

Mosquito-borne infections in Fiji

V. The 1971-73 dengue epidemic

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SUMMARY

A dengue epidemic due to type 2 virus involving some 3,400 cases began in Fiji early in 1971, had a peak during May, June and July, and cases have continued to occur with a low incidence during 1972 and 1973. Many of the notified cases showed classical dengue fever symptoms and there were no confirmed cases of haemorrhagic fever. A serological survey indicated that there had been at least 20,000 subclinical infections. It is probable that the virus was introduced to Fiji either through the port of Lautoka or Nadi international airport in February 1971. The normal travel patterns of residents must have spread the virus to all the more accessible localities but, with the exception of Rotuma, it caused infections only in areas where *Aedes aegypti* was available as a vector. There was no evidence that pre-existing dengue type 1 serum antibody gave any protection during this epidemic.

INTRODUCTION

There have been two major outbreaks of dengue in Fiji since the first epidemic was reported in 1885, one in 1930 and the other in 1943-44. Techniques for the isolation of dengue viruses were not available during these early epidemics, but a subsequent survey of sera for neutralizing antibody suggested that the 1943-44 epidemic was due to type 1 dengue virus (Miles *et al.* 1964). Notifications of dengue continued until 1966, but there is no serological evidence that dengue or any other arboviruses have been active in Fiji since 1950 (Maguire *et al.* 1971).

These authors also noted that the very high proportion of the population with no dengue antibody made Fiji a high risk area for a further dengue epidemic. Another dengue epidemic began early in 1971, reached a peak in the period May-July of that year, and continued through 1972 into 1973. Type 2 dengue virus was isolated from a number of cases. This report describes virological, serological, clinical and epidemiological aspects of the outbreaks.

MATERIALS AND METHODS

Notifications

Cases diagnosed on clinical grounds by medical officers were notified to the Fiji Medical Department. Data on age were available for more than half of the notifications. Blood samples were obtained from patients in the acute and convalescent phases of the illness from a number of cases in Suva, but very few from the other health districts.

Virus isolations

Material for virus isolation was injected intracerebrally (i.c.) into litters of mice less than 48 hours old. The mice were observed daily and any which became sick were killed and brain material was passaged again in mice. Brain smears from most mice which became sick were then tested for the presence of dengue virus antigen by staining with fluorescein-conjugated dengue virus antibody. For the later virus isolations it was found that more rapid and reliable results were obtained by examining stained brain smears from mice killed ten days after injection.

Haemagglutination inhibition (H.I.)

A dengue virus type 2 haemagglutinin for goose erythrocytes was prepared by sucrose-acetone extraction of infected suckling mouse brain (Clarke & Casals, 1958). Sera were treated with acetone to remove nonspecific inhibitors, and with goose red blood cells to remove nonspecific agglutinins. They were tested against 4–8 haemagglutinating doses of antigen in a microtitre system.

A recent survey showed that in 1969 less than 1% of people born since 1948 had serum H.I. antibodies against dengue viruses (Maguire *et al.* 1971). It was therefore possible to investigate the origin and spread of this epidemic by testing sera taken randomly from people in this age group for the presence of dengue virus antibodies. An antibody incidence more than two standard deviations above 1% indicated that dengue virus infections had occurred in the population from which the serum samples were drawn.

Experimental infection of mosquitoes

Laboratory-hatched mosquitoes were infected by intrathoracic injection or by allowing them to feed on viraemic mice, or on a mixture of mouse blood and infected mouse brain through a mouse tail-skin or from a cotton pledget. They were kept at 25° C–30° C for periods up to 23 days and were tested for the presence of virus either by staining salivary gland smears with fluorescein-conjugated dengue virus antibody, or by injecting mosquito extracts i.c. into suckling mice. Brain smears from any mice which became sick were stained with fluorescein-conjugated dengue virus antibody.

RESULTS

The first clinical case of dengue was diagnosed in March 1971 at Lautoka (Fig. 1) and was confirmed by demonstrating an increase in dengue virus antibody during the course of illness and convalescence. Six of 27 sera collected from young people

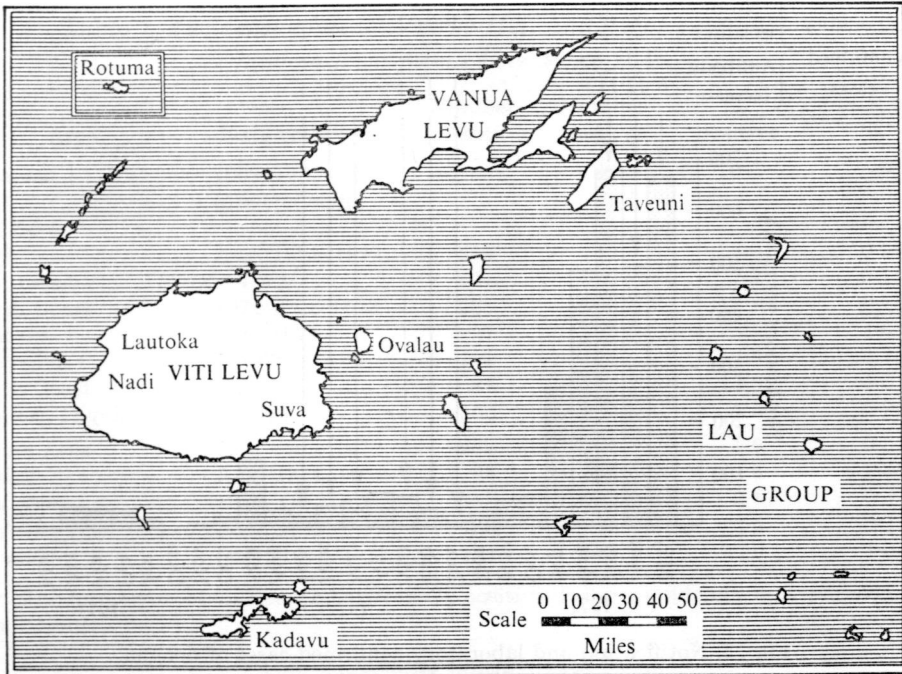


Fig. 1. Map of Fiji Islands. Rotuma is 240 miles NNW of Suva.

at Lautoka in February had HI antibodies to dengue virus, indicating that virus infections had occurred several weeks before the first diagnosed case.

By the end of March a number of other cases had been reported, but no formal notifications were received until May. The incidence of notifications and of laboratory-confirmation by virus isolation and serology is shown in Fig. 2. The number of cases notified remained high until the end of August when they began to decrease steadily to reach a minimum figure of 3 cases in January 1972. Dengue virus was isolated from the blood of one of these three cases. The number of notifications then increased each month to a second peak of 79 cases in April. Cases continued to be notified until April 1973 when the total had reached 3,413. The abrupt increase to 106 dengue notifications in the week ending 2nd September 1972 was probably due to erroneous diagnoses at the beginning of an influenza epidemic.

A substantial proportion of the cases showed the classical dengue fever syndrome but many cases were mild and difficult to differentiate clinically from cases of rubella which were occurring concurrently in 1971. Only three cases showing haemorrhagic manifestations were notified. All were adults. Attempts to isolate virus from the blood of these patients were unsuccessful, and no antibody was detected in their sera.

Seventeen virus isolations were made from blood or serum of acutely ill patients (Fig. 2). In ten cases the virus was shown to be dengue by examining infected mouse brain smears stained with fluorescein-conjugated antibody, and in 13 cases the patient developed dengue virus antibodies during the course of the illness. The H.I. antibody titres were much higher to type 2 than to type 1 virus. Dengue

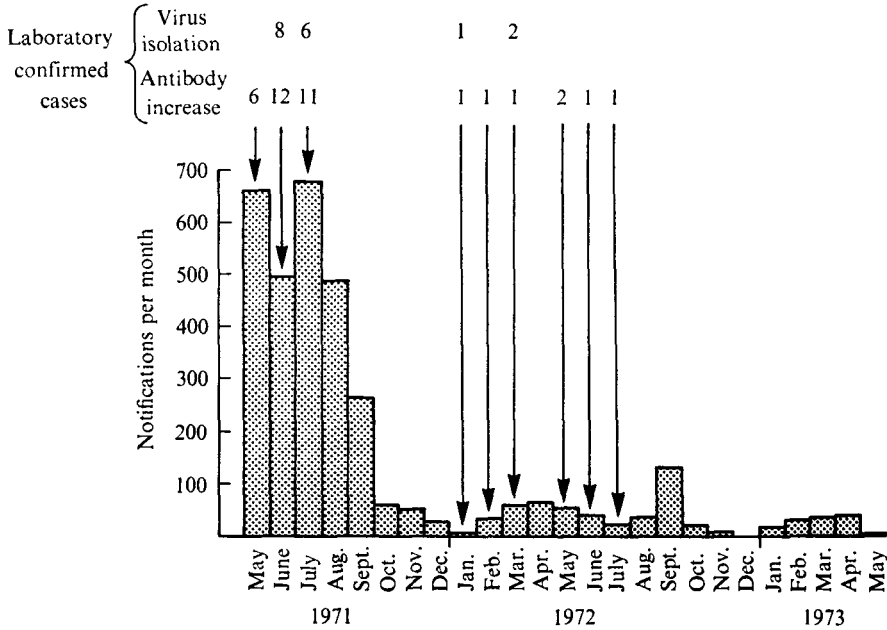


Fig. 2. Notification and laboratory-confirmed cases of dengue. May 1971 to May 1973.

virus infection was diagnosed in 36 other patients from whom no virus was isolated, on the basis of a four-fold or greater increase in H.I. antibody during the course of the illness. Serological studies confirmed by Dr R. L. Doherty of Brisbane and Dr Leon Rosen of Honolulu showed the virus strain to be type 2 dengue.

The virus was readily isolated in suckling mice as it caused illness about 14 days after primary i.c. inoculation. After ten passages in mouse brain the incubation time in mice was reduced to seven days. The virus grew in MK2 cells, the only cell type which has been tested.

Most of the notifications and clinical cases were from the Suva district, but the disease also affected people to varying degrees in other parts of Viti Levu, on the adjacent island of Ovalau, and on the remote island of Rotuma. The results of the survey of sera from people born since 1948 for the presence of dengue virus H.I. antibodies are shown in Table 1. In a number of areas the incidence of antibody positive sera is significantly higher than that prevailing in the age group before this epidemic. This confirms the evidence from notifications that dengue virus was active in all coastal areas in Viti Levu but not in the Western Highlands, and that infections also occurred on Ovalau and Rotuma but not on Vanua Levu or in the Lau Islands, and probably not on Kadavu. Twenty-six cases notified from Vanua Levu were shown serologically to be rubella virus infections.

The distribution of dengue notifications according to age, where information was available, is shown in Table 2. Seventy-three per cent of the notifications were from people over 20 years of age although they comprised less than 43% of the population, and 35.4% of them had dengue virus antibodies before the

Table 1. Incidence of dengue virus H.I. antibody in sera taken at random from people born since 1948

Area	Date collected	Number tested	Number positive	% positive	S.E.D. %*
All areas	1967-1969 (pre-epidemic)	4,886	29	0.6	—
<i>Viti Levu</i>					
Suva	Aug. 1971-1972	204	53	26.0	0.90
East Coast	1972	127	10	7.9	0.79
North Coast	1972-Jan. 1973	260	36	13.8	0.71
Lautoka	Feb. 1971	27	6	22.2	1.62
South West	1972	121	4	3.3	0.75
South Coast	1972	81	11	13.6	1.01
Western Highlands	1972	68	1	1.5	0.95
<i>Vanua Levu</i>					
Jan.-June 1972		259	4	1.5	0.51
<i>Ovalau</i>					
Aug. 1971		86	17	19.8	1.04
<i>Lau group</i>					
1971-1972		455	2	0.4	0.37
<i>Kadavu</i>					
June 1972		120	3	2.5	0.74
<i>Rotuma</i>					
Sept. 1972		191	82	42.9	1.08

* Standard error of difference between % positive for pre-epidemic and post-epidemic populations.

Table 2. Dengue notifications by age*

Age (years)	Percentage of population. (1966 census) [Total 476,727 persons]	Approximate % of age group with dengue virus antibodies before 1970	Number of notifications	Percentage of notifications
0-19	57.2	0.6	390	27
20-39	26.2	21.0	742	51
40+	16.6	54.3	320	22

* No age information was available from 1,961 notifications.

onset of the epidemic. Serological surveys of young people have indicated that in epidemic areas up to 43% of people born since 1948 were infected during the epidemic (Table 1).

Except on Rotuma, dengue occurred only in areas where *Aedes aegypti* was present. A 2½ day search of the most likely *Ae. aegypti* breeding places on Rotuma revealed *Ae. rotumae* as the only *Stegomyia*. Since there is evidence that *Ae. polynesiensis* and *Ae. pseudoscutellaris* had been dengue virus vectors in an earlier epidemic (Maguire *et al.* 1971) experiments were performed to compare the infectivity of an epidemic strain of virus for *Ae. aegypti* and *Ae. pseudoscutellaris*. The results are shown in Table 3. It was found that 40% or more *Ae. aegypti* could be infected by feeding them on blood containing 10^{6.5}LD 50 of dengue virus per ml. but not one of 59 *Ae. pseudoscutellaris* became infected when fed in the same way on a virus preparation containing 10^{6.0} LD 50 per ml. Further experiments with *Ae. aegypti* showed that they could be infected by feeding on viraemic mice in which the amount of dengue virus was less than 10^{0.5}LD 50 per ml. of blood,

Table 3. *Mosquito infection experiments with Fiji dengue virus strain 1070*

Mosquito species	Method of infection	Virus content of material used (log ₁₀ LD 50/ml.)	Days after infection	No. infected/No. tested	Method used to detect virus*
<i>Ae. pseudo-scutellaris</i>	Fed through mouse tail skin	6.0	17	0/32	s.m.i.
<i>Ae. pseudo-scutellaris</i>	Fed on cotton pledget	6.0	20	0/27	s.m.i.
<i>Ae. aegypti</i>	Fed through mouse tail skin	6.5	18	10/23	s.m.i.
<i>Ae. aegypti</i>	Fed on cotton pledget	6.5	18	6/15	s.m.i.
<i>Ae. aegypti</i>	Fed on viraemic mice	< 0.5	23	2/15	s.m.i.
<i>Ae. aegypti</i>	Intrathoracic injection	5.6	20	3/3	f.a.

* s.m.i. = suckling mouse inoculation.

f.a. = fluorescent antibody staining of salivary glands.

and that 20 days after intrathoracic injection dengue virus was concentrated in the salivary glands. Laboratory colonies of *Ae. polynesiensis* and *Ae. rotumae* were not available for infectivity studies.

DISCUSSION

Serological evidence indicates that in Fiji the only arboviruses which have commonly infected man are dengue viruses. The prevalence of antibody in relation to year of birth indicates that dengue virus epidemics have occurred from time to time and that little or no infection has occurred between these epidemics. The last dengue outbreak was in 1943–44 and serological responses of individuals involved in that outbreak strongly suggest that it was due to type 1 dengue virus (Miles *et al.* 1964; Maguire *et al.* 1971).

Dengue recurred in 1971 and, although the disease was first diagnosed in Lautoka in March, serological studies indicated that it had been present for some weeks at that time. The epidemic rapidly built up and reached a peak in June and July. The limited number of notifications in 1972 and 1973 brings the total number notified to 3,413 (Fig. 1).

Although there were many classical dengue cases, there were also very many mild atypical cases, and serological studies show that there were large numbers of subclinical immunizing infections (Table 1). When there was a concurrent rubella epidemic the clinical differentiation of mild dengue from rubella proved difficult, and the beginning of an influenza epidemic led to a sudden rise in dengue notifications. The difficulty of making a differential diagnosis between dengue and other acute febrile infections is well recognized (Clarke & Casals, 1965), and our problems merely emphasize this fact.

Three cases of possible haemorrhagic dengue were reported but it could not be shown that any of them were due to infection with dengue virus. This is in contrast to the 1971 dengue 2 virus epidemic in Tahiti in which a number of cases with haemorrhagic manifestations were observed (Moreau, Rosen, Saugrain & Lagraulet, 1973). However, Tahiti has had three dengue outbreaks since 1960, and Moreau *et al.* (1973) noted that their observations were consistent with the hypothesis that haemorrhagic manifestations due to infection with dengue viruses are the results of a secondary response in a previously sensitized individual. Nevertheless other factors must be involved as no haemorrhagic manifestations were observed by Likosky *et al.* (1973) in a similar situation in Puerto Rico where a dengue type 2 epidemic in 1968–69 followed a dengue type 3 epidemic in 1963.

The age distribution of notified cases was surprising in view of the incidence of dengue virus antibody before the epidemic. Although approximately 57% of the population had been born since the 1943 epidemic, and less than 1% of them had dengue virus antibodies, only 27% of the notifications came from this group. On the other hand more than half the notified cases were in the 20–39 year age group which formed about 26% of the population, and there was serological evidence that 21% had been exposed to dengue viruses before this outbreak. Although the infection rate was higher than indicated by the notifications, due to subclinical infections, the age distribution of notified cases suggests that pre-existing dengue virus antibodies in people born before 1950 gave little protection against infection in this epidemic.

The virus was probably introduced into the country in February either through the port of Lautoka or through the international airport at Nadi, which is only about 20 miles from Lautoka. The origin of the virus is unknown, but during 1971 and 1972 outbreaks of dengue type 2 occurred in Tahiti (Moreau *et al.* 1973), Gilbert and Ellice Islands, New Hebrides, Western Samoa, New Caledonia, Niue and New Britain (Marshall & Hawkes, 1972). After the first case was diagnosed at Lautoka in March the epidemic spread during the next four months to most coastal areas of Viti Levu, to the adjacent island of Ovalau and to Rotuma, 240 miles to the north. Although the normal travel patterns of residents must have introduced dengue virus into all the more accessible localities in Fiji so that all human-biting mosquitoes would have had adequate opportunities of becoming infected in the field, the geographical distribution of the notifications indicates that, except for Rotuma, the disease spread only to areas where *Ae. aegypti* occurs.

Mosquito infectivity experiments showed that the strain of dengue virus responsible for this epidemic could infect *Ae. aegypti* but not *Ae. pseudoscutellaris*. Technical problems prevented testing the infectivity of the virus for the other possible vector mosquito, *Ae. polynesiensis*.

In apparently having only one virus vector, this dengue epidemic differs from previous outbreaks. The distribution of dengue virus antibodies amongst the population in 1969, particularly in Vanua Levu and Taveuni, indicates that in previous outbreaks dengue virus must have been readily transmitted not only by *Ae. aegypti* but also by *Ae. polynesiensis* and *Ae. pseudoscutellaris* (Maguire *et al.* 1971).

In view of the apparent ineffectiveness of type 1 serum antibodies in protecting people against infection with this virus, it is fortunate that the strain was a relatively avirulent one. It caused little serious illness and the subclinical infections stimulated the production of serum antibodies in many people born since the last epidemic. The increasing efficiency of communication between Fiji and areas where dengue viruses are endemic make it unlikely that another 28 years will elapse before the next introduction of a dengue virus into Fiji. As this virus may be more virulent, close surveillance for future outbreaks should be maintained.

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