

Hepatitis B Vaccine Studies in Alaska

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Long-term HB Vaccine and Booster Studies Conducted in Alaska

- Vax Demo
 - Vax Demo Booster
- Long-term Infant
 - LTI Child Booster
- Child Booster
- Employee Booster
- Yo Hep
- Long-term Protection of Vaccine on Incidence and Prevalence of HBV

Hepatitis B Vaccine Demonstration Program (Vax Demo): Conducted in 1981 in Western Alaska

- 1630 Seronegative Yupik persons ages 6 months and older from 17 villages vaccinated with plasma-derived vaccine at 0, 1 and 6 months
- Follow-up serology testing yearly for first 11 years then at year 15
- HBV DNA tested on all persons who acquired anti-HBc during study period
- Report of interim analysis published at 5, 7 and 10 years; 15 year results submitted

Vax Demo: Initial Results

- 94% developed protective antibody levels
- Persons < 20 years old had:
 - The highest response rate (99%)
 - The highest antibody levels
- Persons > 50 years had lower response rate: (70%)

Hepatitis B Vaccine Demonstration Program: Long-term Follow-up

- 10 year follow-up
 - 76% still had protective anti-HBs levels
 - 0.09% got HBV infection (anti-HBc+)
 - None developed clinical hepatitis or became a carrier
- 15 year follow-up
 - 66% still had protective anti-HBs levels
 - None developed clinical hepatitis or became a carrier

Hepatitis B Vaccine Demonstration Program: Long-term Follow-up

Follow-up Period	% protected (anti-HBs)	No. Infected Incidence	No. HBV-DNA +
5-Year	81%	4 (0.45/1000)	Not Done
7-year	74%	8 (0.85/1000)	Not Done
10-year	* 76%	13 (0.94/1000)	Not Done

Vax Dem: 22-Year Follow-up

- 22 year follow-up study in 2003-2004
 - Contact 1030 of the original participants from 7 villages
 - Test for hepatitis B markers
 - If anti-HBs < 10 mIU, give booster dose of hepatitis B vaccine and retest at
 - 10-14 days
 - One month
 - One year

Conclusion: Vax Demo Study

- Long-term protection in children and adults lasts at least 15 years after hepatitis B vaccination
- Booster doses in these groups are not needed for at least 15 years.

Long-term Protection of Infant Hepatitis B Vaccination: LTI Study

- Objectives
 - To determine the persistence of protective anti-HBs among a cohort of AN successfully immunized with HB vaccine beginning at birth
 - To determine the frequency and characteristics of breakthrough infections among this cohort

Manuscript in preparation

LTI Study: Methods

- **Study population**

- Convenience sample of AN infants who completed the recommended series of HB vaccine during 1984-1995
- Responded to vaccine (anti-HBs \geq 10miu/ml)

LTI Hepatitis B Study: Methods

- **Laboratory**

- Serologic testing for anti-HBs and anti-HBc done every other year until age 16 years old
- Specimens positive for anti-HBc
 - Tested for HBsAg
 - Tested for HBV DNA using PCR

LTI Results

- Total number of children: 334
- Median specimens per child: 5
 - Range 2-11 specimens
- Median years of follow-up: 10
- Percent males: 55%

LTI: Results

- Vaccine type
 - Plasma-derived 99 (30)
 - Recombinant 235 (70)
- Maternal HBsAg status
 - Positive 136 (41)
 - Only 8 (6%) HBeAg-positive
 - Negative 198 (59)

Hepatitis B Vaccine: Long-term Protection when Administered to Newborns: Conclusions

- No evidence of serious breakthrough infections at 16 years of follow-up, but asymptomatic anti-HBc+ infections occur
- Loss of protective anti-HBs when vaccinated in infancy more rapid than persons vaccinated >6 months of age
- Protection from hepatitis B lasts for at least 16 years

Other Studies involving Long-Term Follow-up on Infant Hepatitis B Vaccination

- Most studies have been performed in Infants of HBsAg/HBeAg+ mothers
- Marked variability in vaccine schedule and number of immunizations:
 - starting at birth vs. at 2-3 months of age
 - Administering last dose at 6 vs. 12 months
 - Administering 3 vs. 4 doses

Other Studies involving Long-Term Follow-up on Infant Hepatitis B Vaccination

- 51%-85% of children of HBsAg/HBeAg+ mothers vaccinated in infancy had anti-HBs levels ≥ 10 mIU/ml at 10 years
- Study from Hawaii in low risk infants given 2.5 mcg recombinant vaccine at birth: Only 19% had anti-HBs levels > 10 mIU/ml at 6-years but all responded to a booster dose
- Our study suggests anti-HBs decline more rapid in children of HBsAg+/HBeAg- or HBsAg- moms

Hepatitis B Child Booster Studies

- Purpose: To determine the response to a booster dose in children who received hepatitis B vaccine during infancy.
 - Child Boost: 310 children whose initial response to hepatitis B vaccine is unknown
 - LTI Boost: 47 children who had documented anti-HBs level of ≥ 10 mIU after vaccination

Long-Term Immunogenicity & Efficacy: Vaccination in Infancy

- 310 children immunized on schedule starting at birth but response to vaccination unknown
 - 208 tested at age 5: children with anti-HBs < 10 mIU were given a booster dose
 - 102 children deferred testing until age 9, then those with < 10 mIU were given a booster dose

Long-Term Immunogenicity and Response to a Booster Dose in Low Risk Children Immunized in Infancy: Vaccine Response Unknown

No.	Vaccine Type	Maternal HBsAg	Mean Age	%Anti-HBs \geq 10 mIU	Booster Response
102	Plasma	negative	8.9 years	41%	33/54 (61%)
208	Recomb	negative	5.1 years	12%	120/134 (90%)

Long-Term Immunogenicity and Response to a Booster Dose in Children Immunized in Infancy: Responded Initial Vaccination

No.	Vaccine Type	Maternal HBsAg	Mean Age/years	%Anti-HBs \geq 10 mIU	Booster Response
17	Plasma	negative	12.6	4/17 (24%)	8/12 (67%)
36	Recomb	negative	7.5	0/36 (0%)	32/35 (91%)
16	Plasma	Positive	12.1	5/16 (31%)	9/10 (90%)

LTI Conclusions

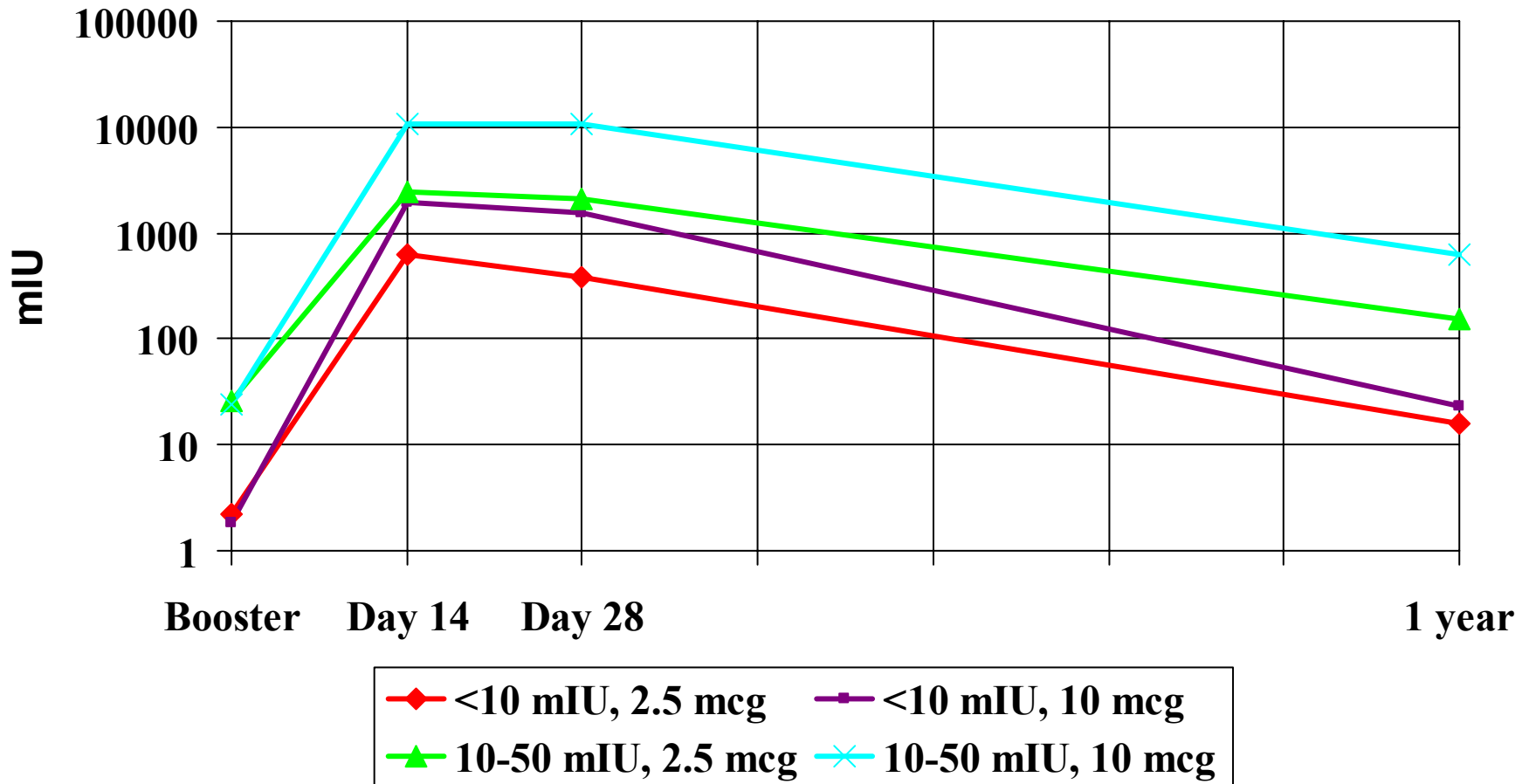
- Anti-HBs levels over time in children vaccinated in infancy decline at a rapid rate with those receiving recombinant vaccine falling the fastest
- Response to a booster dose of vaccine at 5 to 7 years of age is good (90%)
- Some children at 9 to 12 years fail to respond to a booster dose including 10% to 30% of those who were known to respond to the initial series

Long-Term Immunogenicity & Efficacy: Health Care Workers

- 59 HCR who responded to vaccination 5 to 15 years previously with low or absent anti-HBs levels were randomized into a 10mcg or 2.5 mcg booster dose
 - 98% anamnestic response at 10-14 days
 - 100 % anamnestic response at 1 month

Vaccine 2001;19:4081-85

Anti-HBs levels following a booster dose of hepatitis B vaccine



Yo-Hep (Youth Hepatitis) Booster Study in Alaska Natives

- Effectiveness of hepatitis B booster dose in children who were vaccinated with recombinant vaccine starting at birth
- Groups studied:
 - 200 children ages 4-5 years
 - 200 children ages 10-13 years
- Follow-up anti-HBs testing at 10 – 14 days and one month
- Results: Fall 04

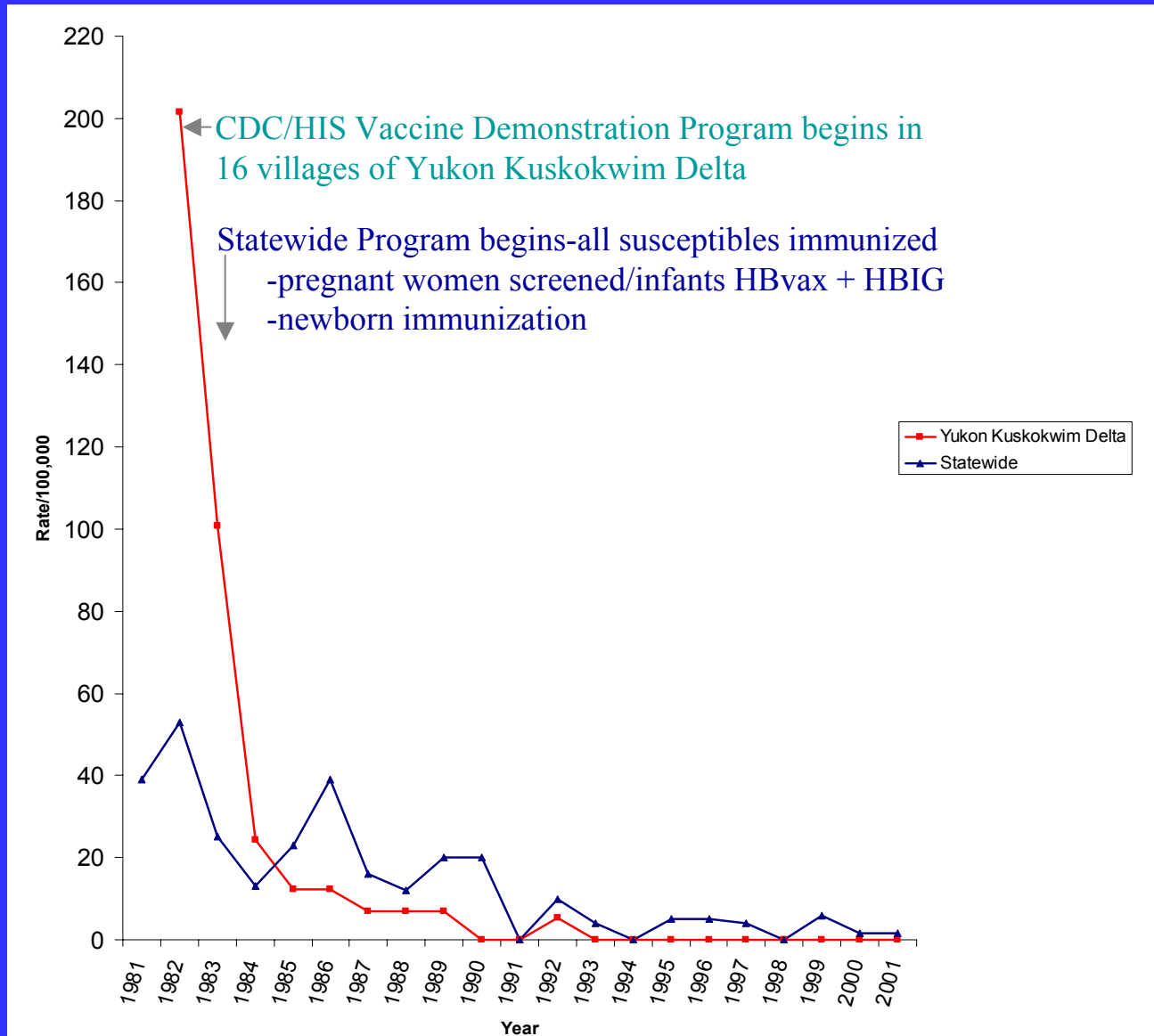
Hepatitis B Vaccination in Alaska

- 1980: Screening Pregnant women in 2 hospitals; HBIG to infants HBsAg+ mothers
- 1981-82: Hepatitis B vaccine demonstration project in Southwest Alaska
- 1983-87: 53,000 Alaska Natives (75%) screened and 40,000 susceptible were vaccinated
- 1984-present: Universal Hepatitis B vaccination of all infants
- 1987: Estimated 90% susceptible persons in endemic areas immunized

Impact of Hepatitis B Immunization Program on the HBV in Alaska Native Population

- Declining incidence of acute hepatitis B
- Generation of children free of chronic HBV
- Impact of immunization on the portion of HBeAg-positive (infectious) Carriers in population
- Trend toward decreasing incidence of HCC in persons < 30 years of age

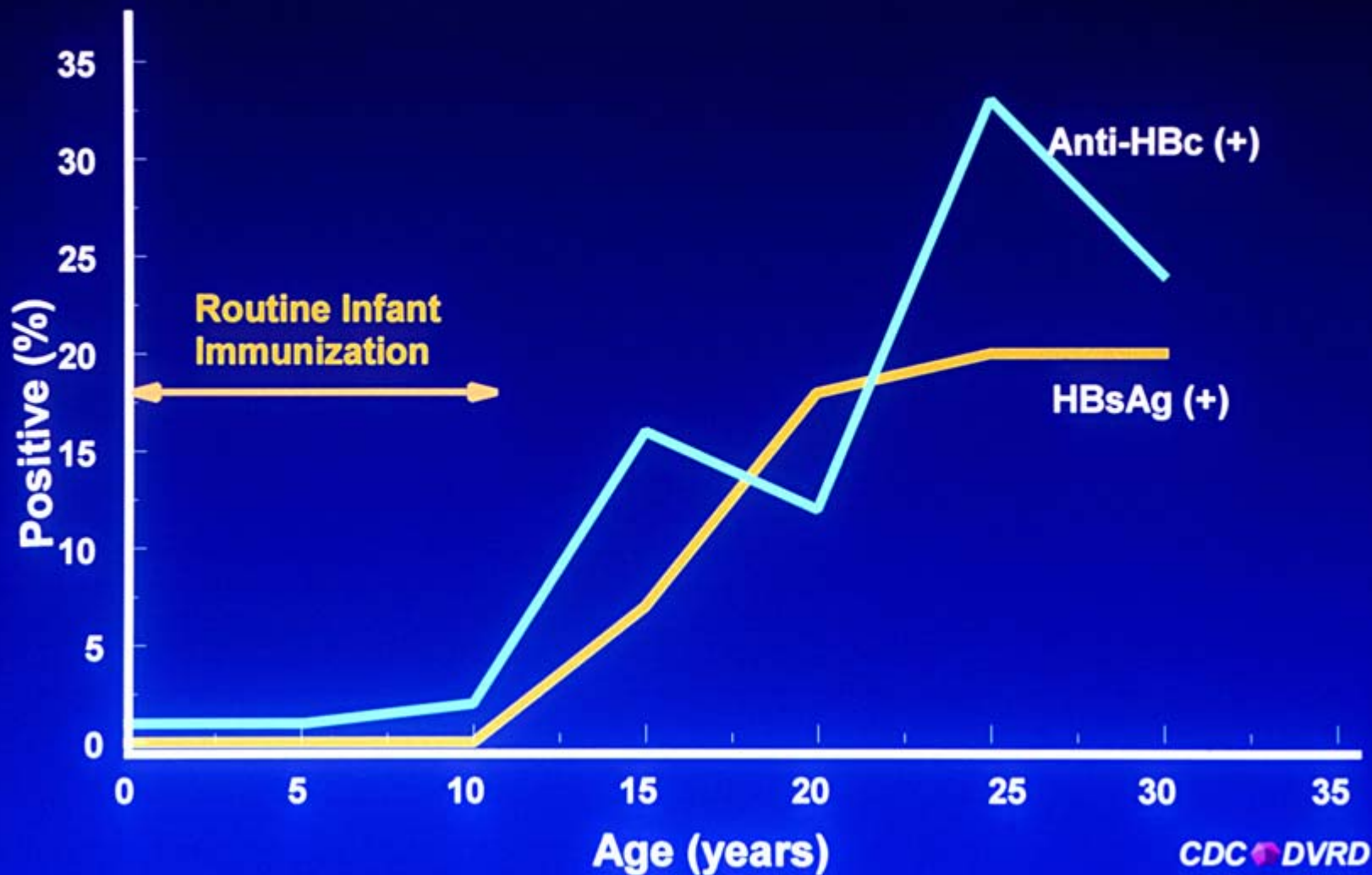
Incidence Symptomatic Hepatitis B in AK Natives 1981- 2001



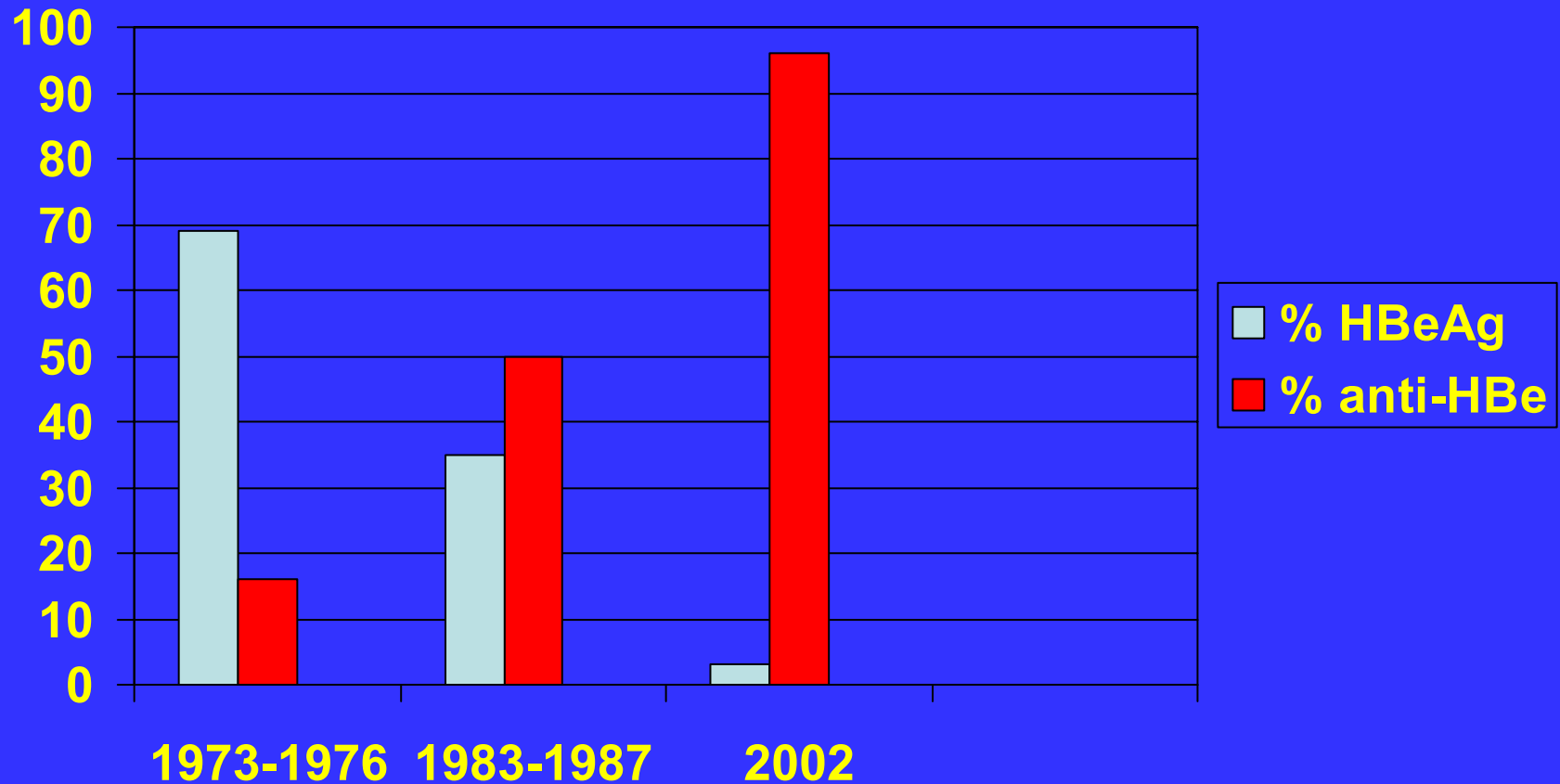
Bristol Bay Hepatitis Survey

- Serosurvey in 1984 of 603 persons \leq 30 years of age 10 years after initiation of universal hepatitis B Immunization
 - Prevalence of HBsAg in 1984 was 13%
 - Prevalence of HBsAg in 1994:
 - Ages 0-10 0
 - Ages 11-15 8%
 - Ages 16-20 18%
 - Ages 21-30 21%

Age-specific Prevalence of HBV Infection Bristol Bay Eskimos, 1994



Impact of Hepatitis B Vaccination: HBeAg and Anti-HBe Over Time



Chronic Hepatitis B in Alaska Natives Outcome Study

- All Alaska Natives are offered testing every 6 months for liver enzymes and AFP
- Consented participants also at baseline have:
 - HBV Genotype
 - HBV DNA levels
 - A sample is tested for viral mutations that may be associated with liver disease:
 - Pre-core mutant: Development of cirrhosis
 - Core-promoter mutation: Development of liver cancer

HBV Immunization: Questions

How do we determine when, if ever, to boost.

- Wait for symptomatic hepatitis to occur in vaccinated individuals (i.e. measles)
- Vaccinate at time when we can no longer demonstrate anamnestic response

