HBV Vaccination Effectiveness in Greenland

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HAV EPIDEMICS

- **1970-74**
  - 11/15 districts
  - 4,961 cases (11%) of clinical hepatitis
  - Incidence: 2,606/100,000 persons per year
  - 93% of cases among persons aged 0-25 years
  - Immunity in older persons compatible with 1947-48 epidemic
  - Attack rate Danes: 1/6 AR for Greenlanders
  - Case-fatality rate 0.3%
HAV AT PRESENT

HAV antibodies
Sisimiut & Ilulissat 1994 (Langer et al).

Estimated HAV prevalence

Age, years

Seroprevalence (%)

0-9 10-19 20-29 30-39 40-49 50-59 60-69 69+

Low, intermediate, and high.

This map generalizes currently available data, and patterns might vary within countries.
HCV, HDV, HEV

- **HCV, Langer et al 1994**
  - 0.8% seroprevalence
  - None HCV RNA positive
  - 0.09% in routine tests

- **HDV**
  - 11% (1989, Olsen), 40% (1994, Langer), 30% (2009, Børresen) of HBsAg-infected HDV positive

- **HEV, Langer et al 1994**
  - 3% seroprevalence (~rate of false test positivity)
  - None HEV RNA positive
By September 2010, the HBV vaccine was included in the childhood vaccination program in Greenland.
HBV screening of pregnant women in Greenland

Established in 1992

• HBsAg testing at first pregnancy examination
• Test result and date of testing recorded on the perinatal chart
• Children born to HBsAg positive mothers should be vaccinated according to National Guidelines
Children born to HBsAg-positive mothers

- Birthday 1 Month
  - 1. Hep B
  - 2. Hep B + immunoglobulin

- 2 Month
  - 3. Hep B

- 12 Month
  - 4. Hep B
  - HBV vaccine: 10 mikrogram recombinant
Aims of the study

Part I

• HBsAg prevalence among pregnant women

Part II

• Vaccination coverage and timeliness of given vaccinations among children of HBsAg-positive mothers

• Prevalence of break-through infections among vaccinated children of HBsAg-positive mothers

• Levels of protective antibodies among vaccinated HBV-negative children.

Materials and Methods

Hepatitis B database

- Established in 2004
- All HBV test results (HBsAg and anti-HBs) from Greenland from 1992 to 2009, 2000-2004 missing due to errors in the database under construction

CRS – Civil Registration System

- Identifying children born in Greenland from 1992 to 2007
- Linkage by the mothers CRS-number, children born to HBsAg-positive mothers identified
HBV prevalence and vaccination coverage – methods and result

- 4050 pregnant women with HBV test results
- 248 children included
- 207 (83%) children with information on vaccination coverage
- 3.2% (135) HBsAg-positive regional differences
- 31 children excluded due to death, emigration, mother HBsAg-negative during current pregnancy
- Review of perinatal chart: Immunoglobulin and 1. vaccination
- Medical and vaccination chart: (1.) 2. til 4. vaccination
HBsAg positive mothers by area (birthplace of child)

4050 women. HBsAg prevalence at first pregnancy after 1992

<table>
<thead>
<tr>
<th>Area</th>
<th>HBsAg Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>North</td>
<td>2.08%</td>
</tr>
<tr>
<td>West</td>
<td>4.81%</td>
</tr>
<tr>
<td>Nuuk</td>
<td>2.08%</td>
</tr>
<tr>
<td>South</td>
<td>1.23%</td>
</tr>
<tr>
<td>East</td>
<td>3.87%</td>
</tr>
</tbody>
</table>

P < 0.001
Vaccination coverage for 207 children from 1992 to 2007

<table>
<thead>
<tr>
<th>Children n.</th>
<th>No vac.</th>
<th>1. vac.</th>
<th>2. vac.</th>
<th>3. vac.</th>
<th>4. Vac.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>207</td>
<td>42 (20.3%)</td>
<td>24 (11.6%)</td>
<td>21 (10.1%)</td>
<td>50 (24.2%)</td>
</tr>
<tr>
<td>Vaccination “on time”&lt;sup&gt;a&lt;/sup&gt;</td>
<td>165</td>
<td>143/165 (87.2%)</td>
<td>110/141 (78%)</td>
<td>67/120 (55.8%)</td>
<td>64/70 (91.4%)</td>
</tr>
<tr>
<td>Birth period</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1992-1995</td>
<td>79</td>
<td>20 (25.3%)</td>
<td>11 (13.9%)</td>
<td>12 (15.2%)</td>
<td>25 (31.7%)</td>
</tr>
<tr>
<td>1996-2000</td>
<td>88</td>
<td>11 (12.5%)</td>
<td>10 (11.4%)</td>
<td>6 (6.8%)</td>
<td>14 (15.9%)</td>
</tr>
<tr>
<td>2001-2007</td>
<td>40</td>
<td>11 (27.5%)</td>
<td>3 (7.5%)</td>
<td>3 (7.5%)</td>
<td>11 (27.5%)</td>
</tr>
<tr>
<td>Area</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High-Endemic</td>
<td>163</td>
<td>34 (20.9%)</td>
<td>22 (13.5%)</td>
<td>14 (8.6%)</td>
<td>35 (21.5%)</td>
</tr>
<tr>
<td>Low-Endemic</td>
<td>44</td>
<td>8 (18.2%)</td>
<td>2 (4.6%)</td>
<td>7 (15.9%)</td>
<td>15 (34.1%)</td>
</tr>
</tbody>
</table>

<sup>a</sup> 48 hours, 2 months, 4 months, 18 months, <sup>b</sup> p < 0.001, HBIG 131/165 (79.4%)
Follow-up study 2008/2009

248 children candidates for follow-up study

35 excluded dead (n=5), emigrated (n=8) excluded areas (n=24)

213 children invited for follow-up

140 children (66%) HBV tested in 2008/2009

3% (4) chronic carriers*
3% (4) immune *
94% (132) negative
HBsAb level >10 IU/L among 'at-risk' children by age group

HBsAb level > 10 IU/L

% 80

60

40

20

0

All

1½-4

5-9

10-14

15+

Age at follow-up (years)

All HBcAb- neg. children

3+ vaccinations

All
HBcAb-negative children with 3+ vaccinations

antibody level by age and Area
Conclusions I

- Regional difference in HBV prevalence among pregnant women
- Every fifth child born to HBsAg positive mother received no immunoglobulin or vaccination postnatally
- Only every third received full vaccination program (4 vaccinations)
- 6% (8) of ‘at-risk children’ had break-through infections
- 50% of these were HBsAg-positive
- Of the 8 HBcAb positive children, 7 had received at least 3 HBV vaccinations, but only half of them immunoglobulin
Conclusions II

- 59% of HBcAb-negative children with 3+ vaccinations had HBsAb < 10 IU/l
- 73% of all included children had HBsAb < 10 IU/L
  - NON – RESPONDERS?
  - COLD CHAIN?
- There was no expected fall in HBsAb level with time since vaccinations in the Western part of Greenland
- Older children with HBsAb > 100 IU/L
  - NATURAL BOOSTING

Does the cellular immune system work eventhough we found low HBsAb levels?
Perspectives

- The program did not work!
- Sep. 2010, HBV vaccination was included in the Childhood Vaccination Program in Greenland (birth, 3 month, 5 month and 12 month)
- HBV testing of pregnant women and HBIG continues
- Better information to the HBsAg-positive mothers as well as the health care personnel
- HBsAb level measurement of vaccinated infants of HBsAg-positive mothers at 15 month of age.
- Booster later in life.
On-going studies

Children with break-through infections

• Looking at escape mutations in the α-determinant of the s-gene

Vaccinated HBcAb-negative children

• Proposal to look at correlation between the HBsAb level and perfluorinated compounds (PCF)
Thank you for your attention
HBV vaccination breakthrough infections

GL8 Mother of Family 4

MENITSGFLGPLLLVLQAGFFLLLTRILTIPQSLDSWWTSLNFLGG
TTVCLGQNSQSPTSNSHTSPTSCPPTC*PGYRWMCCLRFIIIFLFLI
LLCLIFLLVLLDYQGMLPVCPLIPGSSSTTSTGPCRRTCTTPAQGT
SMYPSCCCTKPSDGNCIPIPPSSWAFGKFLWEWASARFSW
LSLLVDFVQWFVGLSPTVWLSVWMMWYWGPSLYSILSPFLP
LL*PIFFCLWVYI.               (F8L, G44E, Y134F)
1527 ♂ Born 1998
- HBsAg +
- HBV DNA: 9.3 x 10^7 IU/ml
- ALT: 56
- HDV:neg

5192 ♂ Born 1993
- HBsAg+, anti-HBe+
- ALT: 358
- HDV: pos

5193 ♂ Born 1994
- HBsAg+, HBeAg+
- HBV DNA: 5.1 x 10^7 IU/ml
- ALT: 357
- HDV: pos

5185 ♂ Born 2003
- HBsAg+, HBeAg+
- ALT: 321
- HDV: pos

1529 ♂ Born 1996
- HBsAg +
- HBV DNA: 5.0 x 10^7 IU/ml
- ALT: 54
- HDV:neg

Mixed WT/Mut also found in 2623

MENITSGFLGPLLVLQAGFFFFFFLLTRLTTIPQSLDSWWTSLNFLGG
TTVCLGQNSQSPTSNHSTSCPPTTPG Tyr WMCLRRFIIFLF
ILLCLIFLLVLILLDYQGMLPVCPLIPGSSTTSSTGPRCTCTTPAQ
GTSMPYSCCCTKPSDGNCNTCIPIPSSWAFGKFLWEWSARF
SWLSLLVPFVQWFVGLSPTVWLSVWMWMWWYGPSLYSILSP
FLPLstopPIFFCLWVYI.