Hepatitis B Vaccine.

Pages with reference to book, From 28 To 29

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Through out the world, some 200 million persons are chronic carriers c;f Hepatitis B virus, most of them being silent, and a good percentage suffer from chronic active hepatitis, cirrhosis and 11CC (Alter, 1982). In 1968 Dr. Baruch Blumberg was awarded nobel prize for his discovery of Australia antigen. The complete hepatitis B virus (Dane particle) consists of a core component containing EN A and EN A polymerase enveloped by a lipoprotein surface matrix (HBsAg). Due to defective production of the virus, the surface component (HBsAg) is produced and released in blood stream in excess, as compared to the core. The HBsAg in the blood takes two particulate forms (spherical & tubular) and thus 100 billion to a trillion particles cf incomplete virus per millimeter of blood circulate in blood. It was this massive volume of circulating antigen that helped in the detection of HBsAg (Australia antigen) by even least sensitive tests as agar gel diffusion. This same mass of non infectious defective virus has served as the particulate immunogen in most current vaccines, called subunit vaccines. HBsAg positive cases, mostly blood donors, who were previously rejected to donate blood due to high risk of infectivity, have now become the prime source for vaccine synthesis. PurifIcation and subsequent inactivation steps have made it almost impossible for the live virus to contaminate the vaccine. Large volumes of plasma is obtained from antigen positive cases with high titers by plasmapheresis. The Dane particle is separated from the two particulate forms, and later tubular forms are inactivated by treatment with formaldehyde and enzyme digestion.

Safety tests of this vaccine have been tried successfully in chimpanzees, selected local human population and later large scale clinical trials. No untoward side effects except mild pain at the injection site and low grade fever have been observed over a period of several years. No hepatitis B vaccine has produced hepatitis B infection or any other infection which might be taken as a contamination of the original plasma pool.

Subunit vaccines have been produced by National Insitute of Allergy and Infectious diseases, National Institutes of Health, workers in France (Maupas et al., 1978), Netherlands (Reesink et al., 1978), China (Tao et al., 1978) and Japan (Shikata et al., 1981).

The aqueous vaccine (Merk Sharp and Dhome) was highly immunogenic in chimpanzees but not in man, so it was incorporated in aluminium hydroxide(Alum) and v'as found highly effective. The recently licensed alum adsorbed hepatitis B vaccine produces antibody formation against HBsAg in 80-90% of the recipients after primary immunization with two doses 20-4Oug at one month interval. After the third dose the positivity of antibody in the recipients rises to more than 95% once antibody (anti HBs) is formed. Individuals are protected from all but massive exposures to hepatitis B virus. The antibody developed has specificity for the common HBsAg determinant 'a' and hence is protective against both ad and ay subtypes of HBV. The booster dose after 6 months not only increases the çroportion of vaccine recipients but also increases the antibody titers dramatically from 20% to 70%.

The efficacy trial of this vaccine was conducted by Szmuness et al.(1980) against placebo in male homosexuals, a group which is known to be at the highest risk for HBV infection in the United States. It was found that 77% cases developed antibody within 2 months of the initial inoculation which increased to 90% after the six month booster dose. The effect of vaccination on the incidence of HBV infection was dramatic and no matter which parameter of infection was analyzed, the difference between vaccine and placebo recipients was striking.

Few cases of HBV infection did occur in the vaccine group in the early months of the study, but it is presumed that they had contacted the infection prior to inoculation. Moreover, the incidence of hepatitis B was significantly less in this group than amongst the controls, suggesting that the vaccine

might afford post exposure prophylaxis. The efficiency of this vaccine against hepatitis B immunoglobulin in the post exposure protection cannot be determined at th.is time.
This vaccine may also serve indirectly as the first anti-cancer vaccine, for possible association of HCC and HBV infection (Kew, 1981). Prospective epidemiologic study by Beasley et al. (1981) found, that relative risk for development of Hepatocellular carcinoma was 223 times greater in HBsAg carriers than among non carriers, and that the antigen is present in these patients years before the development of cancer. If such is the case, the use of hepatitis B Vaccine in areas of high HBV endemicity should prevent new HBV infection and in long term should also lower the occurrence of liver cancer.
The target population for hepatitis B Vaccine administration are health care personnel (physicians, dentists, nurses, paramedical and paradental staff, laboratory technicians), selected patients in hemodialysis, hematology and oncology units, children with thalassemia and hemophilia, residents of mental hospitals, contacts of carriers, homosexually active males, pros titutes, drug addicts, infants and young children in high risk areas (Krugman, 1982) and infants of antigen positive mothers.
The highly effective vaccine has brought a break through in the prophylaxis of Hepatitis B, which is endemic throughout the world. This will in the long run reduce morbidity as well as the post hepatitis B complications.

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