Epidemiology of Viral Hepatitis in Alaska

Brian J McMahon
Alaska Native Tribal Health Consortium and Arctic Investigation Program/CDC
Hepatitis A: Background

- Prior to the availability of hepatitis A vaccine Alaska experienced large recurrent outbreaks of acute hepatitis A with the highest impact in rural areas.
- Introduction of universal childhood vaccination has dramatically reduced the incidence of acute HAV in Alaska from the highest in the US to the lowest in the world.
Geographic Distribution of HAV Infection 1990

Anti-HAV Prevalence
- High
- Intermediate
- Low
- Very Low
Hepatitis A in Alaska Natives and Non-Natives in Alaska, by Year

- Alaska Native
- Non-Native

State of Alaska vaccination programs


Rate per 100,000
Geographic Distribution of HAV Infection 2010

Anti-HAV Prevalence

- High
- Intermediate
- Low
- Very Low
Alaska Population-Based HBV Cohort

- 1560 patients identified between 1974 and 1987 with chronic HBV infection
- 1350 patients are still alive
- Acute HBV in Alaska previously reviewed by Lisa Bulkow
Alaska HBV Genotype Distribution Survey

- Genotype D: 55%
- Genotype C: 13%
- Genotype F: 17%
- Genotype A: 9%
- Genotype B: 6%
Alaska HBV Genotype Distribution Survey

Genotype A
Genotype B
Genotype C
Genotype D
Genotype F

Dr. Vladimir Chulanov
Alaska HBV Genotype Distribution Survey

Genotype A
Genotype B
Genotype C
Genotype D
Genotype E
Genotype F
Genotype H

NJ, K80, S-gene, 410 bp

Dr. Vladimir Chulanov
Genotype A

- All Alaskan genotype A strains belong to A2 subtype
- This subtype is typical for Europe and North America
- Encode serotype adw2
- Highest percent of variability within 410 bp
  S-gene fragment is 2.5%

Dr. Vladimir Chulanov
Genotype D – Two subtypes divided

Dr. Vladimir Chulanov
Genotype D – Two subtypes divided

Dr. Vladimir Chulanov
Genotype F

- Highest percent of variability within 410 bp S-gene fragment is 1.4%
- ~ 70% of strains were identical.

Dr. Vladimir Chulanov
Genotype F Identified Primarily in Southwest Alaska

HCC Patients: 33% (1/3)  Controls: 0% (0/25)
HCC Patients: 50% (1/2)  Controls: 5% (4/81)
HCC Patients: 60% (3/5)  Controls: 25% (37/149)
HCC Patients: 81% (22/27)  Controls: 38% (48/126)
HCC Patients: None  Controls: 7% (2/27)
HCC Patients: 56% (5/9)  Controls: 16% (33/212)
Migration of Genotype F throughout Southwestern Alaska

Circle size is proportional to Number of carriers
HBV Genotype and Transmission in Alaska

• In northwest Alaska where genotype C predominates maternal infant transmission of HBV was common prior to vaccination.

• In areas where genotype C was not found such as southwest Alaska, transmission was predominantly child to child through open cuts and scratches and adults through sexual exposure and perinatal transmission played a minor role.
HBV Genotype Associations

• Genotype C associated:
  – Perinatal transmission
  – High rates of HCC compared to A2, B6 and D2,3 and cirrhosis starting age 40

• Genotype D3: Associated with HBV vasculitis which disappeared post vaccination

• Genotype F associated with HCC in children and young adults

• Genotype B6: No serious sequelae to date
<table>
<thead>
<tr>
<th>Genotype</th>
<th>No. HBeAg+</th>
<th>Age 50% lost HBeAg</th>
<th>Age 75% lost HBeAg</th>
</tr>
</thead>
<tbody>
<tr>
<td>$A_2$</td>
<td>34</td>
<td>19.8</td>
<td>32.1</td>
</tr>
<tr>
<td>$B_6$</td>
<td>6</td>
<td>19.5</td>
<td>27.5</td>
</tr>
<tr>
<td>$C_2$</td>
<td>36</td>
<td>47.8</td>
<td>58.1</td>
</tr>
<tr>
<td>$D$</td>
<td>305</td>
<td>18.0</td>
<td>27.3</td>
</tr>
<tr>
<td>$F_1$</td>
<td>126</td>
<td>16.1</td>
<td>24.5</td>
</tr>
</tbody>
</table>

*P<.001 genotype C vs. other genotypes
Estimates of Chronic HBV in State of Alaska Using 2010 Census

- Alaska Population: 710,231
  - Foreign born: 6.6%
  - Asian ethnicity: 5.4% vs. 4.8% US
  - Pacific Island: 1.0% vs. 0.2% US
- Ethnicity Numbers:
  - Asian: 38,131
  - Pacific Islander: 7,400
  - Plus unknown number of Eastern European and other potential high risk groups
- B McMahon’s quasi accurate estimate of number of chronic HBV in non Alaska Native persons
  - 5% infected: 2,300
  - 10% infected: 4,600
Alaska Native/American Indian Persons in Alaska with Hepatitis C

- Anti-HCV positive (living & dead) 2,300
- Anti-HCV positive (living) 1900
- Enrolled in outcomes cohort
  - 1,234 (living and dead)
  - 986 (living)
  - 967 HCV RNA positive (78.4%)
  - 260 HCV RNA negative (21.1%)
  - 7 no HCV RNA RNA done
Figure 1: Primary Risk Factor/Behaviors in Alaska Natives with HCV

Possible High Risk Behaviors: Snorting, High Risk Occupation, ≥10 Sexual Partners, HCV Household Contact, Tattoo, HCV Sexual Partner, IDU Sexual Partner, Toothbrush/Razor Sharing
Genotypes in Hepatitis C Cohort

- Genotype 1: 65%
- Genotype 2: 21%
- Genotype 3: 14%
- Genotype 4: < 1%
Age Breakdown of HCV Cohort

(86% > age 40. Mean age = 49 years. 54% female)
Conclusions: Epidemiology of HCV in Alaska Natives

- Prevalence of HCV within NHANES estimates for US
- Risk Factor distribution same as US
- Proportion who recovered from HCV same as NHANES study
- Genotype distribution similar to NHANES except slightly increased proportion of genotype 3
Alaska HCV Outcome Study

- Retrospective-prospective population-based study
- 960 patients followed 1994-2005
  - 695 chronic HCV; 214 recovered (RIBA +)
  - Mean years prospectively: 7.2 years
  - Mean years retrospectively: 12.1 years

McMahon et al Gastroenterology 2010; 138:922-31
HCV Outcome Study: Initial Evaluation

- Alcohol usage measured at enrollment
  - 13% consumed ≥ 50gms ETOH/day
- Incidence calculated per 100 person years of follow-up
  - End stage liver disease
  - Liver related death
  - HCC
- Persons with chronic HCV were compared to those who recovered.
## Incidence End Stage Liver Disease per 100 Person Years

<table>
<thead>
<tr>
<th>Factors</th>
<th>Chronic HCV</th>
<th>Recovered HCV</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol ≥50 gms/day</td>
<td>3.21</td>
<td>5.69</td>
<td>P=0.13</td>
</tr>
<tr>
<td>Alcohol &lt;50 gms/day</td>
<td>1.58</td>
<td>0.36</td>
<td>P=0.002</td>
</tr>
</tbody>
</table>

Gastroenterology 2010
# Incidence Liver Related Death per 100 Person Years

<table>
<thead>
<tr>
<th>Factors</th>
<th>Chronic HCV</th>
<th>Recovered HCV</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol ≥50 gms/day</td>
<td>2.28 vs.</td>
<td>3.50</td>
<td>P=0.34</td>
</tr>
<tr>
<td>Alcohol &lt;50 gms/day</td>
<td>0.77</td>
<td>0.09</td>
<td>P=0.01</td>
</tr>
</tbody>
</table>
Mortality in Alaska Natives with HCV Infection vs. Those without

• AN persons with chronic HCV are 17 times more likely to die a liver related death than rest of the US population as a whole

• AN persons who recovered from HCV are 12 times more likely to die a liver related death than AN population
Survival Probability for free from end stage liver disease (ESLD) or liver-related death (LRD)

Predicted probabilities are calculated for a person infected with HCV at 25 years of age
Estimate of HCV Infected Persons in State of Alaska

- Number on non duplicate names in Alaska State database: 13,944 anti-HCV positive
  - 2,300 Alaska Native Persons (1.8%)*
  - 11,644 non Alaska Natives (1.6 %)*

- B. McMahon’s quasi accurate estimates of HCV number and prevalence in Alaska^
  - 25% of infected identified: 55,776 (7.9%)*
  - 50% of infected identified: 27,288 (3.8%)*

*Estimated population prevalence
^Rates in Alaska Natives may be lower as only 1/3rd are urban
Conclusions:

• Alaska Natives have similar prevalence, genotypes and risk factors as US as a whole
• Alcohol is a potent co-factor in development of adverse outcomes
• State of Alaska as a whole may have a higher prevalence of HCV than US