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Hepatitis B

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Study: Hepatitis B Vaccine Protection Continues Even After 22 Years

For how long does protection continue after hepatitis B immunization? Researchers have been trying to answer that question in order to determine when or if vaccine boosters are needed, especially by those living with people chronically infected with the hepatitis B virus (HBV).

In a recent study, researchers screened 493 Alaska natives 22 years after they were vaccinated. During immunization, only the hepatitis B surface antigen (HBsAg) component of the virus is injected, in order to spur the immune system to generate surface antibodies

to ward off any future infection.

Among those immunized, 60% (298) still had adequate protective levels of surface antibodies (above 10 mIU/mL). Doctors administered a single booster dose to the 164 people with low antibody levels and 81% of them responded with protective antibody levels within 60 days.

Those who responded to the booster dose tended to be younger. Researchers also reported that none of the people whose antibody level declined over the 22 years developed acute or chronic hepatitis B, and that 87% of those in the study either had sustained protection against infection or quickly developed adequate antibody protection after getting vaccine boosters.

“The protection afforded by primary immunization with plasma-derived hepatitis B vaccine during childhood and adulthood lasts at least 22 years,” they wrote in the September 2009 issue of *The Journal of Infectious Diseases*. “Booster doses are not needed.”

Another study reported in the August 2009 issue of *Vaccine* followed 2,342 college applicants in Taiwan, who had been immunized as newborns, about 23 years earlier.

Those testing positive for HBsAg (which showed current HBV infection) was 11.6%, 3.5% and 1.0% for participants who were born before 1984, during 1984-1986, and after 1986 (when universal immunization began).

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All 572 participants who no longer had protective antibodies quickly developed protective antibodies after receiving boosters.

Researchers concluded that the antibody levels decreased to 50% among the students over 15 years following vaccination, and that vaccine boosters were 100% effective. "The necessity and age for boosters among (uninfected adolescents with low surface antibody levels) and the timing of the first immunization should be further evaluated," researchers wrote.

Delayed Second Vaccine Dose Puts Infants Born to HBV-Infected Mothers at Three-fold Higher Risk of Infection

To prevent mother-to-child transmission of HBV infection, experts recommend immediate vaccination of the infant at birth, followed by a second vaccine dose after 30 to 60 days and a third dose six months after the first dose. In the United States, infants born to infected mothers are

also given hepatitis B immune globulin (HBIG) at birth.

Thai researchers found that infants who received a delayed second dose (without HBIG) faced a three-fold increase in infection.

According to the study published in the August 2009 issue of *Vaccine*, researchers followed 521 infants born in HBV-infected mothers. Fifteen of these infants became chronically infected with HBV.

In case control comparisons, (when hepatitis B "e" antigen – HBeAg-status was similar in all mothers), the risk of an infant becoming chronically infected was 3.74 times higher if the interval between the first and second vaccine doses exceeded 10 weeks.

"This finding suggests it is important that immunization programs ensure timely second dose vaccination to infants born to mothers with chronic HBV infection," they wrote. Due to the small sample size, researchers called for larger studies to verify the findings.

Vaccination of Chinese Newborns Results in Decline of Chronic Infection Among Children

Fourteen years ago, China began attempting to vaccinate all newborns against hepatitis B. Recently, researchers conducted a national sampling of Chinese citizens, ages 1-59, to determine the prevalence of HBsAg (chronic infection), surface antibody (anti-HBs, showing immunity through vaccine or a resolved infection), and hepatitis B core antibody (anti-HBc, which shows past exposure) in order to assess the success of the vaccination program.

In the August issue of the journal *Vaccine*, researchers reported that the prevalence of HBsAg, anti-HBs and anti-HBc was 7.2%, 50.1%, and 34.1%, respectively.

HBsAg prevalence was greatly diminished among those ages 15 or younger. Among children younger than 5, the chronic infection rate was only 1%, which showed a 90% reduction in chronic infection rate in this age group.

Infection among adults was associated with male gender, residence in Western China, certain occupations, and members in certain ethnic groups. Children who were at highest risk of infection were born at home or in small hospitals.

Researchers estimated that the infant immunization program has prevented an estimated 16 to 20 million new chronic infections, and they called for programs to be strengthened and expanded.

Liver Cancer Cases in Younger Population Reduced By Vaccination

A 20-year follow-up study found a steep decline in liver cancer cases among 6- to 19-year-olds who were vaccinated against hepatitis B at birth, according to a report published in the *Journal of the National Cancer Institute*.

Taiwanese researchers collected data from 2,000 patients with liver cancer who were aged 6-29 years at time of diagnosis in Taiwan between 1983 and 2004. Age- and sex-specific incidence were compared among vac-

cinated and unvaccinated enrollees.

Sixty-four cancer cases were found among people vaccinated compared to 444 cancers identified among unvaccinated people over the study period. Those who were vaccinated and developed cancer were not given enough vaccine doses or were insufficiently protected when they were born to HBV-infected mothers.

Caucasians Have Highest Rate of HBV Recurrence After Liver Transplantation

Caucasians who undergo liver transplantation for hepatitis B have a greater recurrence of HBV infection than Asian- and African-Americans, according to a study published in the September issue of *Liver Transplantation*.

Caucasians had a four-year HBV recurrence rate of 19%, which was two- to three-times higher than other ethnic groups. Recurrence also occurred most frequently in those who tested positive for HBeAg, and often have high viral load.

This review showed no race-related disparities in the time patients spent on the organ transplant waiting list. As expected, patients with liver cancer had lower survival rates.

“Our research showed transplant indication and Model for End-stage Liver Disease (MELD) score for end-stage cirrhosis patients were the only predictors of transplantation, but race was not,” researchers noted.

Until recently, this data for HBV-infected liver transplantation was not available. The National Institutes of Health-sponsored HBV-orthotopic Liver Transplantation study examined outcomes in patients transplanted for HBV-related end-stage liver disease. The large number of patients enrolled made it possible to compare waitlist times and post-transplant outcomes by ethnicity.

The authors analyzed data on 274 participants, including 116 Caucasians, 135 Asian-Americans, and 23 African-Americans. Transplantation after one, three, and five years on the waiting list increased from 48% to 63% for Caucasians,

48% to 66% for Asian-Americans, and 53% to 88% for African-Americans.

Irrespective of race, patients with acute liver failure spent the least time on the waitlist, followed by patients with liver cancer and those with end-stage cirrhosis. The five-year survival following transplantation was 94% for African-Americans, 85% for Asian-Americans, and 89% for Caucasians.

Asian-Americans were three times as likely to have liver cancer when they were placed on the waiting list (47%), versus 16% of African-Americans and 17% of Caucasians.

The probability of infection recurrence four years after transplantation was 6% among African-Americans, 7% among Asian-Americans, and 19% among Caucasians.

Lamivudine Effective in Preventing HBV Recurrence in Both HBsAg-positive and HBsAg-negative Patients During Chemotherapy

Chemotherapy suppresses the immune system and enables a recurrence of hepatitis B in patients who test positive for HBsAg or who have resolved infections and test negative for HBsAg.

Taiwanese doctors, reporting in the August 2009 issue of the *Annals of Hematology* journal, followed 115 B cell lymphoma patients who were treated with rituximab to gauge the impact of the therapy on hepatitis B reactivation.

Fifteen of the cancer patients treated tested positive for HBsAg. Of the 15, five received lamivudine (Epivir-HBV) to suppress viral replication during treatment. None of them experienced any resurgence in HBV during treatment. However, eight of 10 HBV carriers who did not receive lamivudine experienced HBV-related hepatitis, resulting in one death.

Four (4.2%) of 95 HBsAg-negative patients developed HBV-related hepatitis and two died. The researchers concluded that rituximab-based therapy could cause serious HBV-related complications and even death in

patients with active or resolved HBV infections.

Researchers Find Unique HBV Infection With Positive HBeAg and Surface Antibody, But No Surface Antigen

Writing in the *Journal of Clinical Virology*, Chinese researchers reported on a unique patient who tested positive for the HBeAg and HBs-anti, but negative for HBsAg, which usually denotes infection.

Increasingly, researchers are finding people who have hepatitis B—marked by HBV DNA in their bloodstream—but who test negative for HBsAg. This phenomena is called occult hepatitis B.

The patient in the report had high levels of surface antibodies, low HBV DNA (viral load), and HBeAg.

An analysis of his virus revealed two sets of HBV coexisting—the normal type, and a mutated virus with mutations in its surface antigen that had never been identified before.

Slave Trade and Prevalence of Hepatitis B in Africa Tracked Through HBV Genotypes

The hepatitis B virus, which has existed for thousands of years, has differing viral strains or genotypes based on the region of the world where it evolved. In Haiti, 90% of the population descends from African slaves. Researchers sampled 7,147 pregnant Haitian women and tracked their genotype subgroups (called subgenotypes) to see if they could link them to specific regions in Africa.

Reporting in a recent issue of *Emerging Infectious Diseases Journal*, researchers found that 44% of Haitian HBV infections were caused by genotype A1, which today is found in eastern Africa, and 20% belonged to a rare subgenotype, A5, which is found only in the former Bight of Benin, once a slave trading post.

However, the Haitian A subgenotypes appear to have separated very early from the subgenotypes that are found in western Africa today. Today, the most

prevalent genotype and subgenotype found in West Africa (subgenotypes E and A3, respectively) are rare in Haiti.

This indicates that the dominant HBV subgenotypes in Africa today emerged and spread throughout the general population after the slave trade ended, researchers wrote.

Researchers extrapolate that the high prevalence of genotype E in Africa must be a recent phenomenon, and probably results from extensive use of reused and unsafe hypodermic needles.

“The conspicuous absence of genotype E in Haiti suggests recent and rapid spread of genotype E in Africa during the past 200 years, probably as the result of public health interventions,” they wrote.

Genotypes E, F and H Appear to Respond to Interferon Treatment

There is little information about how HBV genotypes E, F, G and H respond to interferon and antiviral treatments, because much research on response to interferon treatment has been fo-

cused on the genotypes found in Asia and the United States.

Researchers, writing in the October 2009 issue of the *Journal of Medical Virology*, followed 23 patients with genotypes E-H who received interferon, 12 who received antivirals, and 14 patients who were untreated. HBV genotype E was found in 61.2% of the patients, 8.2% had genotype F, and 10.2% had genotype H.

End of treatment response, marked by normal alanine aminotransferase (ALT) levels and lowered viral load, was 70% (16/23) and sustained response, continuing for several months after treatment ended, was 35% (8/23) for patients treated with interferon. Sustained response was 36% for genotype E, 50% for genotype F or H, and 20% for genotype G.

Virus suppression at week 48 was achieved in 67% of patients treated with antivirals.

“According to the preliminary data, HBV genotypes E, F, and H appear to be sensitive to interferon,” researchers wrote.

Adefovir and Entecavir Equally Effective in HBeAg-Positive Patients with Lamivudine Resistance

South Korean researchers compared the effectiveness of adefovir (Hepsera) and entecavir (Baraclude) in HBeAg-positive patients who had developed viral resistance to the antiviral lamivudine.

Researchers monitor ALT levels, which rise when liver cells are damaged or die, HBeAg seroconversion, and HBV DNA in 91 adefovir-treated patients and 50 entecavir-treated patients.

After 52 weeks of treatment in the adefovir and entecavir groups, HBV DNA became undetectable in 25 (27.5%) and 21 (35.6%) patients respectively, normal ALT levels occurred in 67/78 (85.9%) and 43/47 (91.5%), and HBeAg seroconversion occurred in 4 (4.4%) and 1 (1.7%).

Virological breakthrough, which occurs when the therapy is no longer effective due to viral resistance, occurred in two adefovir

patients and one entecavir patient, according to the report published in the journal of *Antiviral Therapy*.

Drivers With Cirrhosis and Impaired Cognitive Abilities Have More Accidents

U.S. researchers report that patients with cirrhosis (from a variety of causes) who also develop minimal hepatic encephalopathy (MHE) have a 16% higher rate of motor vehicle crashes, compared to 4% among those without MHE, according to their report published in the October issue of *Hepatology*.

MHE is a common neurocognitive complication resulting from cirrhosis. Up to 80% of cirrhotic patients are diagnosed with MHE, which causes impaired attention, slow response, and poor visual-motor coordination.

The study followed 167 cirrhotic patients from Wisconsin and Virginia who had a diagnosis of MHE. Median age was 53 years, an age group considered to have the safest driving record, and patients had an average

36 years of driving experience.

Longer Antiviral Treatment Enables More HIV-HBV Coinfected Patients to Clear HBeAg and HBsAg

HIV-HBV coinfecting patients receiving highly active antiretroviral therapy (HAART) for four years or longer have three-times the chance of clearing HBeAg, according to a report by U.S. researchers published in the *HIV Clinical Trials* journal.

The study also revealed that elevated ALT levels indicate that patients are at high risk of developing HBV-related liver damage and should be treated.

The researchers followed 72 coinfecting patients between 1990 and 2008. During follow-up, 64 (or 88.9%) of the patients had HAART containing antiviral drugs that are effective against hepatitis B, including tenofovir (Viread), lamivudine, or emtricitabine (Emtriva). Most patients took at least two drugs during follow-up, but 11.1% took only one antiviral that was effective against

hepatitis B.

Six out of 34 HBeAg-positive patients (17.6%), who used HAART the longest, cleared HBeAg. For those who cleared HBeAg, the average use of antivirals was four years, compared with 1.7 years among those who did not clear HBeAg. Additionally, 5.5% of patients who used antivirals long-term cleared HBsAg.

