Protection and Antibody Levels 35 Years after Primary Series with Hepatitis B Vaccine and Response to a Booster Dose

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Disclaimer

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.
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Collaboration between

– Arctic Investigations Program, CDC
– Division of Viral Hepatitis, CDC
– The Alaska Native Tribal Health Consortium (ANTHC)
– The Yukon Kuskokwim Health Corporation (YKHC)
– The Norton Sound Health Corporation (NSHC)
Hepatitis B in Alaska Natives

• 1970’s
  – Highest rates of hepatitis B in the United States
  – Among the highest rates in the world
  – High rates of liver cancer and cirrhosis
Incidence of Symptomatic Hepatitis B in Alaska Native People, 1981-2008

- CDC/IHS Vaccine Demonstration Program begins
- Statewide Program begins

Graph showing the rate per 100,000 people for Yukon Kuskokwim Delta and Statewide programs over the years from 1981 to 2008.
Long-term immunogenicity of Hepatitis B vaccination in Alaska

• Hepatitis B vaccine first used in Alaska in 1981 – plasma-derived hepatitis B (HB) vaccine
• Studies of immunogenicity began at that time
Long-Term Immunogenicity & Efficacy
Children & Adults

• Alaska HBV Vaccine Demonstration Project:
• 1530 children and adults immunized in 1981
  – Followed yearly for 11 years, at years 15, 22 and 30
  – No booster given at 1-11 and 15 years
  – % with anti-HBs levels ≥ 10 mIU/ml
    • 5 years: 81%  (JAMA 1989)
    • 7 years: 74%  (Arch Int Med 1991)
    • 15 years: 66%  (Ann Int Med 2005)
    • 22 years: 60%  (JID 2009)
    • 30 years: 51%  (JID 2016)
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Objectives

– Determine proportion of persons with anti-HBs ≥ 10 mIU/mL 35 years after HB vaccine series
– Evaluate response to a booster dose of HB vaccine among those with anti-HBs < 10mIU/ml
– Compare characteristics of persons with and without protective antibody levels
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Methods

• Study Design
  – Serologic survey
  – HB vaccine booster dose

• Study Setting
  – All 16 of the original villages in the YK Delta and Norton Sound
    • 3 visits X 16 villages = 48 visits
  – Anchorage for those who have moved since the start of the study
Map of Alaska
Participating Regions
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Methods

• Study Population
  – All village residents (6 months or older) who received three doses of plasma-derived HB vaccine with a documented response of ≥ 10 mIU/mL or 10 SRU in the original study in 1981
  – Excluded persons who received a booster dose of HB vaccine anytime over the past 35 years
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Methods

- Visit 1 - initial blood draw, assess anti HBs levels
- Visit 2 - booster to persons anti-HBs <10 MIU/mL
- Visit 3 - post booster draw
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Preliminary Results

• Two Groups
  – Group 1: Persons who did not participate in the 22- or 30-year study
  
  – Group 2: Persons who participated in the 22- or 30-year study, but were not boosted
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Preliminary Results

• Two Groups
  – Group 1: Persons who did not participate in the 22- or 30-year study  Naïve Group
  – Group 2: Persons who participated in the 22 or 30-year study, but were not boosted Group biased toward higher antibody response
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Visit 1

• Group 1: Naïve Group* (N=112)
  – 53 (47.3%) had anti-HBs ≥ 10 mIU/ml

* Did not participate in the previous 22 or 30-year studies
Antibody Decline

Levels of antibody to hepatitis B surface antigen (anti-HBs) decline over 35 years among 2 groups in Alaska.

Group 1 persons had not participated in the 22 nor 30-year follow-up study.
Group 2 persons had participated in the 22 or 30-year follow-up participated but were not given an HBV booster dose.
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Visit 3 (Booster follow-up)

- Booster doses were given only to persons (Groups 1 and 2) who had anti-HBs < 10 mIU/ml
Proportion who Responded to booster dose with anti-HBs ≥ 10 mIU/ml at 35 years

|            | Group 1 | Group 2 |
|------------|---------|---------|
| Anti-HBs levels ≥ 10 mIU/ml | 28/38 (74%) | 23/27 (85%) |
Proportion who Responded to booster dose with anti-HBs > 10 mIU/ml at 35 years

- **Group 1:** 28/38 (74%)
- **Group 2:** 23/27 (85%)

74% responded to booster dose.
Anti-HBs level 35 years after Hepatitis B Vaccination, by Post-vaccination Antibody level after Primary Series Alaska (Group 1)

| Anti-HBs after Primary Series | N   | > 10 MIU at 35 years | P-value |
|-------------------------------|-----|----------------------|---------|
| 10 - 199 mIU/ml               | 17  | 6% (1)               | <0.0001 |
| 200 - 499 mIU/ml              | 16  | 13% (2)              |         |
| 500 – 999 mIU/ml              | 10  | 20% (2)              |         |
| ≥1000 mIU/ml                  | 69  | 70% (48)             |         |

- No association between protective antibody level and:
  Age, gender, BMI, Diabetes, or comorbidities associated with poor immune response
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Results

- 8 persons were anti-HBc positive
  - 4 not previously identified
  - All HBV DNA-negative
  - In the 35-year period, 27 persons had detectable anti-HBc breakthrough infection
  - None had clinical hepatitis or developed chronic HBV
Limitations

• Loss to follow-up over 35 years
• Participants in our study received the primary hepatitis B vaccination series with the plasma-derived vaccine, which is no longer used in the United States
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Summary

• Antibodies have continued to decline over the past 35 years
Summary I

- 47% had anti-HBs level $\geq 10$ mIU/ml at 35 years
- 74% boosted to $\geq 10$ mIU/mL

- Overall, **86%** had evidence of immunity: either boosted **or** had anti-HBs $\geq 10$ mIU/mL at 35 years

- Protection by primary immunization with plasma-derived Hep B vaccine lasts at least 35 years
  - Booster doses not needed
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Summary II

• Our study findings likely apply to populations currently using the recombinant vaccine
  – ACIP closely follows data from the Alaska cohort
    • No recommendation for booster at this time

• Higher anti-HBs after primary series was associated with protective antibody levels at 35 years
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