

# First Documented Outbreak of Dengue in the Peruvian Amazon Region<sup>1</sup>

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*This article describes a classical dengue outbreak caused by dengue serotypes 1 and 4 that occurred from March to July 1990 in the city of Iquitos and surrounding areas of Loreto Department in the Peruvian Amazon. Epidemiologic data indicate that more than 150,000 persons may have been affected in Iquitos alone. Another dengue outbreak occurred in Tarapoto, a city in the neighboring department of San Martín. Laboratory data indicate that the same dengue serotypes were involved in both outbreaks. No cases of dengue hemorrhagic fever/shock syndrome appear to have occurred. Prior to this outbreak, no indigenous dengue cases had been documented in Peru.*

Dengue virus has circulated throughout Central America and the northern portions of South America for at least two decades. In Colombia, Venezuela, and Suriname, illnesses caused by dengue vi-

ruses 1, 2, and 4 have been documented; and cases of dengue 2 and 4 have been reported in French Guiana (1). More recently, outbreaks have occurred further to the south and east. Major outbreaks of classical dengue associated with dengue 1 were recorded in Bolivia, Ecuador, and Paraguay (1); and others associated with dengue 1 and 4 occurred in Brazil during the 1980s (2). The first outbreak of dengue hemorrhagic fever/shock syndrome in the Americas, caused by dengue 2, occurred in 1981 in Cuba (3), underscoring the need for more effective surveillance.

With respect to the situation in Peru, as of 1958 the dengue vector mosquito *Aedes aegypti* was considered eradicated throughout the country (4). However, in October 1984 the mosquito was detected anew by Ministry of Health officials in Iquitos, the largest city in the northeast portion of the Peruvian Amazon (see Figure 1). Thereafter, rapidly increasing *Ae. aegypti* counts were documented by Ministry of Health officials—so that whereas in 1985 only 1% of the households were found to be infested, by 1988 this mos-

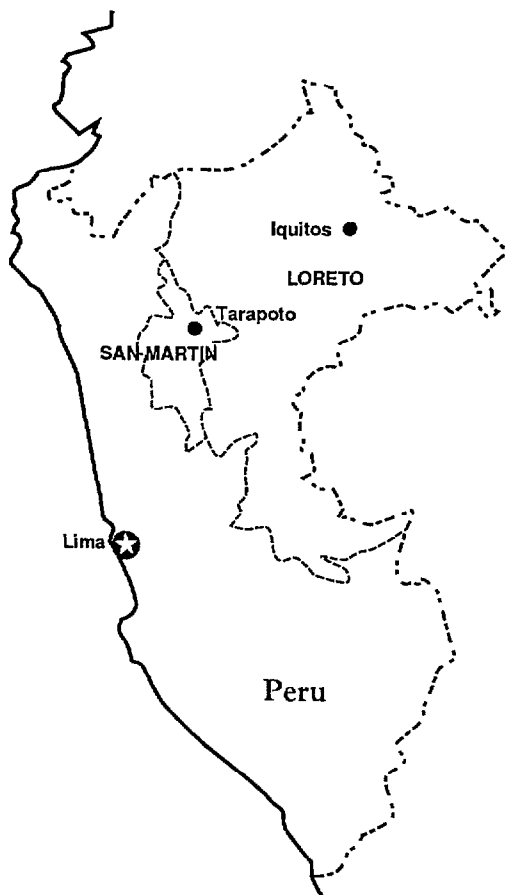
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**Figure 1.** A map of Peru showing the locations of Iquitos and Tarapoto.

quito species was found in 26% of the homes examined.

Prior to the outbreak described here, indigenous cases of dengue had not been reported in Peru. Moreover, a random selection of human sera collected from the country's coastal, mountain, and jungle areas in 1985–1987 showed that only two individuals out of 1,015 (0.20%) had antibodies to dengue; both had low titers to dengue 1.

The first cases of the epidemic reported here appeared among residents of Yavari Avenue in Iquitos near the end of March 1990. The major clinical features of the

disease included fever, osteomuscular pain, and rash.

## MATERIALS AND METHODS

### Clinical Description and Course of the Illness

From the outset, the facilities of the Naval Medical Research Institute Detachment (NAMRID) at the Centro Médico Naval (Naval Medical Center—NMC) became the central reference point for special study and laboratory confirmation of dengue-like illness. One of us (EC) examined all patients presenting at the NMC. Most of these patients were referred by physicians from throughout the city, but many others appeared of their own volition. Both civilians and military personnel were examined at the NMC; no one was turned away. Examination of dengue-like cases and confirmatory diagnostic laboratory tests were conducted free of charge on an outpatient basis.

After the initial cases appeared, a working case definition was developed at the NMC to facilitate rapid and accurate assessment of the epidemic. Three major criteria (fever, headache, and osteomuscular pain) and various minor criteria (rash, ocular pain, cervical adenopathy, etc.) were considered in determining cases. A "case" was identified as any illness meeting at least two of the major criteria and one minor one.

### Virology and Serology

Acute-phase blood samples were collected at the NMC from patients whose illness fit the case description of dengue. A portion of whole blood was immediately placed in a cryotube and frozen in dry ice for transport. In addition, serum was separated from clotted blood, stored at  $-70^{\circ}\text{C}$ , and then transferred on dry

ice to our central (NAMRID) laboratory in Lima.

In an effort to isolate the virus, portions of the frozen blood samples were inoculated into a mammalian cell line (Vero 76, African Green Monkey Kidney) and a mosquito cell line (Clone C6/36, *Aedes albopictus*). One passage was made from cultures that showed no cytopathology after 14 days of incubation.

In addition, mosquitoes trapped using standard human and animal bait methods from various locations in Iquitos during the first two weeks of the epidemic were cultured for viruses using the same types of cell lines. The trapped mosquitoes employed for this purpose consisted of 20 pools containing 20 to 25 female mosquitoes per pool.

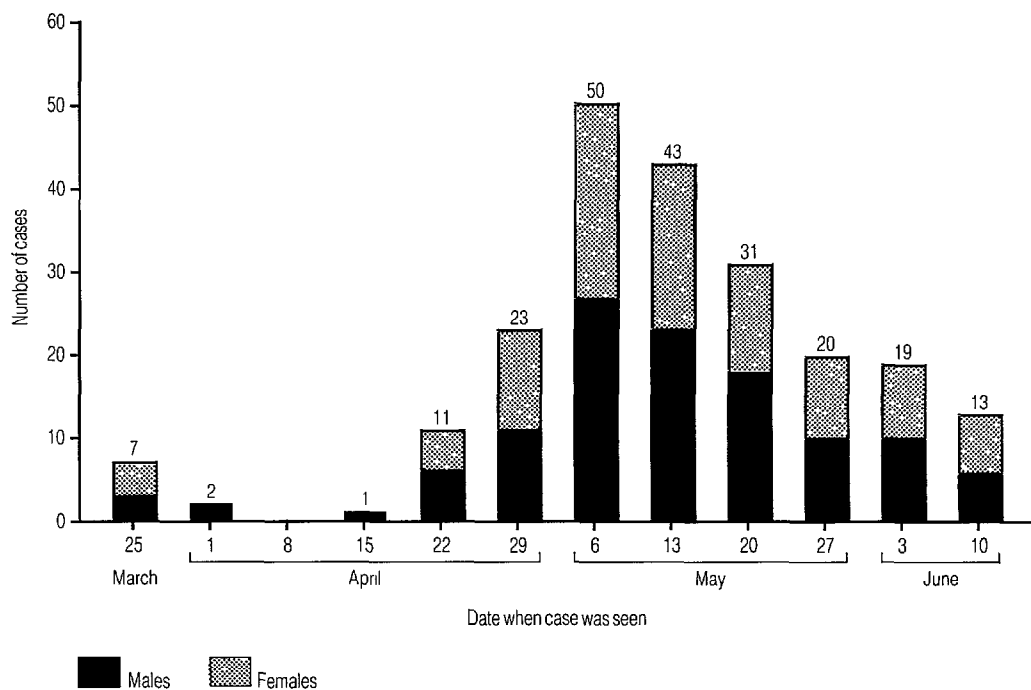
Acute and convalescent sera were obtained from 183 acutely ill patients examined at the NMC. The paired sera were

tested using both indirect fluorescent antibody (IFA) and hemagglutination inhibition (HI) methods (5).

## RESULTS

Of the patients examined at the NMC, a total of 220 with dates of illness between 25 March and 15 June fit the dengue case description (Figure 2). Of the 217 patients for whom clinical data were available, 116 (53%) were males. A majority of the patients were seen during the first two weeks of May. Most complained of mild to severe "muscle and bone aches and pains" and were bedridden for three to five days. The frequencies of various signs and symptoms exhibited by these cases seen at the NMC are shown in Table 1.

Two methods were used to calculate attack rates during the outbreak. One was



**Figure 2.** Patients examined at the Naval Medical Center in Iquitos who were diagnosed clinically as having dengue, by the date when each case was first seen by the NAMRID physician. The numbers shown include three patients for whom clinical data were not available.

**Table 1.** Signs and symptoms of patients meeting the clinical diagnosis for dengue who were examined at the Naval Medical Center, Iquitos (N = 217, except where noted).

Signs/symptoms	No.	%
Fever	207	95.4
Headache	199	91.7
Malaise	177	81.6
Myalgia	173	79.7
Low back pain	170	78.3
Arthralgia	168	77.4
Chills	167	77.0
Anorexia	149	68.7
Nausea	110	50.7
Dizziness	80	36.9
Adenopathy <sup>a</sup>	54	33.5
Ocular pain	63	29.0
Pruritus	43	19.8
Asthenia	43	19.8
Altered taste	40	18.4
Dermal rash	27	12.4
Bleeding gums	14	6.5
Epistaxis	6	2.8
Heavy menstrual flow <sup>b</sup>	5	5.0

<sup>a</sup>No. of patients examined = 161.

<sup>b</sup>No. of patients examined = 101

based on interviews of patients with dengue who were seen at the NMC. Results referred to as "interfamily case rates" were obtained by asking each patient for information about the number of members living in his or her dwelling and the number of such members who had suffered an illness similar to the patient's. Eighty-two patients were interviewed during the month of May, at the height of the epidemic, and the information they provided indicated an interfamily case rate of around 44.3%.

A more conventional method, a household survey, was also employed to estimate the attack rate. This entailed interviewing members of households selected by means of a grid system encompassing the residential neighborhoods of Iquitos. The survey, conducted on 18 May 1990 with assistance from students of the Medical School of the Amazonian University (Facultad de Medicina de la Universidad Amazónica), included more than

450 house-to-house interviews. The data gathered revealed that 10% of the individuals interviewed had had a febrile illness on the day of the interviews and another 15% had experienced febrile illness within the 60 days preceding the survey. Since Iquitos' current population is approximately 305,000, these data suggest that about 76,000 individuals may have experienced the disease at a point roughly halfway through the epidemic.

The mean age of those who sought attention at the NMC was 30.6 years. Children under 12 years old were seldom affected, or were affected less adversely than adults and hence did not seek medical attention. Most people who sought medical attention reported a mild to moderately severe illness sufficiently pronounced to cause absenteeism from work or school for three to five days. No crises involving dengue hemorrhagic fever/shock syndrome were documented. One death was reported; its possible association with dengue virus remains to be determined.

Viral isolates were recovered from 93 blood samples collected from acutely ill patients during the middle and late phases of the outbreak. IFA tests found that 79 of the isolates belonged to the dengue 1 serotype and 12 belonged to the dengue 4 serotype. The other two isolates were found to belong to the alphavirus group.

Five of the 20 pools of mosquitoes trapped in or near the city of Iquitos during the early stages of the outbreak yielded dengue 1 virus. However, only two of the five pools were composed of *Aedes aegypti*; the remaining three pools consisted of *Culex amazonensis*, *Aedeomyia scuamipennis*, and *Trichoprosopon digitatum*.

Of the 183 paired (acute and convalescent) sera tested by HI, 151 (83%) exhibited a fourfold or greater increase in the level of antibodies against dengue serotypes 1, 2, and 4. In addition, 17 other paired sera yielded dengue antibody ti-

ters of 1:40 or greater, but no rise between the acute and convalescent samples was documented. This brought the number of HI-positive sera to 168.

Another test, IgM antibody capture enzyme immunoassay (MACEIA), found that sera from 136 (81%) of the 168 HI-positive patients had IgM antibody to dengue antigens. No such IgM antibody was detected in the remaining 32 individuals.

## DISCUSSION AND CONCLUSIONS

Virologic cultures and serologic data have confirmed that a classical dengue outbreak caused by dengue 1 and dengue 4 viruses occurred from March to July 1990 in Iquitos and surrounding areas of Loreto Province in the Peruvian Amazon. Before this outbreak, no autochthonous dengue cases had been documented in Peru.

The outbreak was large. A survey performed at the height of the epidemic revealed that some 76,000 people, approximately 25% of the city's population, may have been infected. Since the epidemic curve was roughly symmetrical, some 152,000 symptomatic cases may have occurred. A post-outbreak serologic survey has yet to be carried out, and so the total number of infected persons cannot be estimated accurately. Assessment of inter-family case rates reported by dengue patients suggests that on the average, among families who experienced the disease, roughly 44% of the people living in the household were affected.

Another confirmed dengue focus occurred in Tarapoto, a population center in San Martín Department adjoining Loreto (see Figure 1). The Tarapoto outbreak, which began in the second week of April 1990, was smaller than the Iquitos outbreak. Laboratory data, not presented here, indicate that the same den-

gue serotypes were involved. Of four febrile illness cases leading to death during the Tarapoto outbreak, three were unequivocally diagnosed as cases of yellow fever. The fourth case yielded IgG and IgM antibody titers of 1:40 and 1:80, respectively, to dengue 4 in the acute blood sample and was nonreactive to the other dengue serotypes. Autopsy and other laboratory tests were not available, and so the cause of death could not be determined.

While mosquito species other than *Ae. aegypti* were found to contain dengue virus, there is no evidence that those species were actually involved in disease transmission. Two other possibilities exist: One or more mosquitoes of the other three species may in fact have taken blood meals from infected people without being involved directly in disease transmission, or body parts of infected *Ae. aegypti* mosquitoes may have inadvertently contaminated the other three species during the collection process.

Control measures were greatly handicapped by a strike of federal government medical workers, and emergency measures directed at reducing mosquito infestations were hampered by the limited availability of equipment for spraying insecticides. Public service announcements about the outbreak were made by means of posters and handbills posted throughout Iquitos and also through local radio and television broadcasts. These announcements instructed the population about various public health measures, including practices to prevent mosquito breeding. The effect of these actions is unknown.

Immune enhancement following sensitization of hosts to prior dengue infection is believed to offer a possible mechanism for hemorrhagic complications produced by the virus (6). In Cuba's large dengue 2 outbreak of 1981 there were 24,000 cases of dengue hemorrhagic fe-

ver, 10,000 cases of dengue shock syndrome, and 158 deaths. This outbreak occurred four years after the introduction of dengue 1 virus into the Caribbean (1). The possibility that other dengue serotypes may soon reach Peru, perhaps causing dengue outbreaks with hemorrhagic manifestations, shock, and high rates of mortality, must be kept in mind.

A nationwide dengue surveillance and control program is essential in order to reduce response time and minimize morbidity and mortality. The following are critical elements for such a program:

1. *Mosquito surveillance.* The distribution of *Ae. aegypti* must be determined in all regions of the country, especially in the jungle areas. The status of *Ae. albopictus*, a second very efficient vector already present in Brazil (1), should also be determined, because this vector could easily be introduced via air and commercial Amazon River traffic.

2. *Mosquito control.* In the absence of a vaccine and effective antimicrobials, mosquito control measures must become the backbone of the program. In areas where the mosquito vector(s) are documented, a campaign to achieve their rapid reduction must be instituted. This campaign should make use of thoroughgoing public information measures including radio, television, and newspaper announcements that discuss the disease and what must be done to eliminate the mosquito.

The program must emphasize that mosquito control is a responsibility of everyone in the community, not just of those in government. Entire families must be educated and encouraged to become involved in vector elimination. Special drives must be carried out to eliminate open cans and other receptacles that may hold water and to apply insecticides, including larvacides, that have proved effective in mosquito control.

3. *Contingency planning.* Physicians, paramedical personnel, and health officials must be organized and made aware of the potential for further outbreaks, and a system of rapid reporting (7) should be established. When an outbreak is suspected, the first step should be to identify the disease foci so that efficient use of critical supplies and attention can be provided to the control program.

In addition, a plan should be developed for handling large numbers of cases should an outbreak occur. This plan must include details covering special contingencies, such as hospitalization and management of severely ill patients.

Samples of blood taken during the acute phase of the illness, as well as acute and convalescent sera, must be obtained and shipped frozen to the proper laboratories for culture and serologic studies. In case of death, heart blood and liver and kidney biopsy specimens should be obtained for special studies.

In sum, the probability that other, perhaps more devastating, dengue epidemics will occur in Peru and other countries where dengue has been documented must be accepted. Only then can careful and conscientious preparations be carried out.

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### *New Chemical Safety Group*

An international group of government-designated experts is to be set up to improve chemical safety. The group, an intergovernmental forum, will work closely with international organizations, industries, trade unions, and consumers to promote comprehensive guidelines on the safe handling of toxic chemicals at all stages, from production to disposal.

The concept of the forum was developed by the International Program on Chemical Safety (IPCS), which was launched in 1980 by the World Health Organization, the United Nations Environmental Program, and the International Labor Organization and whose main work so far has been evaluation of the health and environmental risks associated with some of the 100,000 chemicals in widespread use around the world. In December 1991, an intergovernmental meeting in London endorsed recommendations by specialists from more than 70 countries for the establishment of the forum within the following 12 months. In May 1992, the 45th World Health Assembly also strongly supported the forum and called for an expanded role for the IPCS as well as strengthening of national and international safeguards in the management of toxic chemicals. Plans for the group were finalized at the United Nations Conference on Environment and Development, held in Rio de Janeiro from 3 to 14 June 1992.

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Source: World Health Organization, Press Release WHO/43, 19 June 1992.