Hepatitis B Vaccination of High-risk Hospital Personnel

Hepatitis B has long been recognized as an occupational hazard for hospital personnel, and the risk of infection has been generally considered to be a function of exposure to blood.\(^1\) The development of reliable serologic assays for hepatitis B virus (HBV) antigens (e.g., HBsAg) and for antibodies to them (e.g., anti-HBs, anti-HBc) has facilitated greatly the identification of specific groups at increased risk of HBV infection.\(^2\) Using such assays, Berry et al.\(^3\) have found serologic evidence of prior or current HBV infection in 23.3\% of personnel who administer anesthesia at four hospitals affiliated with Emory University. This is substantially higher than the 3–5\% prevalence of serologic markers of HBV infection found in the general population, and, together with data from other serologic surveys,\(^4,5\) clearly warrants the addition of anesthesia personnel to the list of occupational groups with a high risk of HBV infection.

The application of these serologic techniques has also expanded our knowledge of the epidemiology and natural history of HBV infection. It is now clear that clinical attack rates markedly underemphasize the risk of infection, for only about one-quarter of infected adults develop clinical hepatitis.\(^6\) However, 6–10\% become chronic HBV carriers. In addition to their potential infectivity for others, more than 25\% of these chronic HBV carriers develop chronic active hepatitis, which often progresses to cirrhosis. Furthermore, there is now convincing evidence that HBV plays a critical role in the etiology of primary hepatocellular carcinoma, one of the most common malignant neoplasms in Asia and Africa. In a prospective study of 22,707 Chinese men in Taiwan, Beasley et al.\(^7\) have shown that the risk of primary hepatocellular carcinoma is more than 200 times greater among carriers of HBV than among noncarriers. Clearly, there is good reason to avoid HBV infection, and the increased risk demonstrated by the study of Berry et al. should stimulate anesthesia personnel to consider seriously the means by which this may be accomplished.

Three approaches have proven useful for the prevention of HBV infection: avoidance of exposure, postexposure prophylaxis with hepatitis B immune globulin (HBIG), and preexposure immunization with the recently licensed hepatitis B vaccine. While screening for HBsAg has been effective in reducing the incidence of transfusion-associated hepatitis B, it is not practical to screen all hospitalized patients for HBsAg in order to identify the approximately 1\% with circulating HBV. Moreover, while certain patients may be assigned easily to groups with a high prevalence of HBV carriers (e.g., intravenous drug abusers, male homosexuals, immigrants from Southeast Asia), 80–90\% of HBsAg-positive patients are not identified routinely.\(^4,6\) Thus, it is not surprising that Berry et al. found that “most of the individuals with serum markers of hepatitis B had no clinical history of hepatitis” and that there was no reduction in seropositivity among personnel who wore gloves when contacting patients suspected of having the potential to transmit hepatitis. Most of the exposure of hospital personnel to HBV comes from patients who are not suspect. Moreover, while contact with blood is an important risk factor, every body secretion from HBsAg-positive individuals is potentially infectious, and the source and mode of infection of hospital personnel is often unclear.\(^4,7\) In addition to accidental direct percutaneous inoculation by contaminated needles or other sharp instruments, mechanisms of transmission include inadvertent transmission by contamination of minute cutaneous scratches, abrasions or other lesions, contamination of mucosal surfaces (e.g., eye, mouth, nose) by infectious blood or secretions, and indirect transfer of infectious material via contaminated inanimate objects. Thus, while reasonable precautions designed to reduce the incidence of percutaneous and mucous membrane...
exposure to blood and body secretions will help to reduce the risk of HBV infection, especially if employed routinely for all patients, this approach is unlikely to totally eliminate the risk to anesthesia personnel. Postexposure prophylaxis with HBIG can reduce markedly the incidence of hepatitis B when given after percutaneous (needle stick) or mucous membrane exposure to blood containing HBsAg.\textsuperscript{11} However, since most HBV infections in hospital personnel do not appear to follow such recognized exposures, this form of prevention is also unlikely to markedly reduce the incidence of HBV infection in anesthesia personnel.

In contrast, the recently licensed HBV vaccine provides a practical and highly effective means for the prevention of HBV infection in hospital personnel. The recommended series of three 20-\textmu g intramuscular doses of this inactivated (killed) vaccine induces protective antibody (anti-HBs) in an average of over 90\% of healthy adults, thus providing solid protection against HBV infection.\textsuperscript{9,12} It is estimated that more than a quarter of a million individuals in the United States have received this vaccine since its licensure in 1981. During this time, the CDC, the FDA and the vaccine manufacturer (Merck Sharp & Dohme) have been collecting information on illnesses following vaccine administration. Immediate side effects are minimal, consisting of transient soreness at the injection site in up to 10\% of recipients, and no long-term adverse reactions have been identified. While several serious illnesses, including two cases of Guillain–Barré syndrome, have been reported following HBV vaccination, they were associated only temporally with HBV vaccination, and their frequencies of occurrence in vaccinees fall within the expected background rates among unimmunized adults.\textsuperscript{13} Thus, HBV vaccination provides a uniquely safe and effective means of protecting high-risk hospital personnel from HBV infection.

In spite of the safety and efficacy of the HBV vaccine and recommendations of the CDC's Immunization Practices Advisory Committee,\textsuperscript{9} many individuals at risk have not been vaccinated. The cost of the vaccine (approximately $100) has been one factor delaying the implementation of hospital-sponsored programs of HBV immunization. Another factor has been concern about vaccine safety, especially concern that the vaccine might transmit the acquired immune deficiency syndrome (AIDS), since homosexual male HBsAg carriers are a major source of the plasma from which the vaccine is made. To date, no AIDS cases have been reported among the more than 200,000 persons who have received vaccine since its licensure in 1981 nor among several thousand persons at low risk for AIDS who participated in prelicensure vaccine trials. Two homosexual males who participated in vaccine field trials have developed AIDS, but this represents an AIDS incidence rate lower than that in the population of homosexual males from which the vaccine recipients were drawn.\textsuperscript{14} Moreover, the procedures used to prepare the inactivated HBV vaccine are designed to remove or inactivate infectious HBV, as well as all other known viruses. These procedures, which include ultracentrifugation, treatment with 1 \textmu g/ml pepsin at pH 2.0 and 37\°C for 18 h, treatment with 8 M urea at 37\°C for 4 h, and treatment with 1:4,000 formalin at 36\°C for 72 h, should destroy the infectivity of any known virus, including the "slow" viral agents of kuru and Creutzfeldt–Jakob disease.\textsuperscript{14} Thus, even assuming that the agent responsible for AIDS is present in the starting material, the inactivated HBV vaccine should be totally noninfectious. Furthermore, because the epidemiology of AIDS resembles that of hepatitis B, individuals with exposure to blood who are at increased risk of HBV infection also may be at increased risk of acquiring AIDS. While that risk now appears to be exceedingly low, the risk of acquiring AIDS from the inactivated HBV vaccine is almost certainly very much lower. Moreover, the alternative of postexposure prophylaxis with HBIG involves a greater potential for exposure to the agent of AIDS than does HBV vaccination. While there is absolutely no evidence for transmission of AIDS by HBIG, some of the pooled plasma from which it is derived undoubtedly comes from homosexual men, and the process by which HBIG is prepared does not involve the inactivation procedures employed in the preparation of HBV vaccine. Accordingly, the incremental risk of AIDS associated with the administration of HBV vaccine to hospital personnel at risk of HBV infection is nil, and susceptible anesthesia personnel should be vaccinated without delay.

In our institution, we have chosen to screen potential vaccinees for anti-HBc, which is present together with anti-HBs in most individuals with prior HBV infection who are not HBsAg carriers, and which also is present in HBsAg carriers. In this way, we are able to identify both groups who would not benefit from HBV vaccination without specifically identifying the HBsAg carriers. We then offer vaccine only to susceptible (i.e., anti-HBc negative) individuals.

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References

Cardiototoxicity of Local Anesthetics—The Plot Thickens

In 1978, an editorial by Albright1 alerted the anesthetic community to a new complication of regional analgesia, that of sudden circulatory collapse, often resistant to resuscitation, following the accidental intravascular injection of clinical doses of the long-acting anesthetics bupivacaine and etidocaine. In some cases, the cardiac arrest was preceded by convulsions but in others it occurred almost immediately after rapid injection of the drug such as to make antecedent hypoxia unlikely. Albright concluded that “animal studies are urgently needed” to evaluate the relation between central nervous system and cardiac toxicity of the anesthetics. Consequent to this report, Liu and his co-workers2 studied the acute intravenous cardiototoxicity of four local anesthetic drugs (2% lidocaine, 0.5% bupivacaine, 3% mepivacaine, 2% and 1% etidocaine) in intact ventilated dogs anesthetized with pentobarbital. The results indicated that all four local anesthetics had the propensity for producing profound circulatory depression and that their relative cardiototoxicity was proportional to their in vivo anesthetic potency. These findings appeared to support the role of hypoxemia and acidemia as predisposing factors for the severe cardiac depression observed clinically with bupivacaine and etidocaine, particularly since marked decreases in oxygen tension, pH, and base change had been demonstrated previously during bupivacaine-induced convulsions.3 However, when the cardiovascular effects of bupivacaine, etidocaine, and lidocaine were compared in lightly anesthetized ventilated cats, intravenous infusions at equiconvulsant rates resulted in the development of nodal and ventricular arrhythmias before or at the onset of the seizure with bupivacaine and etidocaine but not with lidocaine.4 The fact that arrhythmias were not seen with subconvulsant doses of lidocaine suggested a specific arrhythmogenic action of bupivacaine and etidocaine, thus corroborating the results of in vitro studies on paced perfused rabbit hearts that showed relatively greater cardiotoxic actions of the two long-acting drugs than of lidocaine.*

In the meantime, additional fatal cardiac arrests occurred sporadically in healthy parturients scheduled for cesarean section after intended epidural injection of bupivacaine. None of these was publicized as a case report, but one parturient, whose circulatory collapse followed administration of 12 ml 0.75% bupivacaine, was included in an 18-month review of deaths during anesthesia reported to the Office of Medical Examiner in New York City.† The major abnormality found on her autopsy was

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