Hepatitis D outbreak among children in a hepatitis B hyper-endemic settlement in Greenland

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Hepatitis B in Greenland

- HBV high-endemic country (HBsAg ≈ 7%)
- Cirrhosis and HCC less frequently observed than in other high-endemic countries. (Børresen et al, JNCI, 2011)
  - Benign genotypes
  - Age at infection might be later than in other high-endemic countries.

![Map of global hepatitis B prevalence](image)
Greenland 1965-1998
HBV Markers by age

40 – 75% exposed (HBcAb+)
7 – 20% chronically infected
(HBsAg+)

Model
HBV age at infection

![Graph showing HBV incidence per 100 person years by age.](image)
Hepatitis B outbreak in the settlement of Itilleq, 2005-2007

Sisimiut (n=5,500)
Sarfannguaq (n=130)
Itilleq (n=135)

Børresen et al.
Hepatitis D outbreak among children in a hepatitis B hyper-endemic settlement in Greenland.
Hepatitis B in Itilleq

- March 2005: 3 children from Itilleq admitted to hospital with severe clinical hepatitis (7, 9, 10 years)
Initiated study: Aims and Methods

- Determine the prevalence of HBV in Itilleq
- Detect the degree of elevated liver enzymes in chronically infected persons
- Determine possible explanatory factors for the sudden occurrence of severe clinical hepatitis among children

- March 2006: HBV screening of total population (n=135)
- March 2007, Jan. 2009 and 2011: Re-testing & follow-up
Results 2006-2007

90% (122/135 persons) tested

Overall sero-prevalence
- 27% chronic infected
- 56% immune
- 17% never exposed

94% (52/54) of children tested
- 29% chronic infected
- 35% immune
- 37% never exposed
HBV genotypes Itilleq

Alle samples genotype D1/2

- A new Greenlandic subgenotype?
- D1: Mongolia, Kamchatka peninsula (Russia), Japan, Germany,
- D2: Alaska, UK, Spain, Greece, Turkey, Russia
- HBsAg subtype: ayw3
Hepatitis B

Done by:
Tanaka Y, Mizokami, M Japan
Phylogenetic tree
Itilleq and neighbouring Sarfannguaq
Hepatitis B - Clinical impact?

Liver enzymes

U/L

250

200

150

100

50

0

ALT

AST

Chronic

Immune

Negative

Chronic

Immune

Negative

ASTALT

U/L
Severity markers for HBsAg-positive, 2006-2007

<table>
<thead>
<tr>
<th></th>
<th>Children (n=15) (%)</th>
<th>Adults (n=16) (%)</th>
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<tbody>
<tr>
<td>ALT &gt; 45 I/U</td>
<td>73</td>
<td>38</td>
</tr>
<tr>
<td>Viral load&gt; 1 mio. IU/mL</td>
<td>47</td>
<td>6</td>
</tr>
<tr>
<td>HBeAg positive</td>
<td>53</td>
<td>0</td>
</tr>
<tr>
<td>Hepatitis D (HDV) positive</td>
<td>40</td>
<td>63</td>
</tr>
<tr>
<td>HDV-seroconversion</td>
<td>33</td>
<td>0</td>
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</tbody>
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Regression model:
Hepatitis D the strongest predictor for elevated ALT (liver damage)
In 2009, additional 2 children HDV seroconverted
# Viral load and ALT

<table>
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<th>Children (n=15)</th>
<th>Adults (n=16)</th>
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<tbody>
<tr>
<td><strong>HBV DNA IU/mL</strong></td>
<td></td>
<td></td>
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<tr>
<td>median, (Q25-75)</td>
<td>137 $\cdot$ 10^6 (3.53–14.300 $\cdot$ 10^6)</td>
<td>327 (71–5.606)</td>
</tr>
<tr>
<td><strong>HDV RNA seq/mL</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>median, (Q25-75)</td>
<td>35.000 (39.000–21 $\cdot$ 10^6)</td>
<td>2.3 $\cdot$ 10^6 (0.15–4.7 $\cdot$ 10^6)</td>
</tr>
<tr>
<td><strong>ALT U/L</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>median, (Q25-75)</td>
<td>68 (49–321)</td>
<td>53 (31–120)</td>
</tr>
</tbody>
</table>
HDV in Greenland

• Worldwide, 8 genotypes, genotype I most adverse outcomes

• Previous studies: HDV prevalence in Greenland uncertain (5-40% of HBsAg+, regional differences, higher prevalence with genotype D)

• In the settlement: 3 different clusters of genotype I, aligned with sequences from Mongolia, Iran, Turkey, US, Canada, Taiwan, France and Italy
HDV, 548 bp
Neighbor-joining, JC
20 Greenland sequences
125 reference sequences

Genotype I
Itilleq HDV Genotype I 3 clusters

Year of birth from 1977 to 2005

Year of birth 1967

Aligned with sequences from US and Canada, Mongolia, Iran, Turkey, Taiwan and Turkey

Year of birth from 1958 to 1990
HBV in Itilleq – Conclusions

- High prevalence of chronic HBV infection, especially among children
- Elevated liver enzymes in chronic infected (HBeAg-positive) children
- Super-infection with Hepatitis D most likely
- Five children HDV sero-converted from March 2006 to June 2007, September 2009 additional two chronically infected children HDV positive
- Ongoing HDV outbreak in Itilleq
- Changing epidemiology of HBV in Greenland?
- HDV – a threat?
Thank You

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