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LIMITED FAMILY CLUSTERING OF HEPATITIS B SURFACE ANTIGEN IN A MELANESIAN POPULATION[1]

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Mazzur, S. (American National Red Cross, Blood Research Lab., Bethesda, MD 20014) and N. Jones. Limited family clustering of hepatitis B surface antigen in a Melanesian population. *Am J Epidemiol* 105:113–117, 1977.

The entire population of Graciosa Bay, Santa Cruz, Solomon Islands, was tested for hepatitis B surface antigen (HB_sAg) by reverse passive hemagglutination and antibody to HB_sAg (anti-HB_s) by passive hemagglutination. Analysis of the distribution of HB_sAg in relatives of HB_sAg carriers and non-carriers showed clustering only in children of carrier mothers. Similarly, there was no clustering of total exposure as measured by serologic tests except in children of carrier parents primarily due to the antibody and antigen of children of carrier mothers. This distribution pattern is probably due to cultural and environmental factors which increase exposure between HB_sAg carriers and people who are not related to them and also reduce the amount of contact between siblings.

anthropology, cultural; carrier state; hepatitis B antigen; human genetics; social environment

Previous studies of the distribution of hepatitis B surface antigen (HB_sAg) in human populations have shown a tendency for asymptomatic carriers of the antigen to cluster in families (1–9). Segregation analyses have not excluded the hypothesis that susceptibility to becoming a chronic carrier of hepatitis B virus (HBV), as indicated by the presence of HB_sAg in the serum, is determined by a simple autosomal recessive gene (1–6). Vertical transmission of HBV from mother to infant has been documented (8, 10–12) and a maternal effect has been observed on the population level (13). Family clustering may result from underlying genetically determined susceptibility or the increased risk of infection associated with close contact (14). This distinction is important because genetic etiology is often inferred from family clustering even in the absence of supporting segregation analysis.

In contrast, we have been investigating the epidemiology of HB_sAg and antibody against HB_sAg (anti-HB_s) in the population of Santa Cruz in the Solomon Islands in the South Pacific. Segregation analysis of our data concerning HB_sAg carriers has shown a distribution pattern which mimics that of an autosomal recessive in children in families where neither parent has HB_sAg. However, this analysis firmly rejects a genetic basis among children of families in the same community where one or both parents are carriers of HB_sAg (15).

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Abbreviations: anti-HB_s, antibody to hepatitis B surface antigen; HB_sAg, hepatitis B surface antigen; HBV, hepatitis B virus; PHA, passive hemagglutination; RPHA, reversed passive hemagglutination.

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This paper presents an analysis of the family distribution of HB_sAg and anti-HB_s on Santa Cruz and discusses some behavioral characteristics of the population which may affect the transmission of HBV and the establishment of the HB_sAg carrier state.

Materials and methods

The people who participated in this study live in 14 villages of leaf houses located along the shore of Graciosa Bay, on Santa Cruz Island in the Solomon Islands. They are Melanesians, well nourished and relatively healthy. Their main health problems are malaria, tuberculosis, filiariasis and other respiratory infections (16). In August and September 1974, 771 residents of Graciosa Bay were tested for HB_sAg and anti-HB_s. This represented over 99 per cent of the resident population and included all ages. Blood was taken in plain Natelson capillary tubes from a finger or toe prick. The serum was separated and tested in the field for HB_sAg by reverse passive hemagglutination (RPHA) (17) in the AusCell system (Abbott Laboratories, N. Chicago, IL) using microtiter equipment. Lyophilized red blood cells coated with HB_sAg were kindly provided by Sandra Paprocki of Abbott Laboratories and were used in passive hemagglutination (PHA) tests to detect anti-HB_s. All samples that reacted in either test were titrated to their endpoints and the specificity of the reaction was confirmed by neutralization with HB_sAg or anti-HB_s, whichever was appropriate. The HB_sAg used as a control and to confirm the anti-HB_s results was an *adw* antigen sample from an asymptomatic American Red Cross blood donor. The antibody preparation used in this study was a pool of human antibody prepared by Spectra Biologicals (Oxnard, CA).

A census of the population was prepared. This consisted of a map of the houses in each village. The people living in each house were listed by name and the following additional information was obtained: age, sex, and the name, age and sex and present location of all first degree relatives and spouses. This census included all live born children regardless of whether they were dead or living away from the village at the time the census was taken. The results of the testing for HB_sAg and anti-HB_s were integrated with the census to yield the following results concerning 117 families.

Results

The overall prevalence of HB_sAg on Santa Cruz was 11 per cent; the prevalence of anti-HB_s was 21 per cent. The results of the HB_sAg testing are tabulated in table 1 according to their occurrence in relatives of HB_sAg carriers. The Chi-square test was applied in each category to compare the number of HB_sAg carriers and non-carriers in relatives of carriers and controls. The controls consisted of persons in Graciosa Bay who were not carriers of HB_sAg. All relatives of these controls were tabulated and entered into the table in the same way as the relatives of HB_sAg carriers. Significant clustering was observed only among children of mothers with HB_sAg in their sera ($0.01 < p < 0.05$).

The same statistical analysis was applied to the distribution of anti-HB_s as shown in table 1. There was no significant clustering of antibody in these relatives of HB_sAg carriers.

Similarly, we analyzed the total infection past and present in these groups, as indicated by HB_sAg and anti-HB_s results taken together. Again there was no significant clustering of evidence of past or current infection with HBV in the relatives of HB_sAg carriers except among children of HB_sAg carrier parents, due primarily to the contribution of carrier mothers.

The prevalence of HB_sAg among siblings of HB_sAg carriers was determined by the following formula: Number of HB_sAg-positive children in HB_sAg sibships minus number of HB_sAg sibships, divided by to-

TABLE 1

Distribution of HB$_s$Ag and anti-HB$_s$ in relatives of HB$_s$Ag carriers

Relationship to carrier	No.	HB$_s$Ag	Anti-HB$_s$	Total
Children of carrier mothers	50	8 (16%)*	15 (30%)	23 (46%)†
Children of non-carrier mothers	314	21 (7%)	61 (19%)	82 (26%)
Children of carrier fathers	57	7 (12%)	14 (25%)	21 (37%)
Children of non-carrier fathers	293	31 (11%)	64 (22%)	95 (32%)
Children of one or both parents carriers	94	13 (14%)	26 (28%)	39 (41%)*
Children of two non-carriers	222	17 (8%)	43 (19%)	60 (27%)
Mothers of at least one carrier	21	4 (19%)	1 (5%)	5 (24%)
Mothers of only non-carriers	78	8 (10%)	13 (17%)	21 (27%)
Fathers of at least one carrier	25	6 (24%)	4 (16%)	10 (40%)
Fathers of only non-carriers	63	10 (16%)	15 (24%)	25 (40%)
Parents of at least one carrier	46	10 (22%)	5 (11%)	15 (33%)
Parents of only non-carriers	141	18 (13%)	28 (20%)	46 (33%)

* $0.01 < p < 0.05$.

† $p < .01$.

tal number of children in HB$_s$Ag sibships minus number of HB$_s$Ag sibships. (HB$_s$Ag sibships are those where at least one child was a carrier of HB$_s$Ag.)

Prevalence of HB$_s$Ag among siblings of HB$_s$ carriers = 37 − 26/111 − 26 = 12 per cent.

Twelve per cent is not significantly different from 11 per cent which is the prevalence in the total population. Thirty-four per cent of the siblings of HB$_s$Ag carriers had anti-HB$_s$. This is more than the 23 per cent anti-HB$_s$ among children in non-carrier sibships but not significantly so at the $p < 0.05$ level.

In three instances, both husband and wife had HB$_s$Ag in their sera; however, there was no significant increase in the prevalence of carriers among husbands or wives of 26 carriers when compared to those of 128 non-carriers by Chi-square. Anti-HB$_s$ was present in 19 per cent of the sera from spouses of carriers and 19 per cent of the sera of spouses of non-carriers.

DISCUSSION

Previous studies regarding the distribution of HB$_s$Ag in other populations have indicated strong family clustering with particular concentrations among sibs and parents of carriers, and a distribution compatible with that of an autosomal recessive trait (1–8, 18). On Santa Cruz we see family clustering only related to a maternal effect, that is, HB$_s$Ag carrier mothers are more likely to have carrier children than are non-carrier mothers. This is not surprising since vertical transmission of HBV infection from mother to infant has been well documented (8, 10–12). However, this difference is significant only between the $p = .05$ and .025 level ($\chi^2 = 3.9100$) and these children of carrier mothers represent only 21.7 per cent of the child carriers. Apparently the HB$_s$Ag carriers in this population are not generally infectious since there is no clustering of antibody around any carriers nor is there clustering of antigen among the parents, spouses or siblings of HB$_s$Ag carriers. Although there appears to be some maternal effect, it is not efficient enough to produce clustering among siblings of carriers. Among all children, 62 per cent are single carriers within their sibships.

Previously published (15) segregation analyses of the distribution of HB$_s$Ag in

this population, testing for an autosomal recessive trait by the maximum likelihood method, indicated that the θ calculated from families where both parents are negative for HB_sAg and at least one child has HB_sAg was 0.182 with a SD of 0.068 and a χ^2 of 0.901. The expected value was 0.25. In families with one carrier parent and at least one child with HB_sAg, the expected value was 0.50. The θ for the Santa Cruz population was 0.244 with a SD of 0.103 and a χ^2 of 5.959. This rejects the hypothesis. When both parents are HB_sAg carriers, all of the children who are infected should become carriers. Of 13 children of carrier parents, only two were carriers, three had antibody and eight were negative for both antigen and antibody. The finding of antibody in these children rejects the simple autosomal recessive hypothesis and confirms the observation of Vyas (19).

We believe that the difference between the strong clustering within sibships and compatability with genetic etiology reported in the literature and the lack of such distribution on Santa Cruz is the result of increased interfamilial transmission of HBV and reduced intrafamilial transmission. The reasons for the increase in interfamilial spread of HB_sAg on Santa Cruz are probably due in part to the social behavior of the population. One factor may be found in the toilet arrangements. There is one area of the coral beach near the villages assigned to women and another to men. There is no separation according to family. There is blood present in feces because of hookworm and other parasitic infections and shoes are not worn. The observed sharp increase in the prevalence of serologic evidence of infection with HBV at the time children begin to use the adult toilet area (20) supports the possibility of HBV transmission here.

Another social factor that may enhance interfamilial and decrease intrafamilial transmission of HBV may be the institution of the mendai, or single men's house (21). From early youth, boys spend much time in association with the mendai in the villages while girls work helping their mothers tend younger children and garden away from the villages. Thus the contact between siblings of opposite sex is much reduced. By puberty the young boys move completely into the single men's house and live there until marriage, sharing with an intimacy usually reserved for family living. Szmuness et al. (22) have shown that male homosexuality is associated with transmission of HBV. Such homosexual behavior is common in Santa Cruz and is accepted as a natural and socially approved substitute for heterosexual activity (23).

These data from Santa Cruz indicate that, at least in this population, infection with HBV and establishment of the carrier state of HB_sAg are not primarily associated with the family unit or genetically controlled. As suggested by Lederberg (14), they are apparently determined by cultural and environmental variables which increase the degree of exposure.

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