References


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With infection acquired from carrier mothers. In a study of family members of 27 PHC cases, we found that 70% of mothers of patients with PHC were HBsAg(+) compared with 14% of mothers of controls [5]. Secondly, we tested the hypothesis that chronic liver diseases (primarily cirrhosis) which were known to be associated with PHC were associated with persistent hepatitis B infection. This hypothesis was also supported. In Mali, we observed that in cases of chronic liver disease 46% were HBsAg(+) compared with 75% of PHC cases and 5% of controls [4].

In the course of these studies, we investigated the association of anti-HBc with PHC. We reported in 1975 that anti-HBc was more frequent than HBsAg in PHC patients; again probably reflecting the low level of HBsAg in the sera of these patients. 90% of PHC cases in Senegal were anti-HBc(+) compared with 28% of controls [4, 6].

We also examined the relationship of HBeAg and anti-HBe to PHC. Werner et al. [11] showed that e antigen was rarely found in patients with PHC but anti-HBe was frequently present. This observation is consistent with the thesis that PHC occurs in individuals who have been infected with HBV for many years and that by the time their tumor becomes clinically evident, active viral replication has ceased.

Our studies now in progress in Senegal are directed at four aspects of the interaction of HBV with humans and ultimately relate to the risk of developing PHC.

a. Studies in other populations have shown variations by ethnic group in the frequency with which carrier mothers infect their infants. The frequency of mother-to-child infection, the age at which it occurs, and the type of response of infants to such infection are important variables in the development of strategies of prevention of hepatitis B infection and PHC. We are investigating mother-to-child transmission of hepatitis B in Thies, a town 70 km east of Dakar. About 2,000 women have had blood drawn at the time of delivery. Approximately 100 children born to HBsAg(+) women and 200 children born to HBsAg(-) women are being tested at the following intervals after birth: 15 days, 3 months, 6 months, 1 year, and annually thereafter for 3 years.

b. Studies of whole communities over time permit evaluation of the impact of infection on the entire population, on family units within the community, and the age at which individuals in the community are most likely to become infected. We are focusing our investigation on the villages of the rural community of Tip, about 220 km east of Dakar. A census of each village has been taken and family relationships identified. Blood samples have been collected annually for the past 3 years from about 80% of the population. This should be extremely useful in evaluating field trials of vaccines and other control measures.

c. We are continuing to study the families of patients with PHC and families of patients with cirrhosis or CAH. Blood samples have been collected from about 170 families of PHC cases and 80 families of cases of chronic liver disease. These studies will evaluate the role of mothers and fathers of PHC patients in the transmission of HBV and the type of response to infection. Hepatitis B infection in siblings and children of cases is also being assessed.

d. Many of the areas of the world with high prevalences of chronic carriers of HBV are also areas where severe malnutrition may occur. We are studying the interaction of protein-calorie malnutrition (PCM) in Senegalese children with their responses to infection with HBV. 132 children with PCM treated in the Pediatric Clinic at Le Dantec Hospital in Dakar have been identified and are being compared with 134 children treated in the same clinic for other conditions. Blood samples have been obtained at diagnosis and 30 days after the initiation of therapy.

Analysis of the data from these four studies is just beginning, but certain interesting points are emerging. Before the age of 6 months, appearance of HBsAg in the serum of infants, born to HBsAg(+) women, appears to be a rare event. Anti-HBs transmitted from mother to child seems to have a limited protective effect. The studies in the Tip population suggest that the peak frequency of HBsAg positivity is in the 10- to 19-year age group. If this is confirmed, it suggests that the hepatitis B vaccine given early in life will probably protect most of the population from HBV infection. That is, even if perinatal mother-to-child transmission is not prevented by the vaccine, the overall incidence of hepatitis B infection in this population would be drastically reduced.

Studies of malnourished children suggest that they become infected at an earlier age than well-nourished children and that they may have a different response to this infection. This information will also bear on prevention strategies. The vaccine may be less effective in malnourished children or may have unforeseen consequences in such children.

We believe that studies of the kind described above and similar studies on other populations in other parts of the world will, in due course, lead to effective methods for preventing hepatitis B infection and most cases of hepatocellular carcinoma in humans.