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Mosquito-borne infections in Fiji

II. Arthropod-borne virus infections

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SUMMARY

Surveys of arbovirus activity in Fiji were conducted over a 10-year period from December 1959 to December 1969. No arboviruses were isolated from over 200,000 mosquitoes, 9000 ticks, or 575 serum samples. Eight thousand human and 1117 bird, bat and animal sera were tested for haemagglutination-inhibiting arbovirus antibody using a variety of group A, group B and Bunyamwera group antigens. Only a small number of low-titre reactions were found among the non-human sera, but 14% of all human sera were found to contain Group B antibody. The antibody prevalence increased with increasing age, from less than 1% for persons born since 1950, to 70% for persons born before 1900. The age differences in prevalence could be used to estimate the time and size of previous epidemics. Differences were found in antibody prevalence between the sexes, between ethnic groups and between persons from different regions. These differences could be explained in terms of climate, location and custom.

Historical and serological evidence both suggest that all the antibody detected was due to past exposure to dengue virus. The very high proportion of the population with no dengue antibody makes Fiji a high-risk area for a further dengue epidemic. Dengue virus is known to be active in the Pacific and South-East Asia.

INTRODUCTION

Periodic epidemics of dengue have occurred in Fiji since the first epidemic reported in 1885. There have been two major outbreaks since then: one in 1930 and the other in 1943–4. Clinical cases of dengue were reported in the intervening periods, suggesting that dengue was endemic in these islands, but in recent years the number of cases notified has declined and since 1955 has not exceeded 40 cases per year. There have been no cases notified since the beginning of 1967.

During the period December 1959 to December 1969 numerous surveys were carried out in order to establish the status of arbovirus infections in the Fiji group. This work included attempted isolation of viruses from ticks, mosquitoes and

human, bird and various animal bloods, together with serological studies on serum samples from humans, animals and birds.

Preliminary results (Miles *et al.* 1964) showed that most, if not all, of the arbovirus activity in Fiji could be attributed to dengue virus. Over the past 10 years dengue, especially haemorrhagic dengue, has become increasingly important in South-East Asia, where it has caused the death of scores of children. The Fiji survey was expanded therefore to learn more of the epidemiology of this virus in Fiji, and to maintain surveillance because of the constant threat of the reintroduction of the virus in an epidemic form. More recently studies have been undertaken to compare the epidemiology of dengue with that of filariasis, which in Fiji is almost certainly carried by the same mosquito vectors (Mataika, Dando, Spears & Macnamara, 1971).

This report describes the results of the survey work and analyses some of the factors involved in the epidemiology of dengue in Fiji.

MATERIALS AND METHODS

Regions surveyed

The surveys conducted up to the end of 1967 covered most of the main regions of Fiji, including coastal and inland Viti Levu, Beqa, Southern Vanua Levu, Northwest Taveuni, the small islands of Qamea and Rabi, Kadavu (a full-scale survey), and Naviti in the Yasawa group. Since some of these surveys were designed primarily to detect recent arbovirus activity, the samples tested came from a higher proportion of children than is found in the total population. The 1968–9 survey was carried out in conjunction with the Fiji Medical Department filariasis

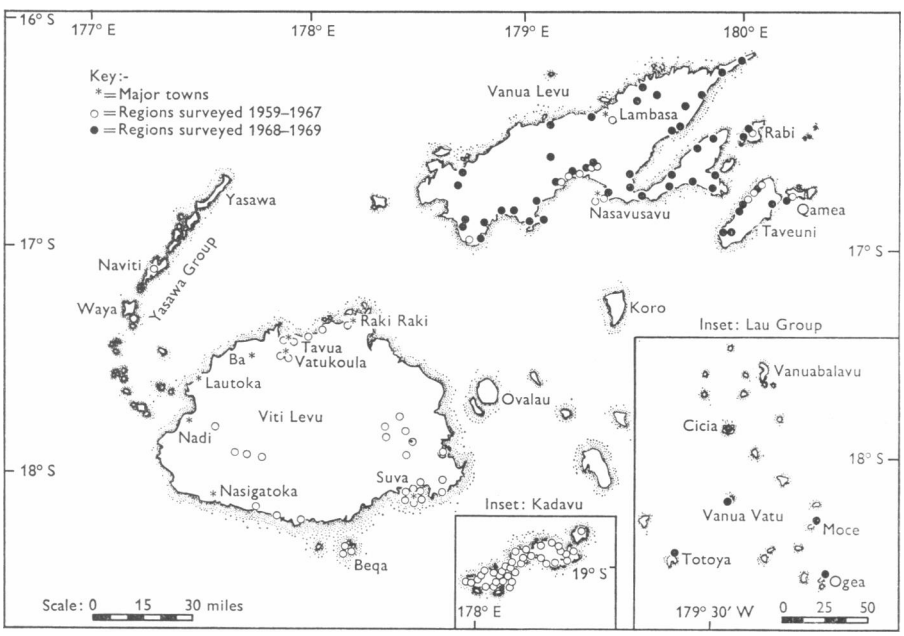

Fig. 1. Arbovirus antibody surveys in Fiji 1959–69.

survey in Northern and Southern Vanua Levu, Taveuni and the Lau Islands. For this survey, the field procedures, sampling methods and climatological and social factors involved in the selection of samples have been described elsewhere (Mataika *et al.* 1971). Detailed recording, punch-card sorting and computer analysis made it possible to gain more information from these collections than from the earlier work. The 1968–9 collections contained over half of the 8000 human sera tested during the total survey period.

The locations of the various regions studied are shown in Fig. 1.

Virus isolation attempts

A total of over 200,000 mosquitoes representing eleven species (but mainly *Aëdes* (*Stegomyia*) *polynesiensis* Marks; *Aëdes* (*Aëdimorphus*) *vexans* Theobald; *Aëdes* (*Finlaya*) *fijiensis* Marks; and *Culex* (*Culex*) *annulirostris* Skuse) and over 9000 ticks representing three species (*Haemaphysalis* (*Kaiseriana*) *longicornus* Neumann; *Rhipicephalus sanguineus*, and *Amblyomma cyprium* Neumann) were tested for virus using the methods described by Miles *et al.* (1964). During the early surveys, insect pools were inoculated into suckling mice, yolk sacs of 6-day embryonated hen eggs, and on chick-embryo cell monolayer tissue cultures, but after 1964 only intracerebral inoculation of suckling mice and inoculation of BHK 21 cell tissue culture tubes were used.

Sera from 140 humans suffering from ill-defined febrile sickness, from 84 fruit and insectivorous bats, and from 351 fowls and other birds were also tested for virus during the survey period.

Serological studies

Sera from 8000 humans, 44 bats, 1062 fowl and other birds and 11 rodents and other animals were tested for arbovirus haemagglutination-inhibiting (HI) antibody using a variety of group A, group B and Bunyamwera group arbovirus antigens. During the first few survey years the sera were tested against 13 or 14 antigens selected from western equine and eastern equine encephalitis (WEE and EEE), Whataroa, Sindbis, Bebaru, Semliki Forest, Chikungunya, Murray Valley encephalitis (MVE), Japanese encephalitis (JE), St Louis encephalitis, yellow fever, dengue types 1 and 2, Cache valley, Ntaya and Batai viruses. During the later years sera were routinely tested against seven antigens only. These were WEE, Whataroa, MVE, JE, dengue 1, dengue 2 and yellow-fever viruses. A set of 44 bat, 36 fowl and 134 human sera was tested against the additional antigens of Getah, Ross River, Tembusu, California encephalitis and Edge Hill viruses.

Antigens were prepared from infected suckling mouse brain by sucrose-acetone extraction as described by Clarke & Casals (1958). Sera routinely were triple-extracted with acetone to remove non-specific inhibitors, then absorbed with excess goose cells to remove non-specific agglutinins. Screening tests were carried out using 4–8 units of antigen and a serum dilution of 1/10. Sera which were positive at this dilution were then titrated against the appropriate antigens. Complete inhibition of 4–8 units of antigen at a dilution of 1/10 or higher was considered a positive reaction.

RESULTS

Virus isolation

No arboviruses were isolated from any of the specimens. Several agents were isolated from mosquitoes and human sera in mice or in tissue cultures (BHK 21) and these were identified as Coxsackie A 6 viruses (Maguire & Macnamara, 1966) and reovirus type 3 (Miles & Stenhouse, 1969) respectively. A Coxsackie A-like virus (TP 275) also was isolated from a pool of *Haemaphysalis longicornus* (A. C. Stenhouse, unpublished observation).

Serology

Five of 44 bat sera were positive at titres of 1/20 or 1/40 against MVE antigen. Each specimen came from a different locality. Four of 36 fowl sera inhibited Getah antigen at a titre of 1/20. All other birds, bats, rodents and domestic animals were negative.

From all areas of Fiji, human serum samples were found which contained arbovirus group B HI antibody. Many, especially those from older persons, reacted broadly to most or all group B antigens, while others reacted with only one group B antigen, usually dengue 1, dengue 2 or MVE. For the purposes of analysis, those sera which reacted only with yellow-fever antigen were classified as negative. This was rare, occurring only with sera from Europeans with a history of yellow-fever vaccination.

Table 1. *Prevalence of arbovirus antibody within the major ethnic groups*

	Fijian			Indian			Other races*			
Sex	+ve	−ve	%+	+ve	−ve	%+	+ve	−ve	%+	Total
Female	502	3039	14·2	25	232	9·7	16	81	16·5	3895
Male	516	3200	13·9	46	232	16·55	26	85	23·4	4105
Total	1018	6239	14·0	71	464	13·3	42	166	20·2	8000

* Includes Europeans, Chinese, other Pacific Islanders and peoples of mixed racial origin.

No human sera were found which reacted with antigens other than Group B. Most positive sera reacted to highest titre with dengue 1 or 2 antigens, and this, taken with the results of dengue neutralization tests reported previously (Miles *et al.* 1964), indicates that practically all the antibody detected could be due to past infection with dengue virus. High titres (up to 1/2560) were found in all age-groups from 20 years of age and upwards. The titres of persons under the age of 20 years were generally much lower. Apart from this there was no correlation between titre and age, sex or race.

Table 1 shows the population tested for arbovirus HI antibody listed according to ethnic group, sex and result of the HI test. There was no difference between the prevalence of group B antibody in Fijian males and females, or between the prevalence in Fijians and Indian males, but the prevalence in Indian females was significantly lower. The total number of specimens from people of other races did

not permit statistical comparison between the sexes, but this group as a whole did have a significantly higher antibody prevalence than the remainder of the survey population.

Table 2. *The effect of age on the prevalence of group B arbovirus antibody*

	Positive			Negative			
Year of birth	M	F	Total	M	F	Total	Positive (%)
Before 1900	34	29	63	23	4	27	70
1900–1904	40	28	68	24	9	33	67·3
1905–1909	45	36	81	32	21	53	60·5
1910–1914	70	58	128	54	42	96	57·1
1915–1919	56	62	118	58	42	100	54·1
1920–1924	68	65	133	81	61	142	48·4
1925–1929	69	70	139	91	73	164	45·9
1930–1934	85	68	153	137	120	257	37·3
1935–1940	61	79	140	132	165	297	32·0
1941–1944	29	26	55	177	230	407	11·9
1945–1949	14	10	24	181	255	436	5·2
1950–1954	5	2	7	508	518	1026	0·68
After 1954	12	10	22	2019	1812	3831	0·57
Total	588	543	1131	3517	3352	6869	14·14

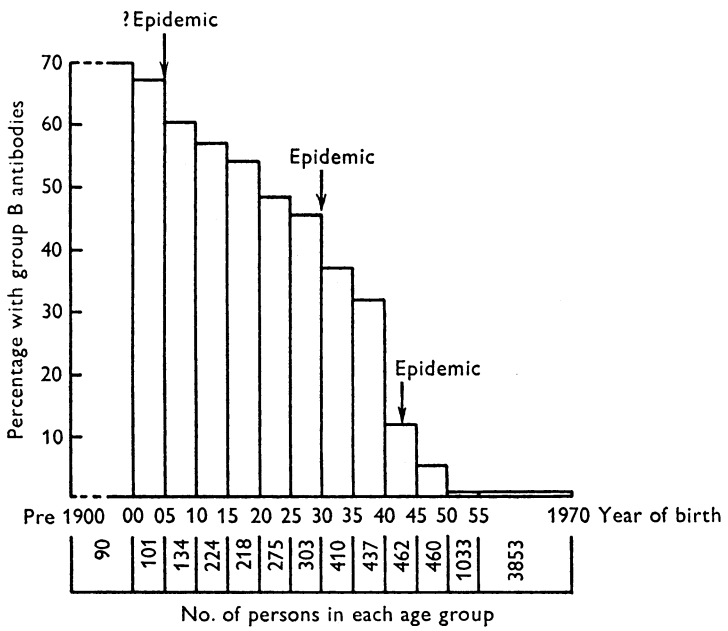

Fig. 2. The effect of age on prevalence of group B antibody.

Table 2 shows antibody prevalence tabulated according to date of birth and sex. The table shows that there is a gradual decline in prevalence with decreasing age and that virus activity must have been virtually absent since 1950. When the totals for males and females born before 1905 are pooled it becomes apparent that there is a significantly higher prevalence in females (81·5% positive) than

Table 3. *Geographical variation in arbovirus antibody prevalence*

Region	Sex						Total		
	Male			Female					
	+ve	−ve	%+	+ve	−ve	%+	+ve	−ve	%+
Northern Vanua Levu									
Inland villages	15	153	8·9	18	156	10·3	33	309	9·65
Coastal villages	40	240	14·3	28	223	11·15	68	463	12·8
Southern Vanua Levu									
Inland villages	32	126	20·25	44	139	24·0	76	265	22·3
Settlements	40	300	11·8	30	309	8·85	70	609	10·3
Coastal villages	89	346	20·45	106	369	22·3	195	715	21·4
Taveuni	132	258	33·9	92	277	24·9	224	535	29·5
Lau Islands	37	350	9·6	72	374	16·15	109	724	13·1
Kadavu	80	770	9·4	106	681	13·5	186	1451	11·4
Viti Levu and remainder of survey area	123	974	11·2	47	824	5·4	170	1798	8·6
Total	588	3517	14·3	543	3352	13·94	1131	6869	14·14

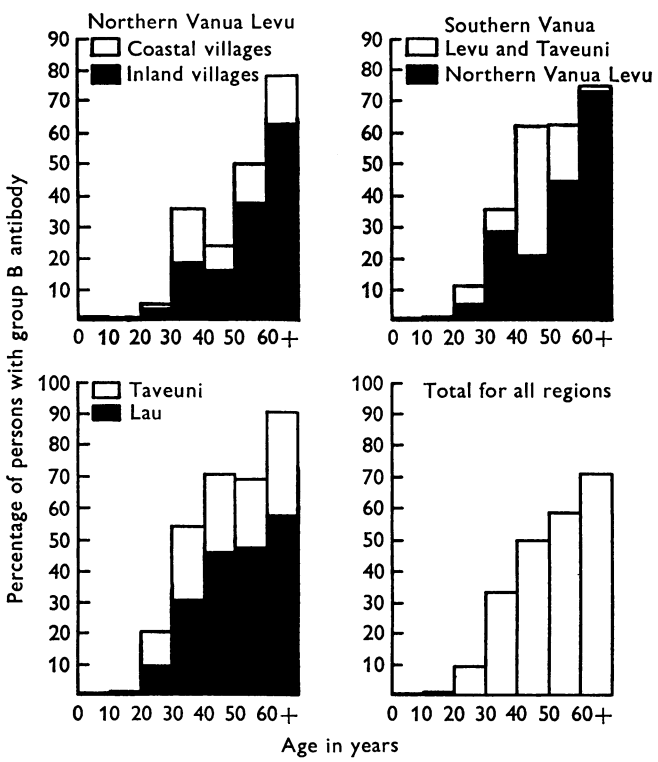

Fig. 3. Antibody prevalence in different geographic regions.

in males (61 % positive). The endemic type of increase in prevalence with age before 1930 and the steps in the incidence rates produced by the 1930 and 1943 epidemics are shown more clearly in Fig. 2.

The variation in antibody prevalence in the various geographical locations is shown in Table 3. Considerable differences were found between areas of differing climate or differing house patterns. As explained above, the rather low prevalence in Viti Levu and the remainder of the survey area can be attributed to the disproportionate numbers of children in these collections, but in all other areas differences in prevalence are real and cannot be explained by differences in the age structures of the populations tested. Some areas showed considerable differences not only in total prevalence, but in prevalences in different age-groups. These differences by region and age-group are shown graphically in Fig. 3.

DISCUSSION

The evidence presented here supports the hypothesis that the only arbovirus which has been active in Fiji is dengue. The low antibody titres in a few bats and fowls probably signify nothing more than non-specific group-reacting substances. The serological evidence that there has been little or no dengue activity since 1950 is supported by the failure to detect virus in any of the material tested. In spite of the lack of recent dengue activity, analysis of the serological results provides a considerable amount of information concerning the epidemiology of dengue in Fiji.

The relationship between race, sex and antibody prevalence

The prevalence of dengue antibody in Fijian males and females, Indian males, and females of 'other races' was essentially the same, but Indian females had a significantly lower prevalence and males of 'other races' had a significantly higher prevalence. The low antibody prevalence in Indian women is readily explained by the fact that they traditionally are extensively covered by clothes and do not work with males on the farms or in the plantations. This lower exposure of Indian women to mosquito bites is reflected in their lower microfilaraemia prevalence. The equal prevalence of dengue antibody in Fijian males and females contrasts with the situation in filariasis, where women are less affected than men (Mataika *et al.* 1971). The reason for the higher prevalence of antibody in males of 'other races' is not clear. Only a small proportion of these men would have come from other regions of known dengue activity.

The Indians of Southern Vanua Levu settlements were found to have lower antibody prevalence (7·1 %) than Fijians from the same area (12·8 %). This difference is probably due to the different housing types. The Indian population in these areas tend to live in concentrated 'barrack'-type houses, whereas the Fijians live in isolated houses. The differences may therefore be due to the better mosquito control in the immediate vicinity of the Indian dwellings.

The differences between the sexes in other regions cannot be explained so readily. In Taveuni there is a significant difference between the sexes, the males having an antibody prevalence of nearly 34 % while the females have a prevalence of only

25 %. This difference was not associated with race ratios in the sample. On the other hand, in Kadavu and Lau the position is reversed. Local custom may play an important role in determining the relative exposure of males and females to mosquito bites, but this is not certain.

The significant difference in antibody prevalence between males and females born before 1905 is puzzling. As far as is known, there has been no change in dress or custom since that time, so that it seems that the only explanation would be that during one of the later epidemics, for some unknown reason, females were attacked at a higher frequency than males.

Variation in antibody prevalence between climatic and geographic regions

It is apparent from Table 3 and Fig. 3 that there are marked differences in antibody prevalence between the regions of Fiji. The rates varied from as high as 29·5 % in Taveuni to as low as 9·65 % in the inland villages of Northern Vanua Levu. The low level of 8·6 % in Viti Levu is abnormal since the sample tested was not a true cross-section of the population.

Taveuni has a high rainfall and a dense mosquito population similar to that found in Southern Vanua Levu. Thus these two regions could be expected to have had higher numbers of infections, while Northern Vanua Levu, which is drier and has a lower mosquito density, would be expected to have fewer cases. In both regions, the observed antibody prevalence fits the climatic conditions. The relatively lower infection rates in the Lau Islands and Kadavu could be due to isolation. Travel and other forms of direct contact with these islands was rather limited at the time of the known epidemics. One observation not shown in Table 2 was the significant difference between the antibody prevalence in people who lived on volcanic islands and that of people who lived on the raised coral islands of the Lau Group. Both island types are populated by Fijians, those on the coral islands living mainly in fishing communities, while those on volcanic islands concentrate more on agriculture, and thus spend more time in the vicinity of coconut plantations. As expected from these observations, the prevalence of antibody on the coral islands was lower (9·2 %) than that found on the volcanic islands (15·2 %).

There was an interesting difference between the coastal and inland villages of Southern Vanua Levu, and the settlements and estates from the same region. Both coastal and inland villages had reasonably high infection rates, but the rates for the settlements were down to less than half that of the villages. It is known that the mosquito *Aë. polynesiensis* is found in the coastal areas and that further inland it is replaced by smaller numbers of *Aë. pseudoscutellaris*. Provided that there was no difference in the vector capability of the two species, one would expect a lower antibody prevalence in the inland villages, but such a difference was not observed. On the other hand, the settlements, being both coastal and inland, could have been expected, on purely geographical grounds, to have the same infection rates as the villages, but instead, they were considerably lower. It thus seems that the difference does not depend on the species of the vector. It seems more likely that the type of housing and the nature of the community are more important, the villages being compact groups of houses close to the bush, while the settlements usually

consist of isolated houses or 'barrack'-type dwellings in more open country. It is also probable that the chances of settlement dwellers becoming infected were considerably lower if the epidemic passed through the community rapidly.

Age differences and the size of previous epidemics

When the age distribution of the population tested during the whole of the survey period is compared with the age distribution of the total population of Fiji (Zwart, 1968), it can be seen that they are nearly identical. It therefore seems reasonable to draw certain conclusions from the serological status of the population as shown in Fig. 2.

The very low antibody prevalence in persons born since 1950 fits well with the fact that few cases of dengue have been notified during this period. Whether the antibody detected in these persons is due to past dengue infection or a low incidence of infection with a related virus, or merely a broad response to a variety of other infections, is not clear, but the fact that the titres in the sera from this age-group are generally lower than in other age-groups would indicate that the antibody may not be due to dengue virus infection.

After the 1943 epidemic in Fiji cases are known to have occurred for several years, and this would explain the antibody detected in person born between 1945 and 1950.

It is possible from the data presented in Fig. 2 to make an estimate of the number of susceptible persons infected during each epidemic. When the data given in the figure are plotted on semi-log paper, three sharp rises in antibody prevalence can be seen. One of these corresponds to the 1943 epidemic and from the graph it can be calculated that 23% of susceptible persons became infected during the 5-year period embracing the epidemic. The next corresponds to the 1930 epidemic, in which 14% of the susceptibles were infected during the 5-year period. The last corresponds to an epidemic which must have occurred around 1905 in which 17% of susceptible persons were infected over a 5-year-period. There is no historical record of such an epidemic. These are figures for the whole population, but if the age distributions of antibody prevalence in different districts shown in Fig. 3 are studied, it can be seen that in some of these regions the infection rate could have been as high as 40%. For the 20-year-period from 1907 to 1927, during which there were no known epidemics, the infection rate was 1·3–1·4% of susceptibles per year.

Fig. 3 gives some indication of the history of dengue in different regions of Fiji. For example, Taveuni and Southern Vanua Levu present similar patterns, but Taveuni had much larger epidemics, as one would expect from the wet climate. On the other hand, Lau seems to have experienced the same epidemics on a smaller scale than Southern Vanua Levu. In contrast to these areas, Northern Vanua Levu inland and coastal villages seem to have missed the 1930 epidemic. Another interesting observation is that in Lau, Taveuni and Southern Vanua Levu there was no increase in antibody prevalence between the years 1910 and 1929. This would suggest that dengue was not endemic in these areas during this period.

Persons under the age of 20 years now represent approximately 57% of the

total population of Fiji and over 99 % of these people have no immunity to dengue virus. Even in the total population the prevalence of non-immunes is 86 %. This must make Fiji a high risk area for a further epidemic of dengue in the future. In the absence of a satisfactory dengue vaccine, it would seem that very vigorous mosquito control programmes would be the only way to minimize this risk. Even if such programmes could be and were carried out, it is difficult to see how Fiji could expect to remain free of dengue when communications between Fiji and areas of known dengue endemicity have become so efficient. Added to the risk of the reintroduction of the same dengue virus type which caused the existing antibodies is the very real risk that a different type of dengue virus will appear there. In an explosive epidemic which occurred in Tahiti in 1964–5 and which was caused by dengue type 3, it was found that many people who had been infected during the 1940s with type 1 became reinfected with the new type (Laigret, Rosen & Scholammer, 1967). This would mean that if a new type of dengue was introduced to Fiji, considerably more than 86 % of the population would probably be susceptible.

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