Serologic Hepatitis B Immunity in Vaccinated Health Care Workers

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Background: Hepatitis B vaccination is recommended for health care workers but has a nonresponse rate of 5% to 32% and an unknown duration of immunity. There is no standardized postvaccination protocol to confirm, monitor, and maintain immunity.

Objective: To assess the hepatitis B serologic immune status in health care workers who were previously vaccinated.

Methods: A convenience survey and an objective laboratory study, which included testing for hepatitis B surface antigen, core antibody, and qualitative and quantitative surface antibody (anti-HBs), were performed. The data collected included vaccination date, number of doses of vaccine, whether and when titers had previously been checked, titer results, sex of patient, job description, and age at the time of our study and at vaccination.

Results: Group A (n = 109, 71%) had detectable anti-HBs titers, and group B (n = 45, 29%) had no detectable anti-HBs titers. Group A was vaccinated 4.80 ± 0.30 (mean ± SEM) years prior to our testing, received 2.91 ± 0.04 (mean ± SEM) vaccinations, and had a mean ± SEM titer of 112.91 ± 5.18 mIU/mL. There was no statistical significance in time since vaccination, number of doses of vaccine, sex, job description, age at the time of our serologic testing, or age at the time of vaccination between groups A and B. Six of 6 subjects given booster doses of vaccine in group B developed anti-HBs. Only 62 subjects (40%) in the entire study population had anti-HBs status previously determined, with 48 (77%) reporting immunity to hepatitis B virus.

Conclusions: Twenty-nine percent of the health care workers who were vaccinated against hepatitis B showed no serologic evidence of hepatitis B immunity. It is unclear whether these subjects are nonresponders, lost immunity, or retained anamnestic potential. Booster vaccination response in 6 of 6 subjects suggests immunity. We recommend (1) postvaccination testing within 1 to 2 months to document immunity, (2) periodic anti-HBs monitoring, and (3) booster vaccination to maintain protective titer levels.

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HEPATITIS B VIRUS (HBV) accounts for 34% of all cases of acute hepatitis in the United States; approximately 53,000 new cases of HVB were reported annually between 1984 and 1993. Of these 53,000 new cases, 8000 were related to occupational exposure. Current recommendations are for vaccination against HBV for high-risk groups, including health care workers. Since the inception of HBV vaccination programs, the compliance has been poor, with fewer than 10% of an estimated 22 million Americans in various high-risk groups having been vaccinated. Although the incidence of HBV infection in health care workers has decreased by 75%, the overall incidence of HBV infection in the general population has declined at a much smaller rate. Therefore, health care workers are still at a high risk for HBV exposure. The duration of immunity imparted by an initial vaccination regimen is not known, and there are no universal recommendations for monitoring immune status and the need for booster doses of vaccine. In an effort to assess possible risk to health care workers, we studied the serologic immune status among health care workers previously vaccinated against HBV.

RESULTS

Initially, 182 subjects were tested. Twenty-eight were excluded because of previous HBV infection or because they had no history of HBV vaccination. The remaining 154 participants were analyzed for this study. There were 98 nurses, 30 medicine house staff physicians, 11 gastroenterologists, 5 surgeons, 5 emergency department physi-
SUBJECTS AND METHODS

Our study group was composed of a group of health care workers with a varied HBV vaccination history. Flyers were posted, and subjects were asked to participate in a study at chance meetings in various areas of the Presbyterian Medical Center, Philadelphia, Pa, from July 1995 to March 1996. Each participant had a sample of serum taken for hepatitis B surface antigen, hepatitis B core antibody, and both qualitative and quantitative hepatitis B surface antibody (anti-HBs) assays (Enzymelinked immunosassay; Abbott Laboratories, Abbott Park, Ill). Data were collected by questionnaire regarding date of vaccination, number of doses received, whether and when titers were previously checked, titer results, sex of patient, job description, and age. Weight, mean age, smoking history, and overall health status were not assessed. The study was approved by the institutional review board of the Presbyterian Medical Center.

Statistical analyses included χ2 test for categorical and frequency data, and continuous data were analyzed using regression analysis, analysis of variance, or the Student t test. Analyses were performed by means of a computerized statistical package (SAS Institute Inc, Cary, NC). The α level chosen to reject the null hypothesis was .05.

The duration of immunity after vaccination against HBV is not known. Ten percent of the patients who receive and respond to vaccination lose anti-HBs after 5 years and 50% lose anti-HBs after 10 years. Many authors believe that protection lasts as long as 10 years, even if antibody titers decrease below “protective” levels of 10 mIU/mL. The loss of detectable antibody titers does not always imply a lack of protective immunity, as intact immunologic memory in B cells from responders has been found 8 years after vaccination. However, data on measles vaccination suggest that the loss of detectable antibody titers does correlate with waning immunity.

In our study, 71% (group A) of health care workers previously vaccinated had detectable anti-HBs titers 4.8 years after vaccination and 29% (group B) had no detectable antibody titers. As only 27% of group B had previously reported that they had had postvaccination vaccination titers checked, we do not know whether to attribute the absence of anti-HBs titers to nonresponse, retained anamnestic potential, or lost immunity.

If we assume the often-stated nonresponse rate of 5%, then 24% (29% − 5%) of the subjects may have lost antibody. This “theoretical loss” of antibody rate of 24% is higher than the expected 5-year postvaccination anti-HBs loss rate of 10%. Whether the group B subjects retained anamnestic potential is unknown. From our data, one can conclude either that there are more nonresponders than expected or that most subjects lost antibody early, yet retained anamnestic potential. The observation that all 6 of our group B subjects who received booster doses of vaccine had antibody production supports the theory of retained immunity with anamnestic potential. Stronger support could have been shown if all 45 subjects in group B had received booster doses of vaccine, but study limitations precluded this.

Alternatively, several of the subjects who make up the above-mentioned 24% may be additional nonresponders. It is possible that the difference (14%) between the theoretical loss (24%) and the expected loss (10%) of anti-HBs represents nonresponders, as they would be expected to have retained anti-HBs at 4.7 years since vaccination. Unfortunately, postvaccination anti-HBs testing to confirm response to vaccination and serologic monitoring on a long-term basis was not commonly practiced.

The Advisory Committee on Immunization Practices recommends that postvaccination testing should be performed within 1 to 2 months in persons at occupational risk and that periodic antibody testing is not needed. These recommendations are controversial. It is clear that postvaccination testing is rarely practiced. Only 62 subjects (40%) in our entire study group (N = 154) had titers previously checked, making interpretation of undetectable titers of anti-HBs difficult. Did they ever initially respond to vaccination? Similar results have been shown in other studies that have demonstrated that only 32% of surgeons have had postvaccination titers checked (only 79% with adequate titers) and that only 75 of 150 of hospitals surveyed in 1992 conducted periodic antibody testing as a guide to giving booster shots.

Some authors suggest that at least 1 booster dose should be administered 5 to 10 years after the initial series, whereas others believe that because of expected immunologic memory, booster shots are not necessary in...
persons with a normal immune status.\textsuperscript{6,12} Fifteen percent of hospitals surveyed from June to August 1992 routinely administered booster vaccinations every 3, 5, or 7 years.\textsuperscript{13} Many authors still suggest that titers should be above 10 mIU/mL at all times.\textsuperscript{15} Conclusions regarding induced immunity.\textsuperscript{7}

Immunologists generally hold the view that booster vaccinations are unnecessary because HBV vaccines and the response to them are effective.\textsuperscript{14} However, study of serum anti-HBs titers in vaccinees who have been followed for long periods of time shows that much variation occurs.\textsuperscript{11,12,15} This variation may not be explainable by the age of the vaccinee, the route of administration of the vaccine, or the number of doses of vaccine received.\textsuperscript{13,11} Furthermore, titers of anti-HBs are not necessarily related to protection against HBV infection.\textsuperscript{11,12}

Our study shows that a majority of health care workers do not routinely check their postvaccination titers and that 29% of these health care workers had undetectable anti-HBs titers on testing. We believe that the lack of information regarding their initial response to vaccination may place them at risk for HBV infection. We recommend that all health care workers have their postvaccination titers checked to be certain that they are responders to HBV vaccination. If the antibody is undetectable at a later date, then there is a strong chance that protection still exists through immunologic memory based on our preliminary data in 6 subjects who received booster doses of vaccine. Vaccinated health care workers should be aware of their postvaccination anti-HBs status, since they may be one of the 5% to 32% of vaccinees who are nonresponders and who remain susceptible to HBV infection.\textsuperscript{10,11}

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REFERENCES