30 Year Follow-up after Hepatitis B Vaccination in Adults and Children

Brian J McMahon MD, Director Liver Disease and Hepatitis Program Alaska Native Medical Center and Arctic Investigations Program, CDC
Declarations and Off Label Use of Medications

- Declarations: None
Vax Demo 30

• Collaborative Study among
  – Alaska Native Tribal Health Consortium
  – Arctic Investigations Laboratory, CDC
  – Division of Viral Hepatitis, CDC Atlanta
  – Yukon-Kuskokwim and Norton Sound Health Corporations
Long-Term Immunogenicity & Efficacy: Children & Adults

- Dates: October 1981- May 1982
- 1630 seronegative Alaska Natives ≥ 6 months of age
- 15 Yukon-Kuskokwim Delta villages
- Plasma-derived vaccine: 0, 1, 6 months
  - 94% had anti-HBs concentrations ≥ 10 mIU/mL
  - Persons < 20 years of age
    • Highest antibody concentrations
    • 99% had anti-HBs ≥ 10 mIU/mL
  - Persons > 50 years
    • 70% had anti-HBs concentrations ≥ 10 mIU/mL
Long-Term Immunogenicity & Efficacy: Children & Adults

- Alaska HBV Vaccine Demonstration Project: 1530 children and adults immunized in 1981
  - Followed yearly for 11 years and at year 15
  - No booster given at 1-11 and 15 years
  - % with anti-HBs levels $\geq 10$ mIU/ml
    - 5 years: 81% (JAMA 1989;261:2362-6)
    - 7 years: 74% (Arch Int Med 1991;151:1634-6)
    - 15 years, 66% (Ann Int Med;2005;142:333-41)

- Test all participants for anti-HBs, HBsAg, anti-HBc
  - Sequence HBV DNA if HBsAg or anti-HBc+
Long-Term Immunogenicity & Efficacy: Alaska Study at 15 years

- No chronic carriers or acute symptomatic HBV cases were identified.
- Anti-HBs GMC decreased from mean concentration of 822 mIU/ml to 27 mIU/ml.
- 23 HBV breakthrough infections defined by appearance of anti-HBc.
- Significantly more breakthrough infections in non-responders compared to responders.
- 6 were transiently HBV DNA positive, 4 of whom had HBV surface mutants and one transiently had 145R escape mutant.

Alaska HBV Vaccine Demonstration Project: 22 Year Follow-Up

- Residents of 7 villages, 9 villages not studied
- % with anti-HBs levels $\geq 10$ mIU/ml
  - 5 years: 81%
  - 7 years: 74%
  - 15 years: 66%
  - 22 years: 59%
- Booster dose Recombivax® 10 mcg given to those who with anti-HBs $<10$ mIU/mL:

McMahon et al. J Infect Dis 2009
Vax Demo 22: Study Design

• Blood Draw/Boost schedule
  – Day 0: Pre booster draw/booster dose
  – Day 10-14: Post booster blood draw
  – Day 30-60 Post booster blood draw

• Booster (anamnestic) response at 2 weeks:
  – 4-fold anti-HBs increase, or
  – Increase to ≥ 10mIU/mL
Vax Demo 22: Preliminary Results in Persons Who Responded to Initial Series

- 5 persons anti-HBc positive (all previously identified, all HBV DNA negative)
- 184 (41%) with anti-HBs <10 mIU/mL
  - 155 received booster and follow up
    - 113/147 (77%) with boost at 10-14 days
    - 125/155 (81%) with boost at 30-60 days
- Overall, 94% (95% CI: 91.0% – 95.6%) had evidence of immunity: either boosted at 10-14 days or had anti-HBs ≥10 mIU/mL at 22 years
Vax Demo 30: 2011-2012

- All 15 Communities will be visited three times
  - Visit one: Draw all participants
  - Visit two: Boost those with anti-HBs <10 IU/ml
  - F/U blood testing of those boosted at 4 wks
Very Preliminary Results

- As of the auspicious date of 11/11/11
- 6 villages have been visited
- Results are available on 165 participants
  - 130 were never boosted previously
  - 35 were boosted at year 22
Results to date

Prevalence of Anti-HBs in Person Who Received Hepatitis B Vaccine 30 Years ago and Did Not Receive a Booster Dose at 22 years follow-up.

<table>
<thead>
<tr>
<th>Age in 2011</th>
<th>No. Participants</th>
<th>% anti-HBs &lt;5 mIU/ml</th>
<th>% anti-HBs 5-9.9 mIU/ml</th>
<th>% anti-HBs ≥ 10 mIU/ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;40</td>
<td>47</td>
<td>45%</td>
<td>6%</td>
<td>49%</td>
</tr>
<tr>
<td>40-60</td>
<td>70</td>
<td>23%</td>
<td>16%</td>
<td>61%</td>
</tr>
<tr>
<td>&gt;60</td>
<td>13</td>
<td>38%</td>
<td>8%</td>
<td>54%</td>
</tr>
<tr>
<td>Total</td>
<td>130</td>
<td>32% (n = 42)</td>
<td>12% (n = 15)</td>
<td>56% (n = 73)</td>
</tr>
</tbody>
</table>
Prevalence of Anti-HBs in Person Who Received Hepatitis B Vaccine 30 Years ago and Received a Booster Dose at 22 years later.

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<th>% anti-HBs &lt; 5 mIU/ml</th>
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</tr>
</thead>
<tbody>
<tr>
<td>&lt;40</td>
<td>8</td>
<td>50%</td>
<td>0%</td>
<td>50%</td>
</tr>
<tr>
<td>40-60</td>
<td>16</td>
<td>50%</td>
<td>19%</td>
<td>31%</td>
</tr>
<tr>
<td>&gt;60</td>
<td>11</td>
<td>100%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Total</td>
<td>35</td>
<td>66% (n = 23)</td>
<td>9% (n = 3)</td>
<td>26% (n = 9)</td>
</tr>
</tbody>
</table>
Conclusions

• There is a high level of humeral protection from hepatitis B vaccination when administered in children > 1 year of age and adults under 50 years of age.
  – For at least 22 years after primary immunization
  – Preliminary 30 results show that > 50% never boosted still have anti-HBs > 10 mIU/ml
  – Only one third of persons boosted at 22 years maintained anti-HBs levels ≥ 10 mIU/ml
  – Complete 30 follow-up results will be available in 2012
  – Cellular immunity may last much longer than humeral immunity can be demonstrated