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DENGUE EPIDEMIC IN HONDURAS, 1978-1980[1]

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A serologic survey was conducted in Honduras to determine the extent of the 1978-1980 dengue epidemic in that country. The results indicate that at least 134,000 dengue cases occurred. Though no dengue-related fatalities were confirmed, the epidemic highlights the potential for future problems and the need to maintain Aedes aegypti *control programs in potentially affected regions.*

Introduction

Dengue, a disease caused by group B flavivirus *(1),* has caused serious epidemics in the Caribbean area and in the tropical countries of Asia and Africa. The virus, of which there are four serotypes (dengue 1, dengue 2, dengue 3, and dengue 4), is transmitted by the *Aedes aegypti* mosquito, which also transmits yellow fever; the mosquito *Aedes albopictus* also acts as a dengue vector in Southeast Asia *(2).* Reservoir hosts of the virus are unknown; man is the natural host, although mice and monkeys *(3)* may be artificially infected. In its benign form the disease is characterized by pains in the muscles and joints, which is why in some countries it is known as breakbone fever. In its most severe form, known as dengue hemorrhagic fever, the disease may bring about a hemorrhagic shock syndrome with fatal consequences *(4).*

Over the past 20 years, three major dengue epidemics have occurred in the Caribbean area. The first, which took place in 1963, was caused by dengue 3 and involved Jamaica, Puerto Rico, the Lesser Antilles, and Venezuela *(5).* The second, coming in 1969, was caused by dengue 2 *(6).* It likewise struck Caribbean islands and also spread to Colombia, where in 1972 it caused about half a million cases. The third dengue epidemic, caused by dengue 1, began in February 1977 on Jamaica and came to affect more than 60,000 people on the island. From there it soon spread to other areas—including the Bahamas, Cuba, Puerto Rico, Dominica, Grenada, Suriname, and Venezuela *(7).*

In February 1978 the dengue 1 epidemic entered Central America through the Bay Islands off the Atlantic Coast of Honduras. The virus was probably introduced from Jamaica, since many residents of the islands have relatives on Jamaica, and these related people tend to visit one another, especially around Christmas. Soon after reaching the Bay Islands, this epidemic spread to Honduras, El Salvador, Guatemala, and Mexico.

The most severely affected Honduran city was San Pedro Sula. During the peak of the epidemic, in August 1978, the Epidemiology Department of the Ministry of Public Health estimated that 77,000 cases had occurred in that city *(8).* However, the epidemic also continued to spread throughout the country; and it was largely for that reason that the study reported here was launched—in order to define the spread of the disease and the dengue serotypes in circulation.

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Materials and Methods

Study Groups and Serum Storage

Between October 1978 and January 1980 a sample survey was carried out at each of the country's principal population centers. In each city or town, between 20 and 40 human serum specimens were collected at random, efforts being made to collect them from persons in three different districts and in different age groups. Occasionally a second blood specimen was collected from febrile patients three weeks after the first. In addition, 100 serum specimens from soldiers and prisoners, which had been collected before the dengue epidemic in 1975, were available. These hundred sera and the sera collected from population centers were stored at -20°C until antibody tests were performed. The only exceptions were sera to be used for virus isolation, which were stored at -70°C.

Serologic Tests

Hemagglutination-inhibition (HI) antibodies were detected by the Clarke and Casals method *(9)* adapted to microplates. The serum specimens obtained were tested for antibodies against the following group B flaviviruses: dengue 1, dengue 2, dengue 3, yellow fever, and St. Louis encephalitis.

Virus Isolation

Some serum specimens from febrile patients were sent to the laboratory of the U.S. Centers for Disease Control (CDC) in San Juan, Puerto Rico, for virus isolation by inoculation of *Toxorhynchites amboinensis* mosquitoes *(10)*. In addition, suckling mice were inoculated intracerebrally. These mice were observed for 15 days following their inoculation.

Results

Of the 1,506 serum specimens collected in 34 Honduran cities and towns, 405 (26.9 per cent) were found to contain HI antibodies against dengue 1 at a titer equalling or exceeding 1:40. In 16 of these communities (Table 1), the percentage of positive sera exceeded 20 per cent. All 16 communities, with the exception of Santa Rosa de Copán, are located in hot, low-lying areas; and as Figure 1 shows, a fair number are situated in northern areas.

As Table 2 shows, female subjects yielded a higher percentage of positive sera (30.3 per cent) than did male subjects (21.3 per cent). This difference is statistically significant ($p < 0.001$). Also, the percentage of positive sera increased gradually with age, rising from 21.1 per cent in the 1-14 age group to 39.5 per cent in the group over 59 years of age (Table 3). Most of the serum specimens with antibodies against dengue 1 had titers of between 1:40 and 1:80, the geometric mean being 1:87 (Table 4).

Of the patients reporting dengue-like symptoms (fever, headache, joint pains, petechial rash), 31.2 per cent were found to have anti-dengue 1 antibodies. However, as Table 5 shows, 16.2 per cent of those not reporting dengue-like symptoms also had such antibodies.

The immune response of patients following the dengue attack was verified by testing 11 paired serum specimens collected during the epidemic in Villanueva. Most of the sera obtained three weeks after the acute stage of the disease showed titers of 1:80 to 1:160 (Table 6); one showed a titer of 1:640; and one (from a patient whose acute-stage serum had shown a titer of 1:40) registered a titer greater than 1:1,280.

The first hundred serum specimens found to have antibodies against dengue 1 were also tested against dengue 2, dengue 3, yellow fever, and St. Louis encephalitis. The geometric means of the antibody titers of these sera

Table 1. The percentages of sera with HI antibodies to dengue 1 in 34 Honduran towns and cities, 1978-1979.

Identifying no.	Place	Date of serum collection	No. of sera collected	No. of sera with HI titers ≥1:40	% positive for dengue 1
1	Roatán	7/25/78	165	52	31.5
2	San Pedro Sula	10/14/78	41	25	61.0
3	La Lima	10/14/78	52	2	3.8
4	Puerto Cortés	4/5/79	51	1	2.0
5	San Manuel	7/28/79	30	21	70.0
6	Villanueva	7/31/79	16	13	81.3
7	Santa Rita	6/27/79	37	17	45.9
8	El Progreso	10/14/78	30	11	36.7
9	La Ceiba	3/24/79	55	4	7.2
10	Trujillo	6/28/79	37	14	37.8
11	Tocoa	6/29/79	33	12	36.4
12	Santa Rosa de Copán	7/5/79	31	9	29.0
13	Veracruz	7/4/79	23	3	13.0
14	Dulce Nombre	7/4/79	28	2	7.1
15	Jesús de Otoro	7/10/79	19	1	5.3
16	La Esperanza	7/11/79	62	9	14.5
17	Ocotepeque	11/1/79	46	1	2.2
18	San Marcos de Ocotepeque	10/31/79	71	3	4.2
19	Gracias, Lempira	10/30/79	31	2	6.5
20	Marcala	9/14/79	30	0	0.0
21	La Paz	11/28/79	32	20	62.5
22	Comayagua	11/27/79	15	3	20.0
23	Tegucigalpa	9/7/79	114	12	10.5
24	Talanga	11/11/78	27	14	51.9
25	Guaymaca	10/11/78	11	8	72.7
26	Campamento	4/20/79	31	3	9.7
27	Catacamas	4/19/79	52	2	3.8
28	Juticalpa	12/19/79	37	9	24.3
29	Danlí	6/14/79	43	10	23.3
30	Yuscarán	6/15/79	35	0	0.0
31	Sabanagrande	10/17/78	13	0	0.0
32	Morolíca	7/4/79	20	5	25.0
33	Choluteca	6/7/79	49	4	8.2
34	Nacaome	3/14/79	42	18	42.9

were 1:178 against dengue 1, 1:51 against dengue 2, 1:50 against dengue 3, 1:79 against yellow fever, and 1:55 against St. Louis encephalitis (Figure 2).

Virus was isolated from 10 patients: three from San Pedro Sula; three from Yarumela, an interior town some 10 miles southeast of Comayagua; and four from San Lorenzo, a Pacific Coast town roughly 15 miles northwest of Choluteca. Each of the viruses isolated was identified at the CDC laboratory in San Juan, Puerto Rico, as dengue 1.

Of the hundred serum specimens from prisoners and soldiers in different parts in the country that were collected before the dengue epidemic (1974-75), 11 showed antibodies against dengue 1 at low titers. The geometric means of the antibody titers of these sera were 1:35 against dengue 1 and 1:180 against yellow fever.

Discussion

In 1978 and 1979 dengue affected Hondu-

Figure 1. A map of Honduras showing the towns and cities surveyed. Communities where over 20 per cent of the sera tested positively for HI dengue 1 antibodies are indicated with black circles, those where less than 20 per cent tested positively are indicated with open circles.

Table 2. Distribution of patients with serum antibodies against dengue 1, by sex.[a]

	No. with antibodies	No. without antibodies	Total	% with antibodies
Males	119	439	558	21.3
Females	286	659	945	30.3
Total	405	1,098	1,503	26.9

[a] $X^2 = 14.21$; $p < 0.001$ These data do not include three subjects whose sera were found negative for dengue 1 antibodies but whose sex is unknown.

Table 3. Distribution of subjects with dengue 1 antibodies, by age.[a]

Age (in years)	No. with antibodies	No. without antibodies	Total	% with antibodies
1 – 14	96	359	455	21.1
15 – 34	168	475	643	26.1
35 – 59	101	213	314	32.2
≥ 60	30	46	76	39.5
Total	395	1,093	1,488	26.5

[a] The table does not include data on sera from 18 subjects whose ages were unknown. Ten of these sera were positive for dengue 1 antibodies and eight were negative.

ran communities along the Atlantic and Pacific coasts and in the valleys of the interior, Comayagua, and Juticalpa.

The apparent sequence of these epidemic outbreaks was as follows: Roatán in February 1978, San Pedro Sula in June 1978, Comayagua Valley in August 1978, and Nacaome in December 1978. These outbreaks continued into 1979 and spread to neighboring communities. An outbreak in Danlí was probably responsible for spreading the disease to Nicaragua, since several thousand Nicaraguan refugees fleeing the recent war in that country were present in the area during this outbreak.

It is to be noted that some communities in the departments affected by dengue did not have epidemics, even though their populations were not immune. This was true, for example, of Lima and Puerto Cortés in the Department of Cortés. These circumstances are undoubtedly to be explained by the low *Aedes aegypti* populations present in those places at the time of the epidemic. The same explanation may hold true for the Honduran capital, Tegucigalpa, which was not significantly affected even though some sporadic (mostly imported) cases occurred there. According to the National Malaria Eradication Service *(10)*, the departments at high risk from *Aedes aegypti* infestation in 1978 were Cortés, Santa Barbara, and the Bay Islands, while those at low risk were Francisco Morazán, Atlántida, Choluteca, and Ocotepeque. This information correlates quite well with the data obtained from the serologic survey.

There is no longer any doubt that the epi-

Table 4. Titers of HI antibodies against dengue 1 detected in positive sera from subjects reporting dengue-like symptoms.

Titer	No. of sera	% of sera
1:20	69	17.0
1:40	90	22.2
1:80	131	32.3
1:160	45	11.1
1:320	23	5.6
1:640	23	5.6
1:1,280	8	1.9
1:2,560	14	3.4
1:5,120	2	0.4
Total	405	100.0

Table 6. Increases in HI dengue 1 antibody titers in 11 paired serum specimens collected from subjects with dengue in Villanueva, Cortés Department, in August 1979.

Subject no	Reciprocal HI antibody titers	
	Acute sera[a]	Convalescent sera[a]
1,163	<20	160
1,164	<20	80
1,165	<20	640
1,166	<20	80
1,167	<20	80
1,168	40	>1,280
1,169	<20	160
1,170	20	80
1,172	<20	80
1,173	<20	80
1,175	<20	160

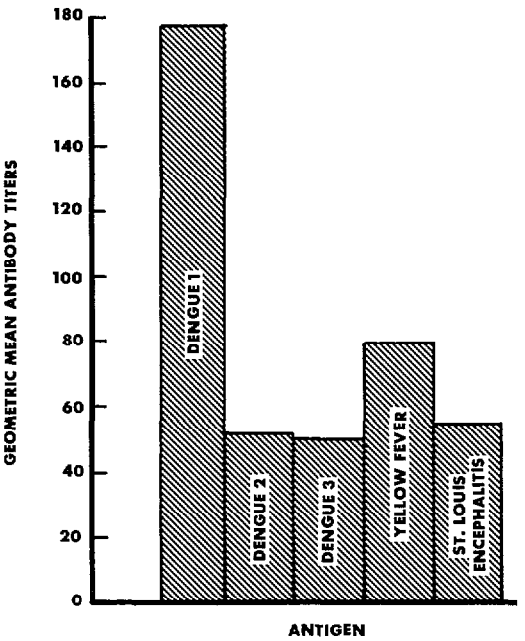
[a]The convalescent serum specimen was collected three weeks after the acute serum specimen

Table 5. Distribution of sera positive for dengue 1 antibodies among subjects reporting dengue-like symptoms and among subjects not reporting such symptoms.

Symptoms reported[a]	No. with antibodies	No. without antibodies	Total	% with antibodies
Yes	334	735	1,069	31.2
No	71	366	437	16.2
Total	405	1,101	1,506	26.9

[a]Typical reported symptoms included fever, headache, joint pains, petechia, and anorexia

Figure 2. The geometric mean HI titers of antibodies against dengue 1, dengue 2, dengue 3, yellow fever, and St. Louis encephalitis viruses in sera obtained from 100 febrile patients.



demic was caused by dengue 1. This was confirmed by the isolation and typing of the virus at the CDC laboratory in San Juan, Puerto Rico. The analysis of antibody titers (Figure 2) also showed that sera positive for dengue 1 tended to react more strongly with that virus than with the other viruses tested.

Overall, the results of the serologic survey, combined with available census data on the localities affected by dengue (Table 7), indicate that at least 134,000 cases of dengue occurred in Honduras. It should be borne in mind that not all the communities affected by the epidemic were surveyed, and in some places the survey was carried out while the outbreak was at its peak rather than afterwards, so that conditions were not ideal for finding the maximum number of positive reactors. This suggests that the actual number of cases could have been slightly higher than the estimated number.

The symptoms of dengue in Honduras, as reported by Romero et al. *(12),* have been confirmed by the authors of this study. These symptoms included headache, fever, anorexia, postorbital pain, joint pains, and muscle pains (especially in the lumbar region). Petechia, pruritis, abdominal pain, and vomiting were observed less frequently. Respiratory symptoms were rare. However, in San Pedro Sula (where doctors reported influenza-like illness) and in other areas (where malaria is endemic) the dengue epidemic may have coincided with another febrile disease outbreak, since 68.8 per cent of the persons reporting dengue symptoms had no antibodies against the disease (Table 5).

Dengue was found to attack females preferentially (see Table 2), perhaps because women who stay at home are more likely to be within reach of domestic *A. aegypti* mosquitoes.

The fact that the percentages of positive reactors increased progressively with age appears to indicate that the risk of exposure to dengue was greater in the older age groups.

The finding that some people had low dengue 1 antibody titers before the 1979 epidemic is probably due to a cross-reaction between yellow fever antibodies in their sera and the dengue 1 antigen tested. This is especially likely because a vaccination campaign against yellow fever was carried out in Honduras in 1952-1954, and also because the antibody titers of the dengue 1 positive sera were higher against yellow fever than against dengue.

Five deaths from the hemorrhagic form of dengue were reported in San Pedro Sula during the epidemic *(8).* Unfortunately, neither virus isolation nor serologic confirmation was attempted, so it cannot be stated positively that these deaths were due to dengue.

In 1980 the number of reported cases of dengue fell sharply. The Ministry of Health of Honduras carried out a malathion fumigation campaign in the principal cities of the country for the purpose of reducing the *Aedes aegypti* population, and this may have affected the course of the epidemic. In any case, the data reported here support the conclusion that

Table 7. Estimated numbers of dengue cases occurring in 15 Honduran towns and cities during the dengue 1 epidemic, as indicated by the results of the serologic survey.

Locale	Estimated population (1974 census)	% of collected sera with dengue 1 antibodies	Estimated no. of cases
Roatán	4,900	31.5	1,500
San Pedro Sula	151,000	60.9	91,900
San Manuel	2,000	70.0	1,400
Villanueva	6,300	81.0	5,000
Santa Rita	5,300	45.9	2,400
El Progreso	28,000	36.6	10,200
Trujillo	4,000	37.8	1,500
Santa Rosa de Copán	12,000	29.0	3,500
La Paz	6,800	62.5	4,200
Talanga	5,000	51.8	2,600
Guaymaca	3,000	72.7	2,200
Juticalpa	10,000	24.3	2,400
Danlí	10,800	23.2	2,500
Morolíca	800	25.0	200
Nacaome	6,000	42.8	2,500
Total	255,900	52.4	134,000

Honduras was struck by a widespread dengue 1 epidemic that affected at least 5 per cent of the population. The communities along the coast and in the interior valleys were most affected. Adults were infected more frequently than children and women more frequently than men. No deaths due to dengue were confirmed, but the resulting loss of working days and cost of drugs were considerable.

All in all, this dengue epidemic points up the need to maintain *Aedes aegypti* control programs. As is well-known, in 1947 the Pan American Sanitary Bureau launched a program to eradicate *Aedes aegypti* from the Americas. The Central American countries joined in this effort, and by 1965 several countries including Honduras had been declared free of the mosquito *(11)*. However, because of technical and administrative problems (especially lack of funds) the maintenance programs could not be sustained, and the mosquito was reintroduced. As a result, we have had a dengue epidemic and face the prospect that introduction of a new dengue serotype could cause hemorrhagic fever cases, as happened on Cuba in 1981. Conditions are also ripe for a devastating epidemic of yellow fever, should that virus be introduced into the region.

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SUMMARY

A serologic survey was carried out in the principal population centers of Honduras to determine the extent of the dengue epidemic that affected the country in the period 1978-1980. A total of 1,506 serum specimens collected in 34 towns and communities were studied. The results confirm that the most affected areas were the departments of Cortés, the Bay Islands, Colón, and Valle, together with some additional communities along the country's principal highway. Virus isolations and antibody titers of human sera demonstrated that the responsible virus was dengue 1. The most commonly reported disease symptoms were fever and joint pains. No dengue-related deaths or cases of dengue hemorrhagic fever resulting from this epidemic have been confirmed. However, the outbreak (together with the recent Cuban experience involving hemorrhagic cases) highlights the possibility of future hemorrhagic cases and the need to maintain *Aedes aegypti* control programs in potentially affected regions.

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