Letters to the Editor

No Seroconversion After Hepatitis B Immunization

In response to the recent question regarding unsatisfactory response to hepatitis B immunization, some reasons have been enumerated(l). It needs to be highlighted that though inactivated hepatitis B vaccines derived from plasma or from yeast recombinant DNA are both immunogenic and safe, about 5-10% of healthy people do not respond to them and variants of hepatitis B virus that are not neutralized by vaccine induced hepatitis B surface antibody have emerged(2,3). Several factors adversely affect the antibody response to hepatitis B surface antigen which include site of injection, deltoid area being preferred to buttock as fat lacks antigen presenting cells, resulting in delay in presenting antigen to B and T cells(4), increasing age, sex, smoking, immunosuppression and immunogenic make up(5).

Though mechanism underlying nonresponsiveness to S component of hepatitis B surface antigen in humans is largely unexplained, evidence is accumulating that different HLA-DR alleles are associated with specific low responsiveness in different ethnic population(5). The pre S_1 and S_2 domains have an important immunogenic role in augmenting hepatitis B surface antigen antibody response, preventing the attachment of the virus to hepatocytes and eliciting antibodies that are effective in clearing virus, stimulating cellular immune response and circumventing genetic nonresponsiveness to the S antigen(6). Recently a phase II clinical trial of a new third generation hepatitis vaccine containing pre Sj pre S_2, S antigenic components has been published. Results reveal that 69% of health workers who did not seroconvert after at least four doses of a licensed hepatitis B vaccine containing the S component seroconverted after single dose of new vaccine(7).

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Reply

The issues regarding unresponsiveness to hepatitis B (HB) immunization, raised by Dr. Anju Aggarwal deserve serious scrutiny. However, these issues are not relevant to the basic question dealt with in the Immunization Dialogue on a specific incident. To recapitulate, a physician having taken 3 doses of HB vaccine in India was found not to have detectable antibody when tested in UK, and two doses of vaccine taken there was followed by a vigorous antibody response. Here the question was specifically about the reliability of the quality (immunogenicity as determined by potency) of the HB vaccines marketed in India.

Since the physician responded to two additional (indeed, a total of 5) doses of the conventional HB vaccine, he cannot be regarded as a non-responder. Dr. Aggarwal uses this opportunity to highlight the problem of unresponsiveness to HB vaccine, and points optimistically to the potential of the new generation HB vaccine incorporating the pre-Sl and pre-S2 antigens in overcoming it.

Many of the statements made by Dr. Aggarwal are direct quotations from the last paper in her list of references. For example, "variants of hepatitis B virus that are not neutralized by vaccine-induced hepatitis B surface antibody" has relevance to the new vaccine, but not to the issue of unresponsiveness, which is the subject of her letter.

There are many studies showing that HB immunization starting in the neonatal period results in the seroconversion of over 95 (often 97-98) per cent of infants. Therefore, the true genetically determined unresponsiveness must be much less than the 5-10% quoted by Dr. Aggarwal. It is true that in adults 5-10% may not respond inspite of 3, or 4 or even 5 doses of the conventional HB vaccine. They are generally referred to as non-responders. In some of them, additional doses of the same vaccine may cause antibody response.

It is true that in the study quoted by Dr. Aggarwal non-responders were given the new generation vaccine and 69% responded to one additional dose. However, the study was not controlled by a group given one additional dose of the conventional vaccine. Therefore, it is difficult to evaluate the study properly. Moreover, we need to know if unresponsiveness will manifest if large numbers of adults are given the new vaccine.

For us in India, the major question still remains as to the assurance of quality of the marketed HB vaccines. Those of you