Seroepidemiology of Infection with Hepatitis A and B Viruses in an Isolated Pacific Population

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To determine the prevalence of infection with hepatitis A virus and hepatitis B virus in an isolated population, samples of serum were collected from 574 healthy subjects living on the remote Pacific island of Funafuti. Each specimen was tested for antibody to hepatitis A virus, hepatitis B surface antigen, and antibody to hepatitis B surface antigen by solid-phase radioimmunoassay. Overall, 79.8% of the population showed evidence of previous infection with hepatitis A virus, and 72.5% with hepatitis B virus; the high prevalence of antibody to both viruses in young adults suggested that the majority of infections were acquired in the first decade of life. Although it is known that hepatitis B virus maintains itself in isolated populations through a reservoir of chronic carriers, the reason for the persistently high rate of infection with hepatitis A virus is unknown.

Over the past 10 years, a number of sensitive serological tests, such as those for hepatitis B surface antigen (HBsAg), antibody to HBsAg (anti-HBs), and antibody to hepatitis B core antigen (anti-HBc), have been developed for the detection of infection with hepatitis B virus (HBV), and these tests are now widely available on a commercial basis. The application of these tests to panels of sera collected from many different populations has led to an improved understanding of the epidemiology of hepatitis B and new insights into its mode of spread. As tests for hepatitis A virus (HAV) and its antibody (anti-HAV) have only recently been developed, less information is available about the epidemiology of hepatitis A. In the past few years, several seroepidemiologic studies have been performed, mainly in developed countries; in each population the prevalence of anti-HAV has been found to increase with age [1–8] and to be inversely related to socioeconomic status [2–10] and standards of hygiene [3, 10, 11].

Almost no information is available about the epidemiology of hepatitis A in developing countries, although the occurrence of cases in travelers [12] and missionaries [13] suggests that the infection is common. To obtain further information on the epidemiology and mode of spread of both types of hepatitis, we have been studying the patterns of infection in a variety of populations of different sizes and degrees of isolation. This paper documents our findings on the remote and isolated Pacific island of Funafuti.

Materials and Methods

Population. Tuvalu (formerly the Ellice Islands) is a British dependency and comprises a group of nine Pacific islands, running NW to SE at latitudes 5°–11° south and longitudes 176°–180° east (figure 1). The islands extend in a winding line over a distance of 400 miles and are separated by distances of 40–90 miles. Most of the islands are coral atolls that have more or less continuous reefs surrounding a deep central lagoon. The level of rainfall is extremely high (over 3,500 mm per annum), and vegetation is limited to coconuts, bananas, and breadfruit. The inhabitants of the islands are Polynesians who are believed to have migrated originally from Samoa. At the time of the last census (December 1973), the total population of the islands was 5,887; it is currently believed to be approximately 7,000 [14].

Funafuti, the main island in the group, is an
Figure 1. Map of Australia, New Guinea, and the major island groups of the central and western Pacific.

Figure 2. Map of Funafuti (the main island of Tuvalu).

oval atoll about 15 miles long and 10 miles wide, consisting of a fragmented reef enclosing a deep lagoon (figure 2). Over two dozen inlets are located on the reef; Fongafale is the largest, taking up about half of the total area of 600 acres. The population of Funafuti has been increasing steadily in recent years and at present stands at about 1,500. Most of this increase has occurred since October 1975, when the Ellice Islands separated administratively from the Gilbert Islands and a number of families temporarily employed in the Gilberts returned home. The current birth rate is 40–50 per year.

Collection of specimens. In July 1976 a roll was prepared by house-to-house visits in which the names of all 595 indigenous inhabitants over the age of 10 years were recorded. Between July and October, when blood samples were collected, an additional 59 adults who had been temporarily employed in the Gilbert Islands returned to Funafuti. Of the 654 subjects available for study, specimens were obtained from 574 (87.8%), of whom 267 (46.5%) were males and 307 (53.5%) were females. These specimens were centrifuged shortly after collection, and the sera were separated aseptically, frozen, and transported in dry ice to Melbourne for further testing.

Test methods. Sera were tested at Fairfield Hospital for HBsAg and anti-HBs by solid-phase radioimmunoassay (RIA) with commercially available reagents (AustriaII-125 and Ausab,
Abbott Laboratories, North Chicago, Ill.). Positive test results for HBsAg were confirmed by neutralization with specific antiserum [15]. Positive test results for anti-HBs were confirmed by blocking of the reaction with HBsAg. Briefly, 100 μl of test serum was mixed with 100 μl of 0.85% NaCl, normal human serum known to be free
of HBsAg and anti-HBs, or a pool of human serum containing a high titer of HBsAg of both the adw and ayw subtypes. This mixture was incubated at 37°C for 1 hr. The RIA for anti-HBs was then performed according to the manufacturer's instructions. Test sera were considered to contain anti-HBs if addition of HBsAg reduced the binding by \( \geq 50\% \). It was sometimes necessary to dilute high-titered sera to 1:10 or 1:100 to demonstrate specific blocking.

Anti-HAV was detected by a competitive solid-phase micro-RIA based on that described by Purcell et al. [16]. HAV was obtained and purified as previously described [5]. The anti-HAV used as coating for microtiter plates and as a source of IgG for labeling with \(^{125}\)I was convalescent serum obtained from a young male with serologically confirmed hepatitis A.

**Results**

The age- and sex-specific prevalences of anti-HAV and of markers of HBV infection (HBsAg plus anti-HBs) are shown in tables 1 and 2, respectively. As no differences were observed between subjects who had spent all their lives in Funafuti and those who had worked for various periods in the Gilbert Islands, the data from the two groups have been combined.

**Discussion**

The results indicate that hepatitis B is endemic in Funafuti. HBsAg (subtype ayw) was detected in 9.8\% of the subjects tested, and anti-HBs was detected in an additional 62.7\%. These figures indicated that at least 72.5\% of the popula-

<table>
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<th>Age (years)</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
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<tr>
<td></td>
<td>No.</td>
<td>HbsAg (%)</td>
<td>Anti-HBs (%)</td>
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<tr>
<td>10–19</td>
<td>81</td>
<td>17.3</td>
<td>61.1</td>
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<td>34</td>
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<td>65.6</td>
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<tr>
<td>&gt;50</td>
<td>54</td>
<td>3.7</td>
<td>61.1</td>
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<tr>
<td>Total</td>
<td>267</td>
<td>12.7</td>
<td>65.5</td>
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infections later in life. Because the probability of becoming a carrier of HBsAg after an acute infection with HBV declines abruptly after the first five years of life, the higher carrier rate in males may be due to the occurrence of a higher proportion of infections during this period.

HBV is endemic in every Pacific island that has been studied [18-20]. Its ability to survive in such isolated populations is presumably related to the presence of large numbers of chronic carriers, who provide a permanent reservoir of infection. The pattern of acquisition of HBsAg and anti-HBs in Funafuti suggests that transmission usually takes place in the first two decades of life, although the mechanism by which it occurs is uncertain. Transmission of the virus from carrier mothers to their babies, at or around the time of delivery, has been documented [23] and is known to be common if the mother's serum contains hepatitis B e antigen (HBeAg) [24]. As >75% of carrier women of child-bearing age in this population are HBeAg-positive [25], “vertical” transmission may be an important factor in the spread of infection and in the maintenance of a pool of chronic carriers.

The pattern of infection with HAV was similar to that observed with HBV. Almost 80% of children had serological evidence of infection by the age of 10 years, and the highest prevalence of anti-HAV was detected among adults aged 30-39 years. Although the prevalence of anti-HAV declined with age, the decline was not as abrupt as in hepatitis B. Also, by contrast with hepatitis B, males were not more frequently infected with HAV than were females.

The epidemiology of hepatitis A in Funafuti differs greatly from the epidemiology of the disease in developed countries, where the highest prevalence of antibody is found among the oldest members of the population, and relatively low rates are detected among children and young adults [1-8]. This lower prevalence of antibody among children and young adults in developed countries is presumably a reflection of higher standards of hygiene and sanitation. The extent of infection with HAV in Funafuti is not surprising, because many features of the lifestyle favor the spread of enteric infections. In general, the standard of hygiene is poor. Drinking water is obtained from household tanks and wells and is frequently contaminated. No adequate means of sewage disposal exists; the majority of the population use reef latrines that empty into the lagoon. The water of the lagoon is used for washing and bathing, and raw fish and shellfish harvested from these waters form an important part of the islanders' diet.

It is interesting to speculate on how HAV is able to maintain itself in an isolated population in which the birth rate is only 40-50 per year and the chance of the virus's persisting as a result of person-to-person transmission is remote. One possibility is the existence of a carrier state in which one or more chronic shedders serves as the reservoir of infection. Although this is an attractive suggestion, there is currently no good virological or epidemiological evidence for the existence of such a state. The fecal shedding pattern of HAV has been the subject of several studies [26-30], and the longest period for which virus has been detected after an acute infection is 16 days (measured from the onset of bilirubinuria). Likewise, repeated outbreaks of the disease in large closed communities imply that, if a carrier state exists, it must be extremely rare. A second possibility is the existence of a nonhuman reservoir of the virus, perhaps in shellfish. Shellfish are known to be able to concentrate viruses from large volumes of water, and, as HAV is relatively hardy, it may persist in an infectious form for a considerable period.

The final possibility is that HAV is unable to maintain itself in this population and that the high infection rate depends upon repeated, chance introductions of the virus by visitors, as has been documented recently in Greenland [31]. If this is the explanation, children born since the latest wave of infection should lack antibody, and it should be possible to detect populations of similar size in which the virus has been absent for many years. Studies to clarify these alternatives are under way.

References
3. Villarejos, V. M., Provost, P. J., Ittensohn, O. L., Mc-


