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Author(s)	Tadano, Masayuki; Okuno, Yoshinobu; Fukunaga, Toshihiko et al.
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SHORT COMMUNICATION

RETROSPECTIVE SEROLOGICAL STUDIES ON DENGUE EPIDEMICS IN OSAKA AND OKINAWA

MASAYUKI TADANO, YOSHINOBU OKUNO, TOSHIHIKO FUKUNAGA and KONOSUKE FUKAI

Department of Preventive Medicine, Research Institute for Microbial Diseases, Osaka University, 3-1, Yamadaoka, Suita, Osaka 565, Japan

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In Japan, dengue epidemics were recorded once before the end of World War II (1942-1945) on the Main Islands and several times (1893-1955) on the Okinawa Islands. Blood samples were obtained from residents in Osaka and Okinawa, and their antibodies were examined by neutralization tests against dengue and Japanese encephalitis viruses. Of 60 serum samples each from Osaka and Okinawa, 11 and 15 sera, respectively, showed positive titers against one or more dengue serotypes. These results confirm that the epidemics had been very large. Moreover, the results showed that the epidemics had been due to dengue type 1 virus in Osaka and to dengue type 1 and 2 viruses in Okinawa.

Several large scale dengue outbreaks have been recorded in this century and one of them occurred in Japan (1942-45). It is considered that World War II contributed to the dengue outbreak in Japan as other large outbreaks were brought about by military exigencies (Schlesinger, 1977). Although there has been only one epidemic on the Main Islands of Japan, there have been more than ten recorded epidemics between 1893 and 1950 on the Okinawa Islands, which are located in a subtropical region.

We obtained sera from aged people in Osaka and Okinawa and examined them serologically. The objects of the present study were to answer the following questions: (1) How large-scale were the epidemics? (2) What type (or

types) of dengue virus was prevalent in the epidemics? (3) Was there any difference in the pattern of antibody rises for different dengue virus serotypes in sera in Osaka and Okinawa? In the present study we titrated neutralizing (N) antibody of test sera because the N test is the most type-specific serological test.

As sera of residents, in Osaka, 60 serum samples (male 30 and female 30) were collected from hospitalized aged patients at Hanwa Senboku Hospital, which is located in the southern part of Osaka Prefecture, and in Okinawa, 60 serum samples which had been obtained from aged people on the Main Islands were kindly supplied from the Department of Parasitology, School of Medicine, University of the Ryukyus.

No histories of the blood donors were given.

The N test was performed by the method of Okuno et al. (1978), in which the focus reduction method using the PAP (peroxidase-antiperoxidase) staining technique is used. The viruses used for the test were dengue viruses

type 1 (DEN-1) Hawaiian strain, type 2 (DEN-2) New Guinea B strain, type 3 (DEN-3) H-87 strain and type 4 (DEN-4) H-241 strain, and Japanese encephalitis (JE) virus, Nakayama strain.

Tables 1 and 2 show the results of N tests

TABLE 1. *Neutralizing (N) antibody titers of aged people in Osaka to dengue viruses*

Serum No.	Sex	Age	N antibody titer (FR50)				
			DV-1	DV-2	DV-3	DV-4	JEV
1	M	61	— ^a	72	15	—	—
16	M	78	70	—	13	—	480
19	M	73	13	—	—	—	850
25	M	71	670	—	—	—	—
29	M	89	1250	12	54	—	240
30	M	76	25	—	—	—	29
32	F	83	78	—	—	—	—
48	F	81	270	10	58	—	—
49	F	69	130	—	—	—	22
50	F	83	22	—	—	—	—
51	F	67	530	16	37	—	—

^a N titer of <10.

TABLE 2. *Neutralizing (N) antibody titers of aged people in Okinawa to dengue viruses*

Serum No.	Sex	Age	N antibody titer (FR50)				
			DV-1	DV-2	DV-2	DV-4	JEV
4	F	62	16	70	— ^a	—	52
34	M	72	50	250	15	72	90
40	M	75	700	—	16	—	330
64	M	68	14	96	15	—	313
67	M	68	120	—	—	—	22
93	F	77	40	25	—	—	60
118	F	64	60	—	—	—	330
144	M	72	165	16	78	—	475
174	M	61	210	28	10	—	150
176	M	61	57	34	10	—	39
204	F	61	400	—	23	—	300
254	M	64	200	12	—	—	46
258	F	60	—	14	—	—	400
316	M	61	240	—	—	—	350
437	M	70	65	84	68	15	64

^a N titer of <10.

on all the serum samples from Osaka and Okinawa which showed a positive N titer against one or more dengue serotypes. Of the 60 samples, 11 (18%) in Osaka and 15 (25%) in Okinawa showed a positive titer against one or more dengue serotype. It was estimated that there was at least 100,000 (Hotta, 1952) or several million (Ura, 1978) cases of dengue fever in the Osaka district, but there is no reliable record of the epidemic in Osaka because of the confusion due to World War II at that time. Although the number of sera examined in the present study was too small to draw a definite conclusion, the high positive rate (18%) of dengue infection seems to confirm the above figures. The positive rate of dengue antibody in sera was higher in Okinawa (25%) than in Osaka, indicating that dengue epidemics had occurred repeatedly in Okinawa, as reported by Ura (1978).

All the sera in Osaka except serum No. 1 showed the highest titer against DEN-1, whereas the sera in Okinawa showed the highest titer against DEN-1 (10/15) or DEN-2 (5/15). Men were dispatched as soldiers to tropical areas during World War II, where they may have been infected with dengue virus. Therefore, results on sera of women probably reflect the features of epidemics more closely.

Consistent with the present results, we report in the accompanying paper that DEN-1 virus was isolated from a patient with dengue fever in Osaka. Moreover, Fujita and Yoshi-

da (1979) found that dengue epidemic in Nagasaki had been due to DEN-1 virus. These observations confirm that DEN-1 was the causative agent for the epidemics that occurred on the Main Islands of Japan.

Although dengue fever is a mild illness and the mortality rate is very low, 470 persons were reported to die of dengue fever in the 1931 epidemic in Okinawa (Ura, 1978). This fact seems to reflect the occurrence of reinfection by a different serotype of dengue virus from that of primary infection, presumably infections with DEN-1 and DEN-2, resulting in increase in severity of the disease. This idea was also suggested by Halstead and Papaevangelou (1980) in a paper on outbreaks of dengue fever in residents of Athens and Piraeus in Greece in 1927-1928, in which both DEN-1 and DEN-2 were transmitted.

Positive titers (≥ 10) for N antibody against JE virus were found in 44 samples (73%) in Osaka and all 60 samples (100%) in Okinawa. Thus Okinawa had been heavily polluted by JE virus.

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