>
<td>32%</td>
<td>INDA</td>
</tr>
<tr>
<td>53%</td>
<td>Body piercing</td>
</tr>
<tr>
<td>33%</td>
<td>Tattoos</td>
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</tbody>
</table>

HCV in High Risk Youth

The Echo Glen Experience

2% of children were HCV positive

- IVDA RR=15.9
- Hx of STDs RR=14.5
- 17% had knowledge of HCV risk factors

Assessing Disease Severity

Tools Normally Used:

- Physical Examination
- Ultrasound examination of the liver
- Liver function tests
- ALT Levels
- Liver biopsy
Liver biopsy in HCV

- **Why:** Extent of Liver damage
  Best prediction of prognosis
  Fibrosis - predictor of Rx response
  Aid in treatment decision making

- **When:** Pre-therapy
  Every 3-5 years if new decisions/progression

HCC Surveillance in HCV

8,500-11,000 New cases/year
≥ 50% due to HCV

Incidence in cirrhotic HCV: 2-8%/year
Non-cirrhotic risk is less; ? Bridging fibrosis
Surveillance for HCC should be offered when risk is ≥ 1.5%/year

www.cancernews.com/data/Article/504.asp
HCC Surveillance in HCV

Tests:  Alpha-fetoprotein in (AFP)
        Ultrasonography (US)

Interval:  Every 6-12 months

Rec:  AFP and US
        - Baseline
        - Every 6 months when bridging fibrosis or cirrhosis

*AAASLD Practice guidelines: Management of HCC. Hepatology 2005.*
Hepatitis C: Who should be considered for treatment?
*individualized*

- Those with advancing liver disease
- Those most likely to respond
- Those who are highly motivated despite the risks of therapy
  - Children > 2 years
  - Normal ALT
HCV IFN Therapy – response definition

- IFN
- End-of-treatment (ETR)
- Sustained (SR)
- ALT
- HCV RNA
- Normal
- Months
Interferon α2b + ribavirin
In Children with Chronic HCV

Hepatology, 2005;42:1010-1-18
The PEG Molecules

2° and 3° interferon protein structure preserved

Peg-Intron
Schering-Plough

Pegasys
Hoffman-LaRoche

Slide from Dr. A. Larson
PEG $\alpha_2a$ + Ribavirin for Chronic HCV

- A = IFN $\alpha_2b$ + Ribavirin
- B = PEG 2a* + Ribavirin

*Not approved for pediatric use

N Engl J Med 2002; 347(13)
HCV in Pediatrics

- Screening at-risk populations important as most patients are clinically silent

- Monitoring tools limited, biopsy still the best

- Treatment options exist; decisions must be individualized