

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 ≥ 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 ≥ 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:

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 $\geq 10\text{mIU/mL}$

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 \geq 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.

Age in 2011	No. Participants	% anti-HBs <5 mIU/ml	% anti-HBs 5-9.9 mIU/ml	% anti-HBs ≥ 10 mIU/ml
<40	47	45%	6%	49%
40-60	70	23%	16%	61%
>60	13	38%	8%	54%
Total	130	32% (n = 42)	12% (n = 15)	56% (n = 73)

Prevalence of Anti-HBs in Person Who Received Hepatitis B Vaccine 30 Years ago and Received a Booster Dose at 22 years later.

Age in 2011	No. Participants	% anti-HBs < 5 mIU/ml	% anti-HBs 5-9.9 mIU/ml	% anti-HBs ≥ 10 mIU/ml
<40	8	50%	0%	50%
40-60	16	50%	19%	31%
>60	11	100%	0%	0%
Total	35	66% (n = 23)	9% (n = 3)	26% (n = 9)

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

