conversions has been clearly demonstrated.[3] However, what is the risk of a nurse or physician developing the disease? Is this risk equal for medical workers of different ethnic origin and sex or, as is more likely, is the risk a function of childhood exposure and length and type of patient care activities?

Neither the attack rate for workers in various patient care occupations nor the attack rate for workers of different ages, sex, race and length of employment is known. Completed studies have looked at the prevalence of hepatitis serum markers and only in a few select groups (eg, dentists) have attack rates been calculated.[4] It may well be appropriate to immunize dentists, dialysis workers and blood banking technicians, but other members of the hospital community may be at much less risk.

How then are we to judge the benefits for those who are at a lesser but as yet undefined risk? This can only be assessed by including an evaluation of the vaccine's potential for serious adverse reactions.

Current production of the vaccine appears to yield a highly purified product. Reactions of an immediate allergic type are unlikely to present a major problem. However, no vaccine can ever be assumed to be entirely safe, and this vaccine cannot be excepted. That it is manufactured from a virus for which there is convincing evidence of oncogenicity in man must raise some concern over long-term exposure and the reimmunization that appears to be necessary.[5]

Unanswered and perhaps unanswerable for years to come are the consequences of administering a vaccine prepared from a human oncogenic virus. Studies in Taiwan have shown that hepatocellular carcinoma is the leading cause of death in men with persistent hepatitis B antigenemia.[5] The mechanism whereby the virus achieves this is not known. There is speculation that the antigenemia must be persistent and present for many years, perhaps from childhood. That repeated exposure to the vaccine could produce such a result is unlikely but the possibility exists. Few vaccines have been introduced without the occurrence of some unforeseen adverse reaction.

The vaccine is extremely difficult and expensive to manufacture by the current process. Initially, it will be in very short supply and great demand. While this will almost certainly lead to other suppliers entering the field, perhaps with new techniques, this too must cause us to review the risks associated with differently manufactured lots.

The cost of an immunization program might be more than equalled by the losses incurred by one or two cases of disease per year in an average sized community hospital. To the very considerable expense of the vaccine, some $100 for a course of the product alone, and the booster immunizations required every few years, must be added the cost of antibody screening of potential recipients. It would seem unwise and expensive to vaccinate those who already are naturally immune. There are some 4.5 million health care workers in the United States. An unselective program to immunize all could cost $450 million for vaccine alone in the first year and $150 million every year thereafter, not considering the usual turnover in the population. Such a program would likely, because of its size, uncover adverse reactions not noted in the smaller clinical trials. This requires that a careful analysis of which health care workers really need the vaccine, and to whom we can afford to give it, must be made.

It is anticipated that the American Committee on Immunization Practices will issue recommendations on the use of the vaccine just prior to its commercial release. These guidelines should address those medical workers known to be at risk and, it is hoped, caution against other indiscriminate use.

These considerations must not undermine our confidence in the vaccine or our resolve to use it appropriately, but encourage us to weigh carefully when and in whom.

REFERENCES

1. Weiss KE, Falvo CE, Buimovici-Klein E, et al: Evaluation of an employee health service as a setting for a rubella screening and immunization program. *Am J Public Health* 1979; 69:281-283.
2. Orenstein WA, Heseltine PNR, Le Gagnoux SJ: Rubella vaccine and susceptible hospital employees. *JAMA* 1981; 245:711-713.
3. Szmuness W, Stevens CE, Harley EJ, et al: Hepatitis B vaccine: Demonstration of efficacy in a controlled clinical trial in a high risk population in the United States. *N Engl J Med* 1980; 303:833-841.
4. Withers JA: Hepatitis, review of the disease and significance to dentistry. *J Periodontol* 1980; 51:162-166.
5. Szmuness W: Hepatocellular carcinoma and the hepatitis B virus: Evidence for a causal association. *Prog Med Virol* 1978; 24:40-49.

Peter N.R. Heseltine, M.D.
Hospital Epidemiologist
Assistant Professor of Medicine
Los Angeles County — University of Southern California Medical Center
Los Angeles, California

Hepatitis B Vaccine Use in Health Care Professionals

In November 1981, the Food and Drug Administration granted a licensure for an inactivated hepatitis B vaccine. The Centers for Disease Control estimates that in the United States there are approximately 200,000 cases of hepatitis B annually and of these, approximately 10% (20,000) become hepatitis B carriers, this despite the dramatic decrease in the last decade of transfusion-related hepatitis B. In addition there are approximately 4,000 deaths annually due to cirrhosis and 800 deaths due to hepatocellular carcinoma, felt directly related to chronic hepatitis B infection.

The feasibility for the development of a hepatitis B vaccine was demonstrated by Krugman and associates[1] who reported that a heat inactivated serum containing hepatitis B surface antigen (HB_sA_g) was partially protective and noninfectious. The current vaccine was developed by Hilleman and associates[2] and consists of a highly purified, formalin inactivated HB_sA_g particles derived from plasma of chronic carriers.

The vaccine has been found to be highly immunogenic for newborns, children and young adults. Immunocompromised individuals and individuals over age 40 do not respond as well. The vaccine series consists of three

Address reprint requests to: Edward J Septimus, M.D., F.A.C.P., Chief of Infectious Diseases, Memorial Hospital, Infectious Disease Consultants, P.A. 7777 Southwest Freeway, Suite 740, Houston, TX 77074.

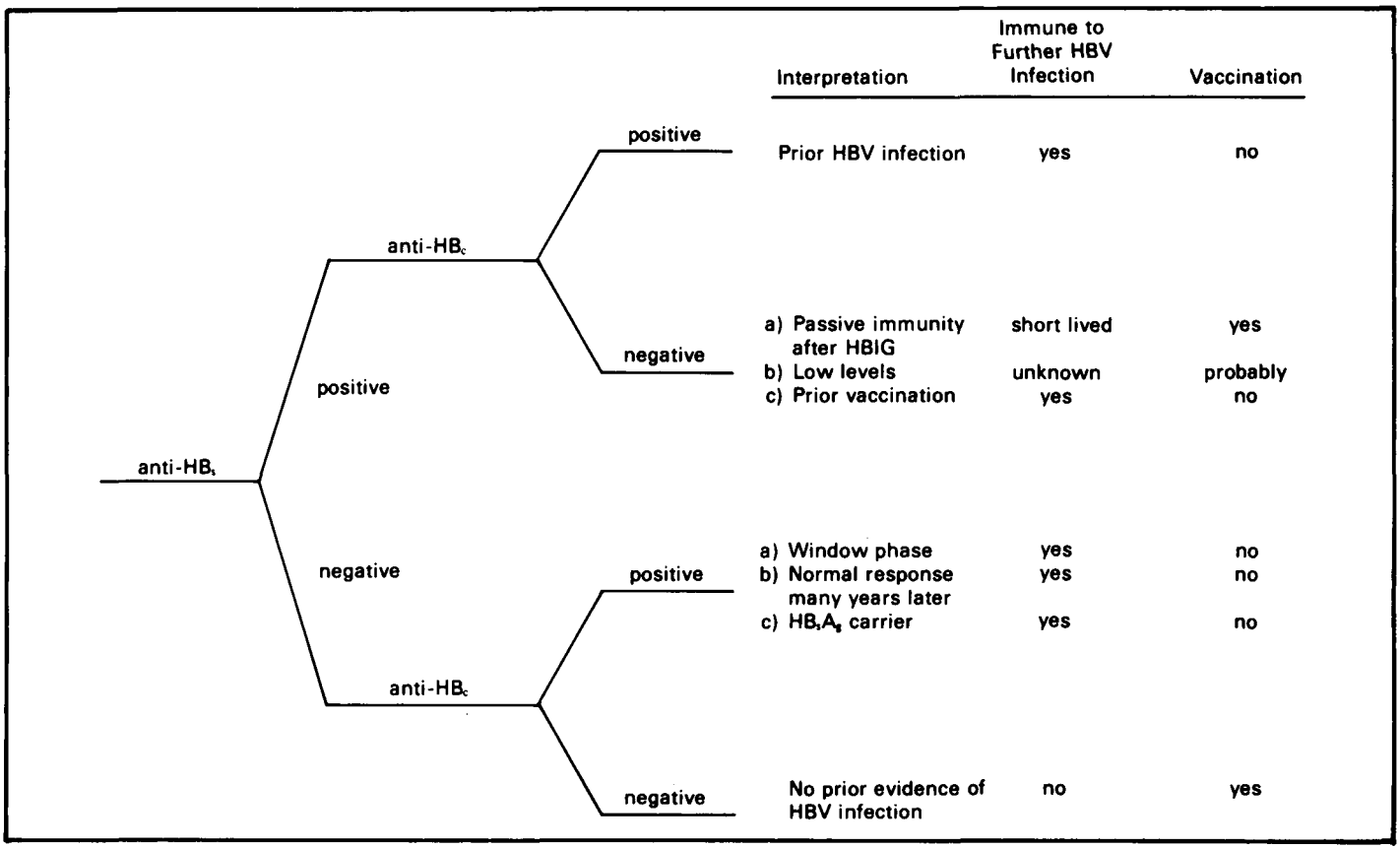

Figure. Hepatitis B vaccine strategies.

injections given intramuscularly; the second dose given one month after the first dose, with the final injection given at six months. The dose is 20 μg per injection for most populations.

In large clinical trials, the vaccine was extremely well tolerated. The most common complaint was soreness at the site of the injection followed by slight temperature elevation.

Szmuness and associates[3] demonstrated a remarkable protective efficacy of 92.3% in a placebo-controlled, double-blind, randomized vaccine trial using inactivated hepatitis B vaccine in over 1,000 homosexual males in New York City. Within two months, 77% of vaccinated persons developed hepatitis B surface antibody (anti-HB_s), which increased to 90% following the booster given at six months. None of the recipients who developed anti-HB_s developed hepatitis B. A second multicenter study also involving over 1,000 homosexual males again showed a vaccine efficacy of greater than 95% among vaccinees who mounted a strong antibody response.[4]

The new hepatitis B vaccine is now available. Since the vaccine is prepared from plasma of chronic carriers, adequate quantities may not be available to meet the demand. In addition, the vaccine is relatively expensive (expected to run $90-120 for the complete series). In light of this, it behooves us to identify high risk groups for vaccination among health care personnel.

Multiple studies have emphasized that it is the frequency and intensity of exposure to blood products, rather than patient contact, that is important in identifying high risk groups. Most studies have shown a three to four times greater risk of hepatitis B virus infection in hospital personnel. Lewis and associates,[5] in one of the earlier studies, demonstrated that anti-HB_s was twice as frequent in health care personnel (physicians, laboratory workers, and nurses) than in controls. Three subsequent studies have examined the seroprevalence in just hospital personnel (excluding physicians). All three studies showed a definite risk to laboratory technicians, intravenous teams and operating room personnel.[6-8] Among nurses, several studies have indicated increased risk in dialysis, oncology and intensive care units.[9-10] Dienstag's recent study also showed a surprisingly high seroprevalence in emergency center nurses.[8]

In an attempt to define comparative risks among physicians and dentists, several serological surveys have recently been reported. All indicate an increased seroprevalence among physicians and dentists vs. controls (14.4% to 16.5% vs. 3.5% to 4.4%).[11-12] Among physicians, surgeons (28%) and pathologists (27%) had the highest prevalence rates. Among surgical subspecialties, cardiothoracic (42%) was the highest. Although dentists have a significantly higher seroprevalance than controls, the highest rate by far was among oral surgeons (21%).[13]

The decision to do prevaccination serological testing may not be routinely necessary. In a recent study by Dienstag and associates,[14] the vaccine was shown to be safe even for persons who were either anti-HB_s or HB_sA_g positive. The cost to most laboratories is approximately $20 for hepatitis-B core antibody (anti-HB_c) and anti-HB_s

https://doi.org/10.1017/S0195941700057325 Published online by Cambridge University Press

per person. The addition of HB_sA_g would add an additional $5 to $10 per person. This has to be weighed against the cost of the vaccine and the seroprevalence of your population. For example, if your group of hospital personnel is highly susceptible (> 75%), it might be more cost effective to vaccinate without prevaccination serologies. However, if your hospital is like most, you probably are not aware of your seroprevalence among high-risk personnel, except in dialysis units. Therefore, you might need to screen all high-risk personnel to determine your susceptibility for future decision making.

Lastly, if you decide to do serological screening, which tests do you order? Most authorities agree that high levels of anti-HB_s are protective. Low levels of anti-HB_s without anti-HB_c have been reported in small percentages of people. Whether this is a false positive or whether this is protective, is not clear at this time. Until further information is available, this group should probably be vaccinated. The advantage of doing both anti-HB_s and anti-HB_c is that this will not only pick up your immune population, but also the individuals who might be chronic HB_sA_g positive, or individuals who have recently acquired hepatitis B virus (HBV) infection. If a person is both anti-HB_s and anti-HB_c positive, most would feel comfortable that that individual is immune. If only anti-HB_c is positive, then I feel that further serological testing (HB_sA_g) and follow-up serologies will be necessary. Anti-HB_c alone may represent either previous infection in which anti-HB_c outlasts anti-HB_s; or a recent hepatitis B infection between the disappearance of HB_sA_g and the appearance of anti-HB_s, the so-called "window" phase; or chronic or low level HB_sA_g (HB_sA_g present below detectable levels) carriers. The figure will hopefully make it easier to interpret various tests and decide on vaccine strategies.

In summary, I feel the licensure of the hepatitis B vaccine will provide us with a safe and highly effective vaccine. Since the vaccine is expensive and will probably be in short supply, I feel that only individuals considered high risk should be immunized as outlined above.

REFERENCES

1. Krugman S, Giles JP, Hammond J: Viral hepatitis, type B (MS-2 strain): Studies on active immunization. *JAMA* 1971; 217:41-45.
2. Hilleman MR, Bunyak EG, Roehm RR, et al: Purified and inactivated hepatitis B vaccine: Progress report. *Am J Med Sci* 1975; 270:401-404.
3. Szmuness W, Stevens CE, Harley EJ, et al: Hepatitis B vaccine: Demonstration of efficacy in a controlled clinical trial in a high risk population in the United States. *N Engl J Med* 1980; 303:833-841.
4. Check WA: Looks like smooth sailing for experimental hepatitis B vaccine. *JAMA* 1981; 246:2111-2112.
5. Lewis TL, Alter HJ, Chalmers TC, et al: A comparison of the frequency of hepatitis B antigen and antibody in hospital and nonhospital personnel. *N Engl J Med* 1973; 289:647-651.
6. Wruble LD, Masi AT, Levinson MJ, et al: Hepatitis B surface antigen (HB_sA_g) and antibody (anti-HB_s), prevalence among laboratory and nonlaboratory hospital personnel. *South Med J* 1977; 70:1075-1079.
7. Pattison CP, Maynard JE, Berquist KR, et al: Epidemiology of hepatitis B in hospital personnel. *Am J Epidemiol* 1975; 101:59-64.
8. Dienstag JL, Ryan DM: Occupational exposure to hepatitis B virus in hospital personnel: Infection or immunization? *Am J Epidemiol* 1982; 115:26-39.
9. Wands JR, Walker JA, Davis TT, et al: Hepatitis B in an oncology unit. *N Engl J Med* 1974; 291:1371-1375.
10. Szmuness W, Prince AM, Grady GF, et al: Hepatitis B infection: a point-prevalence study in US hemodialysis centers. *JAMA 1974;* 227:901-906.
11. Denes AE, Smith JL, Maynard JE, et al: Hepatitis B infection in physicians: Results of a nationwide seroepidemiologic survey. *JAMA* 1978; 239:210-212.
12. Smith JL, Maynard JE, Berquist KR, et al: Comparative risk of hepatitis B among physicians and dentists. *J Infect Dis* 1976; 133:705-706.
13. Feldman RE, Schiff ER: Hepatitis in dental professionals. *JAMA* 1975; 232:1228-1230.
14. Dienstag JL, Stevens CE, Szmuness W, et al: Immunization of chronic hepatitis B surface antigen carriers with hepatitis B vaccine, abstracted. *Hepatology* 1981; 1:506.

Edward J. Septimus, M.D., F.A.C.P.
Chief of Infectious Diseases
Memorial Hospital
Houston, Texas