# Hep B Vaccine Immunity May Wane After 15 Years

BY MIRIAM E. TUCKER
*Senior Writer*

BALTIMORE — Immunity to hepatitis B might wane 15 years after vaccination among those who received the vaccine series beginning at birth, Dr. Stephanie R. Bialek said at a conference on vaccine research sponsored by the National Foundation for Infectious Diseases.

Data from long-term follow-up studies have established that people who received the three-dose hepatitis B vaccine series beginning after 6 months of age have long-term protection against chronic hepatitis B infection and do not need booster shots. In that population, breakthrough infections occur in only about 0%-7% of individuals more than 20 years after vaccination, and most of those are asymptomatic.

Chronic hepatitis B infection is extremely rare, occurring in fewer than 1%, said Dr. Bialek, a medical officer in the division of viral hepatitis at the Centers for Disease Control and Prevention.

However, it is not known whether the same is true for those who begin the vaccine series at birth, a practice that was first recommended in the United States in 1992.

Thus far, 10-year data in that population suggest that breakthrough infections are rare, occurring in 0%-6%, and there have been no reports of chronic infections among vaccine responders.

On the other hand, protective concentrations of antibody to hepatitis B surface antigen (anti-HBs), defined as levels greater than 10 mIU/mL, are present in fewer than 20% at 10 years, compared with more than 50% at 7-22 years among those vaccinated beginning after 6 months of age, Dr. Bialek noted.

Now, new data from an investigation conducted in Micronesia suggest that protection in those vaccinated as newborns may begin to subside at around 15 years.

The Federated States of Micronesia, a U.S.-affiliated jurisdiction in the western Pacific where hepatitis B virus infection had historically been endemic, implemented hepatitis B vaccination beginning at birth in 1989.

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Micronesian adolescents who had received three doses of recombinant hepatitis B vaccine (at birth, 2 months, and 6 months of age) and who had tested negative for antibody to hepatitis B core antigen (anti-HBc) 2 years after the primary vaccination were followed for 15 years after the primary vaccination. Recombivax had been given in doses of 5 mcg at birth, followed by doses of 2.5 mcg at 2 and 6 months. Today, 5 mcg is recommended for all three doses, she noted.

In 2006, investigators were able to track down 105 of the 238 children who had received three doses of hepatitis B vaccine, were anti-HBc–negative, and had been tested for anti-HBs at 35 months. By then, they had a median age of 15.8 years, with a median of 15.1 years since completion of the vaccine series. A total of eight (7.6%) were anti-HBc–positive, but none was HBsAg–positive.

Booster doses of vaccine were given to the 96 who were anti-HBc–negative in 2006. Of these, only 7 (7%) had anti-HBs concentrations greater than 10 mIU/mL at the time they were given the booster, and only about half (45, or 47%) had anamnestic anti-HBs responses at 14 days after the booster (defined as an increase in anti-HBs concentration greater than 10 mIU/mL). Absence of an anamnestic response might indicate waning immunity, Dr. Bialek said at the meeting.

Limitations of this study include the fact that maternal HBsAg status was not known, postvaccination testing had not been performed (some of the participants may have been nonresponders), and the vaccine dose used for the second and third doses was half of the currently recommended dose. And importantly, "Just because they didn't boost doesn't mean they're not protected," Dr. Bialek said in an interview following her presentation. At least two ongoing studies are investigating this issue further, she added. ■



# Analysis Refutes Hepatitis B Vaccine, RA Link

BY MIRIAM E. TUCKER
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BALTIMORE — The hepatitis B vaccine does not appear to be associated with an increased risk for rheumatoid arthritis, Dr. Roger P. Baxter and his associates reported at a vaccine research conference sponsored by the National Foundation for Infectious Diseases.

Both acute and chronic arthropathies have been reported in adults vaccinated with the tetanus-diphtheria (Td), hepatitis B (HepB), and measles-mumps-rubella (MMR) vaccines. However, most of the evidence to support or refute a causal relationship between the Td or HepB vaccine and chronic arthritis has come from isolated case reports, uncontrolled observational studies, or studies that lacked sufficient statistical power, said Dr. Baxter, associate director of the Vaccine Study Center at Kaiser Permanente, Oakland, Calif., and his associates.

**'People who have RA are more likely to be higher utilizers and also more likely to have gotten vaccines.'**

**DR. BAXTER**

A case-control analysis designed to overcome the shortcomings of the previous studies included a cohort of continuous enrollees in Northern California Kaiser Permanente's health plan from Jan. 1, 1995, through Dec. 31, 1999, who were aged 15-59 years during Jan. 1, 1997–Dec. 31, 1999. Individuals who had made clinic visits for rheumatoid arthritis (RA) and other inflammatory conditions prior to their follow-up start date were excluded.

A total of 416 incident cases of RA were identified (based on definitive diagnosis at the time or subsequent assessment by a rheumatologist), and each was matched with three controls based on age and the number of clinic visits made during the year prior to the onset date. Rates of hepatitis B vaccination among the RA patients were compared with those of controls, with adjustment for sex, age, and exact number of clinic visits. Similar comparisons were made for the tetanus and influenza vaccines.

No statistically significant risk of RA was found for any of the three vaccines. Only 1% of RA patients versus 0.6% of controls had been exposed to the hepatitis B vaccine within 1-90 days of onset of RA symptoms, for an adjusted odds ratio of 1.48.

Within 1-180 days, the percentages were 1.9% with RA versus 0.9% of controls, giving a still insignificant odds ratio of 2.01. Within 1 year, 2.4% of RA cases and 1.6% of controls had been exposed to the vaccine, again insignificant at 1.42.

In all, only 10 of the 416 RA patients had received the HepB vaccine within 1 year of symptom onset, suggesting that "If there is an association, these data would imply that hepatitis B vaccine would only contribute to a small minority of cases," Dr. Baxter and his associates said in their poster.

Results for the other two vaccines were also not significant, with adjusted odds ratios of 0.77-1.06 for tetanus and 0.66-1.11 for influenza.

Health care utilization was higher among those with RA, which was a slight confounder in this study despite the attempt to control for number of visits: Even after adjustment, there was still a significant residual effect for number of visits, with an odds ratio of 1.15.

"Basically, people who get vaccines of all kinds are different from those who don't, and underlying differences may confound the relationship with things like RA. We try to control for these factors by matching and analyses, but still we think there are differences. …People who have RA are more likely to be higher utilizers and also more likely to have gotten vaccines than people who don't utilize the system as much," Dr. Baxter said in a follow-up interview.

However, he added, although the difference in utilization was statistically significant, it probably wasn't that different clinically. "We thought initially this was an important confounder. But in the end we found that although they were different, in reality we could adjust for the vast majority of the difference." ■