Prolonged Hepatitis B Surface Antigenemia After Vaccination

Eric R. Lunn, MD, FAAP; Bernard J. Hoggarth, MD, FAAP; and Walter J. Cook, MD, FAAP

ABSTRACT. Infection with hepatitis B virus can lead to serious long-term complications including chronic hepatitis B virus infection leading to hepatocellular carcinoma, liver failure, and death. We report a case of prolonged hepatitis B antigenemia after routine vaccination with Engerix B. A positive hepatitis B surface antigen was found when the individual donated blood 18 days after vaccination. This resulted in rejection of the donated blood and permanent deferral from further donation. It also led to referral to a physician, creating anxiety in the individual and additional unnecessary testing. Additional studies are needed to identify the length of time hepatitis B surface antigenemia after hepatitis B vaccination and, blood collection centers should be aware of the potential for donors to have a prolonged false-positive hepatitis B surface antigen after vaccination against hepatitis B. Pediatrics 2000;105(6).

URL: http://www.pediatrics.org/cgi/content/full/105/6/e81; hepatitis B, hepatitis B vaccine, hepatitis B surface antigen, vaccine-induced positive hepatitis B surface antigen, Engerix B.

ABBREVIATIONS. HBV, hepatitis B virus; HBsAg, hepatitis B surface antigen; EIA, enzyme immunoassay.

Approximately 200,000 to 300,000 acute infections with hepatitis B virus (HBV) occur each year in the United States. More than 1 million persons have chronic HBV infection and ~5000 persons die each year from HBV-induced hepatocellular carcinoma and chronic liver disease in the United States.1,2 HBV is usually transmitted through sexual contact, exposure to blood or blood products, from mothers to neonates at birth, and inapparent percutaneous and permucosal exposures. Previous attempts at controlling HBV infection in the United States consisted of vaccinating high-risk populations and serologic screening of all pregnant women for hepatitis B surface antigen (HBsAg). However, these measures had little impact on the control of HBV infections; therefore, in 1992, the American Academy of Pediatrics recommended universal hepatitis B vaccination for newborns and routine vaccination of adolescents when feasible. Since then, immunization rates for newborns and adoles-
cents with hepatitis B vaccine have steadily risen. The 2 currently available recombinant hepatitis B vaccines are Recombivax HB and Engerix B. Both contain purified recombinant HBsAg obtained by culturing genetically engineered Saccharomyces cerevisiae cells, which carry the surface antigen gene of HBV.

CASE REPORT

As part of a class function, a 17-year-old 8-month-old male donated blood at a local blood collection center. One week later he received a letter indicating he tested positive for HBsAg and recommending review with his personal physician. He was also notified that his name was added to the confidential Deferred Donor Directory stating, “You are now permanently deferred from donating blood, plasma, tissues or organs for others.” He was brought to the pediatric clinic for additional evaluation of HBV infection. On further review of the laboratory studies from the blood collection center, he was noted to have a reactive HBsAg by enzyme immunoassay (EIA), a positive HBsAg confirmatory test by neutralization, alanine aminotransferase (<100 IU/L), nonreactive antibody to hepatitis B core antigen, and nonreactive antibody to hepatitis C virus. Evaluation in the pediatric clinic revealed no risk factors for HBV infection. In further discussion with him, it was determined that he received his third Engerix B vaccination (20-μg dose) 18 days before his blood donation. Physical examination did not reveal any abnormalities. Laboratory studies were obtained 48 days after his third hepatitis B vaccination and revealed a nonreactive HBsAg by EIA, aspartate aminotransferase (25 IU/L; normal: 8–42), alanine aminotransferase (14 IU/L; normal: 0–55), total bilirubin (0.4 mg/dL; normal: 0.2–1.2), and direct bilirubin (2.0 mg/dL; normal: 0–4). Repeat laboratory studies were performed 117 days after his third hepatitis B vaccination and revealed a negative HBsAg by EIA, negative immunoglobulin G and immunoglobulin M antibodies to hepatitis B core antigen by EIA, and a positive antibody to HBsAg. This is consistent with successful hepatitis B immunization.

HBsAg is the most common serologic marker used to identify acute or chronic infections attributable to HBV. It was initially thought that hepatitis B surface antigenemia did not occur after hepatitis B vaccination; however, the study used only the plasma-derived hepatitis B vaccine Heptavax-B. There have been several reported instances of detectable hepatitis B surface antigenemia after hepatitis B vaccination with Engerix B.4,5 Challapalli et al described detectable levels of HBsAg in 55% of 18 newborns tested 33 to 56 hours after administration of Engerix B. Kloster et al described detectable levels of HBsAg in 47% of 19 adult blood donors tested 1 to 3 days after administration of Engerix B. Bernstein et al described detectable levels of HBsAg in 25% of 9 newborns tested after administration of Engerix B. One neonate remained seropositive at 14 days but was seronegative at 18 days. Weintraub et al described detectable levels of HBsAg in 17% of 47 newborns tested after administration of Engerix B. All the newborns were seropositive between 24 and 72 hours after vaccination, and all were seronegative 2 weeks after initial detection. Thus far, there have been no published cases or studies of hepatitis B surface antigenemia after vaccination with Recombivax HB.

Hepatitis B vaccines are noninfectious and do not pose a risk for transfusion-transmitted disease. However, extreme caution should be used when interpreting HBsAg tests performed within a limited time frame after administration of hepatitis B vaccine. Most sources state that the time of antigenemia is brief, usually 1 day.
to 7 days; however, our patient was still HBsAg-positive after 18 days.

Each year in the United States, ~14 million units of blood are donated, by ~8 million volunteer blood donors. These units are transfused to as many as 4 million patients (URL: http://www.aabb.org/does/facts.html). Although there are no national standards, blood collection centers/blood banks may defer donation after hepatitis B vaccination. The US Armed Forces defers donors for 1 day and the Red Cross defers donors for 7 days after hepatitis B vaccination. However, our case suggests that deferral from donation after hepatitis B vaccination may need to be longer. In addition to losing potential donated blood, the false-positive HBsAg results create anxiety and further unnecessary testing of the donor. It also places the donor’s name on the Deferred Donor Directory, permanently disqualifying a healthy individual from donating.

Additional studies are needed to identify the length of time of hepatitis B surface antigenemia after hepatitis B vaccination. Blood collection centers currently screen potential blood donors for recent vaccination, and guidelines exist for temporary deferral of potential donors who received vaccines. Blood collection centers should be aware of the potential for donors to have a false-positive HBsAg (up to 3 weeks) after vaccination against hepatitis B.

**REFERENCES**

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Pediatrics 2000;105;e81
DOI: 10.1542/peds.105.6.e81

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*Pediatrics* 2000;105;e81
DOI: 10.1542/peds.105.6.e81

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