Immunization Dialogue

Hepatitis B Vaccine

Currently, universal infant hepatitis B vaccination is being promoted vigorously. The concept of hepatitis B *immunization is relatively new for our country. In view of the novelty, cost, availability of different brands and the economic constraints of a developing country, several clarifications are required. In this context, Dr. T. Jacob John, Professor and Head, Department of Microbiology and Virology, Christian Medical College Hospital, Vellore, Tamil Nadu 632 004 continues answering important questions posed by us. Professor Jacob John, a leading International Vaccinologist, is an Adviser on Immunization to the World Health Organization and other International Agencies. He is the current Chairman of the IAP Committee on Immunization.*

-Editor-in-Chief

Ql. *Can hepatitis B vaccination be done at the same time as immunizaiion with other vaccines? What sites should be used if giving another injectable vaccine at the same time as hepatitis B vaccine?*

Al. There is no known incompatibility between HB vaccine and any other vaccine in current use. However, if any other vaccine is given by injection simultaneous with HB vaccine, then separate sites must be used.

Q2. Is *the seroconversion to hepatitis vaccine adequate in preterms, small for dates and severely malnourished children?*

A2. I have not seen data specifically addressing the immunogenicity of HB vaccine in preterm or small for date babies, or in malnourished children. Usually a preterm or small for date baby is ready for immunization when weight reaches 2 or more kilograms. Immune responses to other vaccines are usually satisfactory in undernourished children; hence I assume the same for HB vaccine also.

Q3. *Is the seroconversion to hepatitis B vaccine adequate in high risk groups like children receiving multiple transfusions or blood products? Are there any different dosage recommendations for distinct risk groups?*

A3. In general, children requiring repeated transfusions are at increased risk for HBV infection. They should be immunized with HB vaccine; they respond to the vaccine normally unless they are immunodeficient. Patients undergoing chronic hemodialysis and those awaiting kidney transplant also are at increased risk for HBV infection; they do not usually respond to the vaccine like normal children. Therefore, additional doses are recommended for them. One regimen recommends 3 doses at monthly intervals and a fourth dose 2 months later and a booster one year later. When necessary, the immune response can (and should) be measured be quantitating anti-HBs level.

Q4. *Does an individual become HBsAg positive after hepatitis B vaccination?*

A4. HBsAg is a non-infectious subunit of HBV; therefore, it cannot infect a person. Without infection a person does

not become HBsAg positive. The injected quantity of HBsAg (such as 20 meg) is too small to be picked up in an HBsAg test of serum or plasma.

Q5. *Should HBsAg carriers receive hepatitis B vaccination? What happens to a child who is a hepatitis B carrier when he receives the vaccine? Is there any risk of vaccinating individuals with anti HBs +?*

A5. There is no need to give HB vaccine to persons who are HBV carriers, with HBsAg in their plasma/serum. It is most unlikely that a few micrograms of HBsAg will do anything in such persons. There have been some unconfirmed claims that repeated doses of HB vaccine may induce the production of anti-HBs in HBsAg positive persons, thus converting them from positive HBsAg to negative HBsAg and from negative anti-HBs to positive anti-HBs. In my own limited studies, I have not ' been able to document such a response.

Q6. *How does one prevent.-transmission of hepatitis B virus from mother to infant? Is the administration of hepatitis B immunoglobulin absolutely necessary for prevention of vertical transmission?*

A6. With prompt HB vaccine doses given within 24 hours after birth, one month later and 6 months later, the protection rates achieved in babies born to HBV carrier mothers reach upto 90 to 95%. If HB immunoglobulin (HBIG) is also given, the protection rate improves to 95 to 98% . Therefore, I would say that HBIG is not absolutely essential to prevent vertical transmission.

On the other hand, if a mother is known to be an HBV carrier, *i.e.,* HBsAg positive, and also positive for HBeAg, then I would recommend HBIG and vaccine in order to ensure maximum probability of protection. Similarly, if the mother developed HBV infection during pregnancy and remained HBsAg positive at delivery, then again I would recommend HBIG plus vaccine for the infant.

Q7. *Does hepatitis B vaccination have any prophylactic value in an unvaccinated child who comes in contact with a case of viral hepatitis* ?

A7. If an unvaccinated child comes in contact with a person with viral hepatitis, preventive steps would depend upon the etiology of the hepatitis. HB vaccine does have protective effect, very much like the post-exposure prophylaxis in rabies. Neonatal immunization of babies born Jo HBV carrier mothers also illustrate the principle of post-exposure prophylaxis. In such babies, the maximum exposure is during delivery.

Since HBV disease has a long incubation period (6 weeks to 4 months) there is sufficient time to induce protective immunity, especially by passive immunization (by giving HBIG) followed by active immunization. Even when passive immunization is not given, active immunization alone is protective, especially when given as a rapid immunization schedule, in the large majority of infants born of HBsAG positive mothers. Presumably this is the case in cases of a single exposure such as needle-stick.

Q8. *When should the primary vaccination course for hepatitis B vaccination consist of four doses instead of three? Do four doses offer any advantage in seroconversion or it's rapidity* ?

A8. We must remember that the re-

commended schedule of immunization is based on currently available information, and that some changes in the schedule may be made from time to time. The schedule generally accepted was given earlier, as three doses at 0, 1 and 6 months. Two variations of this schedule have been suggested for infant immunization. The first is a four dose schedule, the first three at monthly intervals and the fourth about one year later. This schedule is acceptable for infants born of HBsAg carrier mothers as well as non-carrier mothers. Thereafter, the next booster may be five years later. The second variation is to give two doses at an interval of two months followed by the third dose twelve months later. The next booster dose is five years later. While this schedule may be quite satisfactory for babies born of HBsAg negative mothers, more data are needed to evaluate it's adequacy in babies born of HBsAg positive mothers.

In babies given HB immune globulin (HBIG) at birth (when the mother's status had been checked and found to be a carrier), the four dose schedule mentioned above is preferred to the three dose schedule referred to earlier. Similarly when a health care worker is exposed to HBV *(e.g.,* needle stick injury, the index case being a carrier), then again HBIG and the four dose schedule is recommended for assured long-term immunity.

In the past, there has been a recommendation to give four doses at monthly intervals if 0-1-6 months schedule was considered to be too slow for immunization. HB vaccine manufacturers currently recommend that the fourth dose is better spaced after twelve months, since children do respond well to the three doses given at monthly intervals; here the main problem is the relatively rapid decline in antibody levels. To overcome this drawback, the fourth dose is to be given one year later.

Chronic renal failure and recurrent hemodialysis appear to have adverse effects on the immune response to HB vaccine. In subjects with this problem, one recommendation is to give four injections of double doses (*i.e., 2* ml each) with increasing intervals after each successive dose. For example, the four injections may be spaced at 0, 1, 2, and 6 months of intervals. Such schedules are not simply to be followed blindly, but the patients antibody response must be monitored. In some renal units, single dose injections are repeated until adequate response is documented.

Q9. *Is hepatitis B vaccine required by one ,4pho has already recovered from: (i) acute hepatitis B infection; and (ii) jaundice with etiological agent not determined* ?

A9. HB vaccine is not necessary in subjects previously infected with HBV, whether or not they have anti-HBs response or not. To confirm past infection anti-HBc is a more reliable test.

Since there are many causes of jaundice, HB vaccine is recommended to protect against future HBV infection in subjects with no evidence for past HBV infection. This is particularly true for health care workers. In the case of children, particularly subjects below five years in nearly all cases, and in children below ten years in most cases, we can be reasonably sure that HBV is not the cause of jaundice. In young children HBV infection is almost always asymptomatic !

Q10. *Is it necessary to determine antibody levels after hepatitis* B *vaccination* ?

A10. It is not necessary to monitor antibody levels in infants and children who respond quite well to HB vaccine. In older persons, particularly these over 40 years and in special circumstances such as chronic renal failure, monitoring is a good idea if *cost* is not a problem. In the case of persons on repeated hemodialysis, the benefit is well worth the cost.
