

## DENGUE ACTIVITY IN PUERTO RICO DURING AN INTEREPIDEMIC PERIOD (1995–1997)

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**Abstract.** From 1995 to 1997 dengue was reported in Puerto Rico at an average annual rate of 1.75/1,000 population, compared to 6.73 in 1994, an epidemic year. Dengue virus serotypes 1 (DEN-1), -2, and -4 were isolated each year, with DEN-2 predominating in 1995 and 1996, and DEN-4 in 1997. From 1995 through 1997 incidence was highest (0.61–0.77/1,000) in persons under 30 years of age; males and females were equally affected. Among positive cases, 28.3% to 37.9% were hospitalized; 28.9% to 35.2% had hemorrhagic manifestations; at least 1.1% to 1.6% fulfilled the criteria for dengue hemorrhagic fever/dengue shock syndrome; and 0.2% to 0.3% died. Neither hurricane preparations (1995) nor widespread floods (1996) seem to have affected dengue incidence. Most municipalities with the highest laboratory-diagnosed dengue rates in 1995 were in the eastern foothills of the central mountains, an area relatively spared by the 1994 epidemic. In the next two years, at least half of the municipalities with the highest laboratory-diagnosed dengue rates were in the west. The most intense municipal outbreak of this period (DEN-2, Villalba, 1995, rate of 11.67/1,000) is described to highlight the importance of local conditions and epidemiologic history in determining the risk of dengue.

### INTRODUCTION

Dengue is an acute febrile disease caused by one of four closely related dengue virus serotypes: dengue 1 (DEN-1), DEN-2, DEN-3, and DEN-4. The principal vector of dengue viruses is the urban mosquito *Aedes aegypti*, which has a worldwide distribution in the tropics. In Puerto Rico, as in most tropical areas in the world, dengue is endemic and intermittently epidemic. A clinical diagnosis of dengue fever is reasonable for an acute febrile illness with two or more of the typical manifestations (headache, retroorbital pain, myalgias, arthralgias, rash, hemorrhagic manifestations) in a person who has recently lived in, or recently traveled to a tropical area.<sup>1</sup> Most dengue infections result in relatively mild illness, but many will also cause biochemical evidence of hepatocellular damage, and some can produce more severe disease and shock—dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS).

From June 1994 through March 1995, Puerto Rico experienced the most severe dengue epidemic on record for the island, with DEN-2 as the predominant serotype.<sup>2</sup> Another epidemic, with DEN-4 and DEN-1 predominating, occurred in 1998.<sup>3</sup> Dengue transmission patterns are usually discussed in the context of outbreaks. This article describes the frequency and distribution of dengue in Puerto Rico in an interepidemic period, from 1995 to 1997, including a localized outbreak in the municipality of Villalba in 1995. The bursts of disease activity in different areas from year to year, at a time of relatively low-to-moderate endemic transmission, help clarify the persistence and diffusion of disease throughout time, and highlight the importance of continued laboratory-based surveillance after epidemics.

### METHODS

**Surveillance.** The dengue surveillance system maintained by the Puerto Rico Department of Health (PRDH) and the Dengue Branch, Centers for Disease Control and Prevention (CDC), receives blood specimens from government clinics, public and private hospitals, laboratories, and physicians' of-

fices throughout Puerto Rico. These specimens are sent directly to the Dengue Branch, or collected locally and delivered by PRDH personnel. To evaluate the clinical severity of reported cases, the case investigation form that accompanies samples includes questions on whether the patient had any hemorrhagic manifestations or was hospitalized. Infection control nurses (ICNs) at public and private hospitals throughout the island (the Puerto Rico Association of Epidemiologists) voluntarily provide more extensive clinical information on inpatients with suspected dengue, and the Demographic Registry of Puerto Rico provides copies of all death certificates that mention dengue as a cause of death.

According to the Pan American Health Organization (PAHO), a case of DHF must fulfill all of the following criteria: fever (or recent history of acute fever), any hemorrhagic manifestation, thrombocytopenia ( $\leq 100,000/\text{mm}^3$ ), and objective evidence of increased capillary permeability (e.g., hemoconcentration [hematocrit increased by  $\geq 20\%$ ], pleural effusion [by chest radiography or other imaging method], or hypoproteinemia). A case of DSS must meet all these criteria plus hypotension or narrow pulse pressure ( $\leq 20$  mm Hg).<sup>1</sup>

**Laboratory.** Serum specimens collected less than 6 days after the onset of illness were either processed for virus isolation in C6/36 mosquito cell cultures or inoculated into *Toxorhynchites amboinensis* mosquitoes. Dengue viruses were identified by the use of serotype-specific monoclonal antibodies in an indirect fluorescent antibody test on virus-infected cell cultures or tissues from inoculated mosquitoes.<sup>4,5</sup> Serum specimens collected 6 or more days after onset of symptoms were tested for anti-dengue immunoglobulin M (IgM) by the IgM antibody-capture enzyme-linked immunosorbent assay (MAC-ELISA).<sup>6</sup> IgG antibody determinations were made using an IgG-ELISA.<sup>7</sup> Because the measurement of IgM antibody may fail to diagnose about 5% of secondary dengue infections,<sup>8</sup> specimens with borderline results by MAC-ELISA were tested by IgG-ELISA in an attempt to confirm the diagnosis by detecting an anamnestic anti-dengue antibody response.

A reported case of dengue was defined as a person with

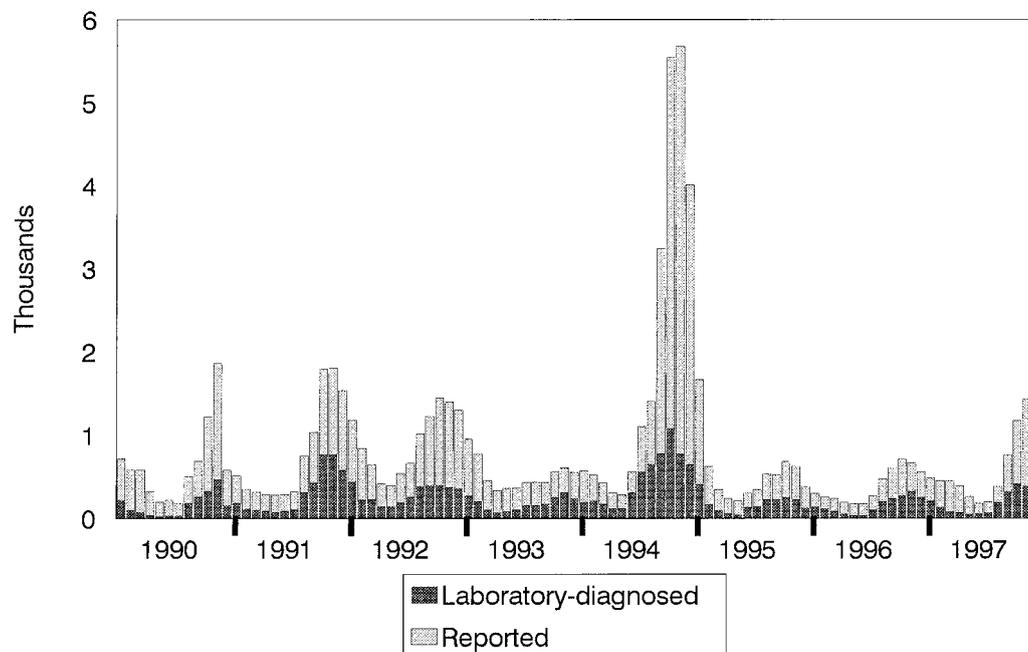


FIGURE 1. Laboratory-diagnosed and reported dengue cases by month, Puerto Rico, 1990–1997.

any illness diagnosed as dengue by a healthcare professional and reported to health authorities. Laboratory confirmation of a current dengue infection was based on one of the following criteria: 1) dengue virus isolation from serum or autopsy tissue samples; 2) seroconversion from negative to positive, or a four-fold or greater change, in anti-dengue antibody titers in paired serum samples; or 3) demonstration of dengue virus antigen in autopsy tissue samples by immunofluorescence or immunocytochemical analysis.<sup>9,10</sup>

Probable dengue cases were those individuals from whom a single serum sample was submitted, and which was IgM positive or had an antibody titer by IgG-ELISA  $\geq 163,840$ . These cases were considered only probable because the persons might have had dengue in the past 3 months (IgM may be present for 90 days or longer), and the symptoms at the time of blood collection might have been due to an illness other than dengue.<sup>7</sup> Unless otherwise stated, probable and confirmed cases are considered together in this publication as laboratory-diagnosed or laboratory-positive cases. In specimens collected 6 or more days after onset of symptoms, the absence of IgM ruled out the diagnosis of dengue, and the case was considered negative. From September 1, 1994 to March 31, 1995, priority was given to samples from more severely ill patients, or from municipalities where an increase in incidence had not been previously detected. Samples not processed because of the laboratory testing priority criteria applied during the epidemic, and single specimens negative for virus and for IgM (if collected 5 or fewer days from onset of illness) were considered non-diagnostic, and the case was categorized as indeterminate. The diagnoses of *Leptospira* infection were made possible by a study carried out after widespread flooding in 1996.<sup>11</sup>

Surveillance information is presented by date of onset of symptoms and municipality of residence of the patient. In the municipality of Villalba, there are eight barrios (municipal subdivisions) as defined by the 1990 census. Each pa-

tient in our analysis was assigned to a barrio according to the residential address provided in the case report form received at CDC. The Puerto Rico Planning Board population estimates for July 1990 were used in calculating rates for the island and its municipalities, and the 1990 US Census population figures were used in calculating rates for the Villalba barrios.

#### RESULTS

**Puerto Rico, 1995–1997.** The average annual rate of reported dengue in Puerto Rico (population 3.5 million) from 1990 to 1993 was 2.64/1,000. Dengue typically had a low season from April through July, and substantially increased in August (Figure 1). After the large epidemic of 1994–95 (23,693 reported cases in calendar year 1994, rate 6.73/1,000 inhabitants), the average annual number of reported cases of dengue in Puerto Rico decreased markedly (Table 1) to 1.75/1,000 during 1995 to 1997. In 1995, low-level disease activity was short-lived (April and May). Cases increased again in June and peaked in October. Dengue activity in 1996 and 1997 returned to the seasonal pattern seen in the years before the epidemic.

Hurricanes Luis and Marilyn passed just north of Puerto Rico on September 6 and 15, 1995, and were preceded by short periods of intense preparation by island residents (e.g., disposal of loose objects in patios and homes), followed by several rainy days. Hurricane Hortense made landfall on September 10, 1996, causing widespread, severe flooding. The epidemic curve by date of onset of symptoms (Figure 1) shows no alteration in the trend of monthly reports for either of those years.

Laboratory-diagnosed cases were documented in all age groups during the 3 years from 1995 through 1997 (Tables 2 and 3). Almost two-thirds of these cases were in persons under 30 years of age. This segment of the population also

TABLE 1  
Reports of suspected dengue cases by year of onset of disease Puerto Rico, 1995–1997

	1995	1996	1997
Total reported cases	6,491	4,645	7,393
Incidence rate per 1,000 population	1.84	1.32	2.10
Laboratory diagnosis			
Positive	2,098 (32%)	1,862 (40%)	2,372 (32%)
Indeterminate	3,761 (58%)	2,218 (48%)	4,200 (57%)
Negative	632 (10%)	565 (12%)	821 (11%)
Hospitalized	1,556 (24%)	1,492 (32%)	2,301 (31%)
Laboratory positive	594	705	780
With hemorrhage	1,578 (24%)	1,334 (29%)	2,027 (28%)
Laboratory positive	607	645	834
DHF and DSS	45 and 3	66 and 3	65 and 5
Laboratory positive	23 and 0	29 and 0	29 and 2
Fatal suspected dengue	23	19	21
Laboratory positive	4	5	7

DHF = dengue hemorrhagic fever; DSS = dengue shock syndrome.

had the highest incidence of laboratory-diagnosed dengue for the 3 years (near 0.70/1,000). About two-thirds of dengue virus isolates was also obtained each year from persons under 30 years of age. Three dengue serotypes were isolated in this period. DEN-2 predominated in 1995 and 1996, followed by DEN-1 in 1995, and DEN-4 in 1996. In 1997, the predominant serotype was DEN-4, followed by DEN-1. The distribution of serotypes by municipality by year is presented in Figure 2. From 1995 to 1997, all three serotypes circulated in the contiguous municipalities of San Juan and Bayamón. The majority of large cities, as well as the smaller municipalities with the highest rates of laboratory-diagnosed dengue, yielded two or three serotypes.

An analysis of monthly dengue incidence by administrative region of the PRDH (Figure 3) shows an early increase in 1995 in the Ponce (southern) region, owing to an outbreak in the municipality of Villalba. While incidence decreased there in September, it peaked in the only two other regions of the island that also had elevated dengue incidence in 1995 (Caguas, east-central, and Aguadilla, in the northwest). In June 1996, the first region to demonstrate an increase in dengue reporting was Aguadilla (it had the highest regional incidence for 1996), followed by increases in July in the other two regions of the island (Ponce to the south, and Mayagüez to the west) with high dengue incidence in 1996. In July of 1997, incidence increased simultaneously in Aguadilla (again the highest regional incidence for the year), Mayagüez (second highest regional incidence for 1997), and the Fajardo region (east).

Analysis at a smaller geographic level (municipality) shows the broad coverage of the surveillance system and the dispersion of disease, with almost every jurisdiction reporting dengue even in 1996, the year with the lowest incidence (Table 4). The municipalities with the highest rates of laboratory-diagnosed dengue (Figure 4) were mostly clustered in the southeastern central region of the island in 1995, while in 1996 the highest rates occurred mostly in the west and the southeast. In 1997, the highest rates were observed in the island municipality of Culebra (an unusual event), the western portion of the island, and Patillas (on the southeast coast). Most of these municipalities went from very low to very high disease activity from one year to the next, except

for Isabela, which showed high activity for 2 consecutive years (1995–1996).

High dengue incidence rates are not due to indiscriminate blood sampling in some locations. The average ratio of reported to laboratory-diagnosed infections for each municipality for the 3 years under consideration was 4:1, with a narrow range (2:1 to 7:1 for 79% of municipalities in 1995; 91% of municipalities in 1996; 96% of municipalities in 1997). The municipalities with the highest attack rates had lower-than-average ratios (1995: 1.7:1 to 3.7:1; 1996: 1.7:1 to 2.1:1; 1997: 2.2:1 to 3.9:1).

The monthly reporting trends for hospitalized cases and those with hemorrhagic manifestations closely paralleled the overall seasonal curve. Of all cases reported from 1995 to 1997, 24% to 32% were reported as hospitalized (Table 1), similar to the proportion among the laboratory-diagnosed dengue cases (28% to 38%). Both sexes were equally represented among the hospitalized laboratory-diagnosed dengue cases from 1995 to 1997. For all municipalities, the mean ratio of reported to hospitalized cases was nearly 5:1, and among laboratory-diagnosed cases, it was about 4:1. Annually, from 54% to 60% of laboratory-diagnosed hospitalized cases were under age 30 years. Among all cases reported from 1995 to 1997, from 24% to 28% reported having at least one hemorrhagic manifestation (Table 1), similar to the proportion among the laboratory-diagnosed dengue (29% to 35%). Two of the three years showed a slight predominance of women among the laboratory-diagnosed dengue cases with hemorrhage (55% female in 1995; 49% in 1996; 57% in 1997).

Table 1 shows the number of hospitalizations for suspected DHF/DSS reported through the special cooperation of ICNs. This is a voluntary system, so it captures only a fraction of the DHF/DSS cases occurring in Puerto Rico. From 1995 to 1997, a total of 187 cases fulfilled the PAHO criteria for DHF or DSS. Of these, 83 were laboratory positive, 90 were indeterminate, and 14 were laboratory negative. Fatal case reports often provide insufficient clinical information; therefore, most fatalities documented during this period are not categorized among the DHF/DSS cases just mentioned. In 1995, dengue was ruled out in 4 of 23 fatal cases, and the results were indeterminate in 15. In 4 cases, all males,

TABLE 2  
Laboratory-diagnosed dengue cases by gender and age group, Puerto Rico, 1995–1997

Age	1995			1996			1997				
	Gender		GNR	Gender		GNR	Gender		Total (%)		
	M	F		M	F		M	F			
0–14	270	264	0	232	232	0	318	352	670 (28.2)	0.48	0.70
15–29	391	340	0	387	280	0	363	380	743 (31.3)	0.75	0.84
30–44	162	226	0	142	193	0	187	219	406 (17.1)	0.47	0.57
45–59	124	126	0	99	106	0	114	146	260 (11.0)	0.41	0.52
60–74	49	53	0	53	44	0	58	55	113 (4.8)	0.30	0.35
≥75	14	13	0	12	13	0	19	17	36 (1.5)	0.18	0.25
ANR	30	35	1	35	33	1	72	72	144 (6.1)	—	—
All ages	1,040	1,057	1	960	901	1	1,131	1,241	2,372	0.53	0.67

GNR = gender not reported; ANR = age not reported.  
\*Number of cases per 1,000 in age group, based on July 1990 estimate of population.

the MAC-ELISA test was positive—a 7-year-old who died in January; a 13-year-old who died in July; a 9-month-old and a 28-year-old who died in November. Since the virus was not isolated from any of these cases nor autopsies performed, there was no indisputable proof of a dengue infection at the time of the fatal illness. Nevertheless, some clinical information was provided for 3 of these 4 patients, and they had symptoms and clinical laboratory findings consistent with dengue infection. In 1996, among 19 fatalities possibly caused by dengue, infection by the virus was ruled out in 8 (5 were positive for leptospirosis), and the result was indeterminate in 6 (including 3 without a diagnostic specimen). Deaths in cases with a positive MAC-ELISA test occurred throughout the year—a 28-year-old woman in March; a 6-year-old boy in April; a 47-year-old woman in July; a 3-year-old boy in August; and a 20-year-old woman in October. Of the 19 reports, 6 were laboratory positive for leptospirosis, 5 among the dengue-negative patients and 1 among the indeterminate. In 1997, 21 suspected fatal cases were notified. Dengue was ruled out in 8 and the cause was undetermined in 6. In 7, the MAC-ELISA test was positive—20- and 24-year-old men who died in January; 21- and 28-year-old women who died in February; a 34-year-old woman (July); a 16-year-old male (September; also had *Leptospira* detected in liver tissue); and a 27-year-old woman (October).

**A special outbreak, Villalba, 1995.** Villalba (population 23,559) is a municipality in the south-central mountainous area of Puerto Rico (18 07 N, 66 30 W), with its urban area (“pueblo”) in a narrow valley at 200 meters altitude, surrounded by mountains up to 1,000 meters high. Smaller communities and individual homes are scattered throughout the municipality. The mean high temperature is 87.9°F (July–August), and the mean low is 63.9°F (January); the average annual precipitation is 63.65 inches of rain. Villalba (Figure 4) had by far the highest municipal rate of laboratory-diagnosed disease in 1995 (11.67 per thousand population, compared to the mean of all municipal rates, 0.70). From 1990 to 1994, the average annual laboratory-positive dengue rate in Villalba was 0.85 (20 cases). In those years, the average proportion of hospitalization among the laboratory-positive patients was 8.0%; and the mean proportion of laboratory-diagnosed cases with hemorrhagic manifestations was 26.0%. The dengue virus serotypes obtained in dengue patients from Villalba from 1990 to 1994 were 4 DEN-1, 4 DEN-2; and 4 DEN-4; nevertheless, DEN-2 was isolated every year except 1993, the only year in which DEN-1 was isolated, while DEN-4 was isolated in 3 of the 5 years.

During 1995, a total of 518 cases of dengue in Villalba residents were reported to the dengue surveillance program. A laboratory diagnosis of dengue was made in 275 (53.1%) of the reported cases; therefore, the reported to laboratory-diagnosed case ratio was 1.9:1. Dengue was ruled out in 20 persons (3.9% of samples); the etiology of the remaining 223 cases remained undetermined. The age of laboratory-diagnosed cases ranged from 6 months to 82 years. Seventy-five percent of the cases were in persons under 30 years of age (Table 5). A similar proportion of dengue virus isolates was also obtained from this segment of the population, which also had the highest incidence of laboratory-positive dengue (14.4/1,000). There were 88 isolates of DEN-2, the only se-

TABLE 3  
Virus isolations by age group Puerto Rico, 1995–1997

Age	Number of isolates								
	1995 (n = 354)			1996 (n = 372)			1997 (n = 357)		
	DEN-1	DEN-2	DEN-4	DEN-1	DEN-2	DEN-4	DEN-1	DEN-2	DEN-4
0–14	23	60	18	26	37	27	49	14	33
15–29	26	88	19	26	86	40	28	52	36
30–44	9	41	16	9	27	27	17	15	32
45–59	5	21	7	3	23	14	5	17	19
60–74	1	2	3	4	5	8	3	0	10
≥75	1	1	0	1	2	2	0	3	4
NR	3	6	4	1	4	0	6	5	9
All ages	68 (19.2%)	219 (61.9%)	67 (18.9%)	70 (18.8)	184 (31.7%)	118 (49.5%)	108 (30.3%)	106 (29.7%)	143 (40.1%)

NR = not reported.

rotype recovered in Villalba. As was noted for Puerto Rico in general for the 1994 epidemic, a sharp increase in virus-positivity rates (but only owing to one positive out of two patients) for Villalba in May 1995 preceded the increase in cases noted for June.<sup>2</sup> The virus-positivity rate for the island did not rise over 20% until the following month. For the rest of 1995, high positivity in Villalba accounted for most of the high weekly rates for Puerto Rico.

An examination of the combined geographic and temporal distribution of dengue cases in Villalba shows that laboratory-diagnosed cases occurred in all eight municipal subdivisions (barrios) in Villalba. In spite of the difference in timing and intensity of the peaks in disease activity (Figure 5), dengue was reported from all but one of the barrios as early as April, and in all subdivisions of the municipality by June. There was a low level of dengue activity from January through May, a peak in August, and a return to low-level activity in December. Similar to the pattern for the rest of the island, the monthly reporting trends for hospitalized cases and those with hemorrhagic manifestations closely paralleled the overall seasonal curve. Of the 518 reported cases, 37 (7.1%) were hospitalized, and 21 of those (56.8%) had

laboratory-diagnosed dengue infection. The ratio of reported-to-hospitalized cases was 14:1. For laboratory-diagnosed cases, the ratio of laboratory-diagnosed-to-hospitalized cases was 13:1 (compared to 5:1 average for the rest of the island). Sixty percent of laboratory-diagnosed hospitalized cases were under age 30. Virus (DEN-2) was isolated in only one of the 21 hospitalized cases.

Of the 518 patients reported as dengue, 93 (18%) had at least one hemorrhagic manifestation. Of the 275 laboratory-diagnosed cases, 56 (20.4%) had at least one hemorrhagic manifestation. Of these, 45 (80.4%) were under age 30, and 28 (50%) were women. Dengue virus serotype 2 was identified in 15 isolates from patients with hemorrhagic manifestations.

Infection control nurses' reports of hospitalized cases included two Villalba residents who fulfilled the criteria for DHF; one was laboratory positive. This 4-year-old male had onset of illness in August and was discharged after a 3-day hospitalization. The other patient, a 16-year-old woman with preexisting diabetes mellitus, developed illness on August 8, was admitted to the hospital on August 9, and died on August 15. She had fever, pleural effusions, hematuria, a plate-

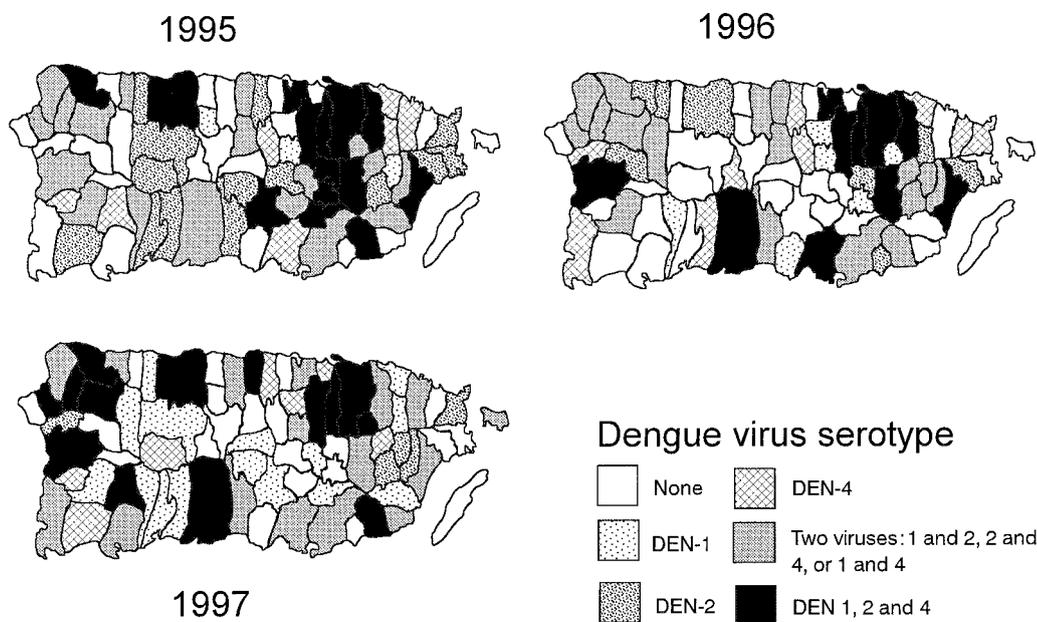


FIGURE 2. Dengue virus serotypes isolated by municipality, Puerto Rico, 1995–1997.

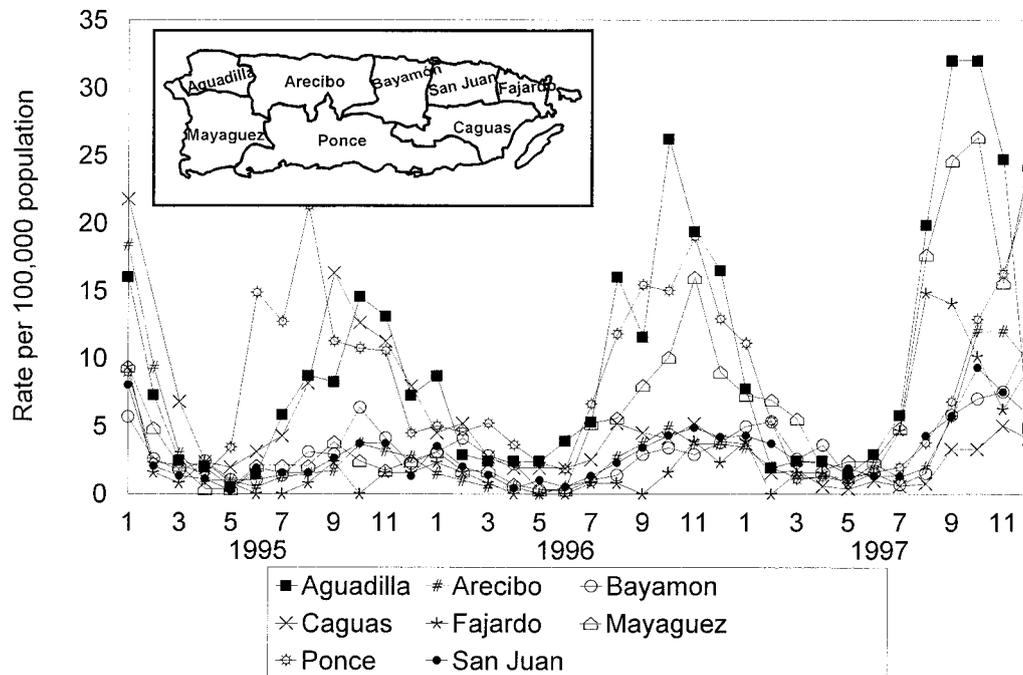


FIGURE 3. Laboratory-diagnosed dengue by region, Puerto Rico, 1995–1997.

let count of 24,000, hemoconcentration, and elevated liver function tests. The dengue laboratory diagnosis was indeterminate.

#### DISCUSSION

The high incidence of dengue in Puerto Rico in 1994 was followed for 3 years by a stable, lower overall incidence rate (average 1.75/1,000). By comparison, the reported rate of Lyme disease in the four states with highest incidence in 1997 (Connecticut, Rhode Island, New York except New York City, and New Jersey) was 0.70 to 0.25/1,000.<sup>12</sup> Dengue activity in Puerto Rico showed a different pattern each of these years. The first 3 months of 1995 were the final months of an extensive epidemic. Localized increases in transmission in July were in essence a continuation of the 1994 epidemic in areas that had been less affected the previous year (1995 rate—1.84/1,000). A year of widespread lower incidence in 1996 (1.32/1,000) was followed by a re-

turn to normal endemic levels in 1997 (2.10/1,000). Every year, some municipalities had periods of higher-than-expected dengue incidence (i.e., outbreaks). All eight barrios of the municipality of Villalba suffered a DEN-2 outbreak in 1995. Between 1969 and 1978, sporadic DEN-2 activity was consistently confirmed in Villalba, even when little dengue transmission was detected on the rest of the island.<sup>13</sup> In the interepidemic period from 1979 to 1981, it was DEN-1 that produced endemic disease in Villalba.<sup>14</sup> From 1990 to 1994, DEN-2 was isolated every year except 1993. Nevertheless, the DEN-2 outbreak in 1995 was so widespread and intense (incidence rate of 11.67/1,000) that it surpassed the highest municipal rate of laboratory-diagnosed dengue detected during the epidemic of 1994 (7.66/1,000). The disease did not spread in discernible concentric waves from a single focus to the rest of the municipality, but rather disseminated quickly to all sectors. Dengue cases were already occurring in all but one of the barrios in April, and in all barrios by June of 1995. This dispersion of cases, which occurred be-

TABLE 4  
Incidence of dengue by municipality, Puerto Rico, 1995–1997

	1995	1996	1997
No. of municipalities (total = 78) reporting dengue	78	78	77
Municipalities with laboratory-positive cases	76	76	77
Average no. of reported cases by municipality	82	59	94
Average rate of reported disease per 1,000 population	1.97	1.34	2.82
Average rate of laboratory-positive disease	0.70	0.52	0.84
Municipalities with rate of laboratory-positive disease above 90% percentile for the year	Villalba (11.67) Aguas Buenas (2.52) Cidra (2.28) Moca (1.70) Aibonito (1.48) Coamo (1.70) Isabela (1.30) Cayey (1.29)	Las Marías (3.65) Guayama (3.08) Arroyo (2.28) Isabela (2.22) Aguada (1.84) Ponce (1.68) Salinas (1.45) Añasco (1.43)	Culebra (16.86) Moca (3.86) Mayaguez (2.37) Patillas (2.24) Hormigueros (2.04) Peñuelas (1.99) San Sebastián (1.68) Lajas (1.39)

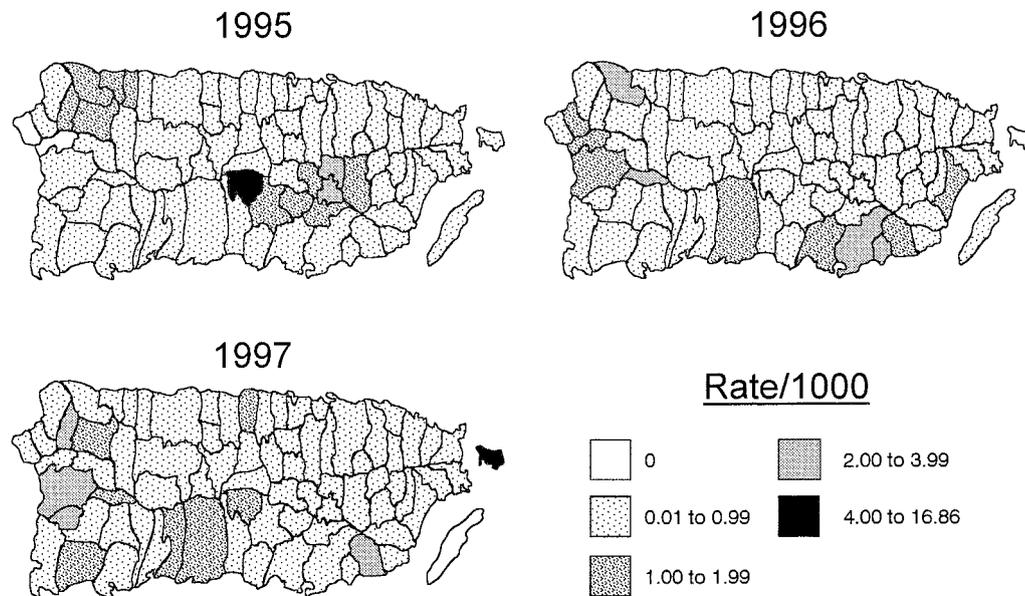


FIGURE 4. Laboratory-diagnosed dengue rates by municipality, Puerto Rico, 1995–1997.

fore a large number of reports signaled the beginning of an outbreak, was also noted in a dengue epidemic in the municipality of Florida in 1991, in a detailed analysis of geographic and temporal referencing of patient locations.<sup>15</sup>

The Villalba outbreak highlights the importance of local conditions and epidemiologic history in determining the risk for increased dengue transmission in a population. A similar pattern (outbreaks in municipalities with relatively low dengue activity in the previous 1 to 2 years) was documented in two (Las Marías and Arroyo) of the four municipalities with the highest laboratory-diagnosed rates in 1996, and three (Culebra, Hormigueros, and Peñuelas) of the five municipalities with the highest laboratory-diagnosed rates in 1997. Most municipalities with outbreaks went from very low to very high disease activity from one year to the next, but three municipalities showed high activity for 2 consecutive years.

In spite of the variation in location and intensity of disease activity from year to year, there was little or no change from the usual patterns of seasonal disease activity, age and sex distribution, and severity of disease. As for previous years, the burden imposed by the disease on the island’s population was high morbidity, measured by incidence rate and hospi-

talization ratio, but low mortality.<sup>16</sup> The low number of reported cases of DHF is considered an underestimate of the true occurrence of disease, and the high proportion of indeterminate DHF and fatal cases reflects the difficulty in obtaining laboratory confirmation of disease through a surveillance mechanism. The relatively high proportion of leptospirosis cases among dengue-negative fatal cases (62.5%; 5 of 8) in 1996 was surprising, but is not an indication of the proportion of leptospirosis diagnoses among dengue-negative patients in general. An investigation conducted that year documented a diagnosis of leptospirosis in only 15% of dengue-negative cases.<sup>11</sup>

We did not conduct a formal analysis of the effects of weather or other events on dengue patterns in these municipalities, but apparently preparations in 1995 for hurricanes or the passing of one that resulted in widespread flooding in 1996 did not affect the shape and height of the dengue epidemic curve for those years. Lower-than-average temperatures and higher-than-average precipitation occurred in 1996, a year with low dengue incidence (but also the year following a major island-wide epidemic). The following year had less rain and clouds than usual, and more hours of sunshine and somewhat higher temperatures.<sup>17,18</sup> Among the areas

TABLE 5  
Laboratory-diagnosed dengue cases by gender and age group, Villalba, 1995

Age	Gender		Total (%)	Incidence rate*	DEN-2 isolated
	Male	Female			
0–14	60	56	116 (42.2)	14.38	32
15–29	47	44	91 (33.1)	14.53	33
30–44	22	14	36 (13.1)	8.04	11
45–59	7	14	21 (7.6)	8.45	8
60–74	1	2	3 (1.1)	2.07	0
≥75	0	2	2 (0.7)	2.47	0
ANR	3	3	6 (2.2)	—	4
All ages	140	135	275	11.67	88

ANR = age not reported.  
\* Number of cases per 1,000 in age group, based on July 1990 estimate of population.

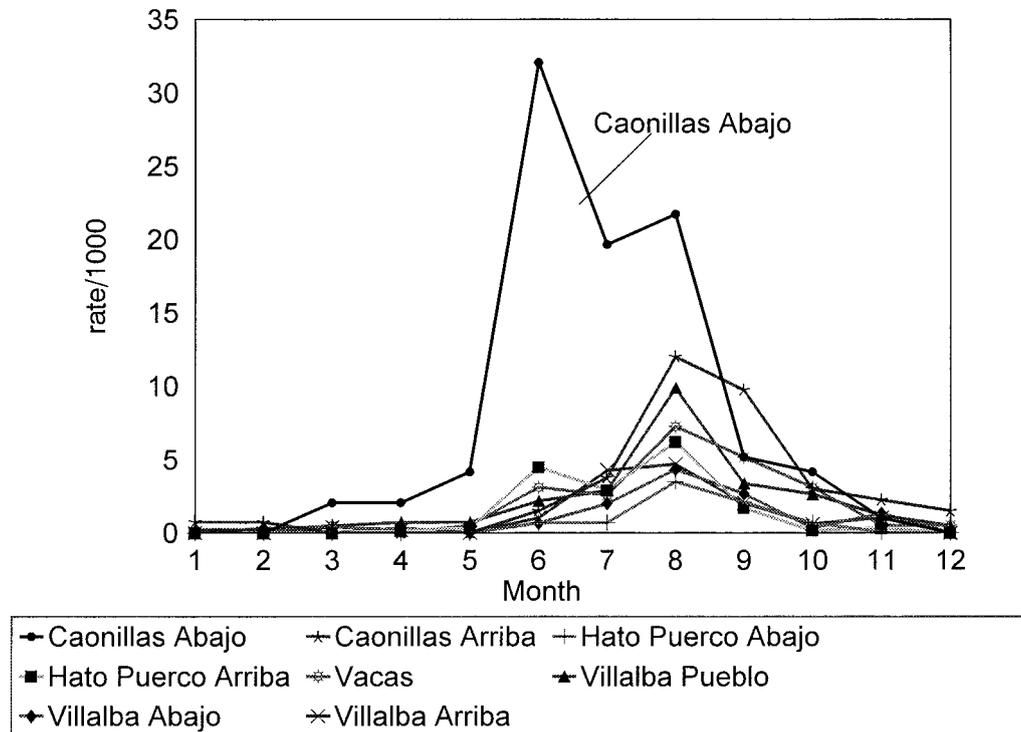


FIGURE 5. Monthly reported dengue rates by barrio, Villalba, Puerto Rico, 1995.

with high dengue incidence in 1997, at least two municipalities (Culebra and Mayagüez) experienced prolonged interruptions in domestic water service, which would have necessitated water storage and thus could have produced many potential mosquito production sites.

Even after the 1994 and 1998 epidemics, the island's population is at risk for still another epidemic, because of the re-introduction of a serotype (DEN-3) that did not circulate in Puerto Rico from 1978 to 1997.<sup>3</sup> The implementation of health reform in Puerto Rico, converting government-operated healthcare delivery to government-insured managed care by private providers, began in 1993 and is still ongoing; this reform may produce changes that will reduce the sensitivity of the dengue surveillance system. However, data through 1996 indicate that the notification of cases to the surveillance system had not been adversely affected (Ayala A, unpublished data). Both the documentation of autochthonous transmission of DEN-3 on the island after 20 years and the early detection of an epidemic in 1998 provide evidence for the current capabilities of the system.

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#### REFERENCES

1. Pan American Health Organization, 1994. *Guidelines for the Prevention and Control of Dengue and Dengue Hemorrhagic Fever in the Americas*. Washington, DC: PAHO.
2. Rigau-Pérez JG, Vorndam AV, Clark GG, 2000. The dengue and dengue hemorrhagic fever epidemic in Puerto Rico, 1994-1995. *Am J Trop Med Hyg* 64: 67-74.
3. Centers for Disease Control and Prevention (CDC), 1998. Dengue outbreak associated with multiple serotypes—Puerto Rico, 1998. *MMWR* 47: 952-956.
4. Rosen L, Gubler DJ, 1974. The use of mosquitoes to detect and propagate dengue viruses. *Am J Trop Med Hyg* 23: 1153-1160.
5. Gubler DJ, Kuno G, Sather GE, Vélez M, Oliver A, 1984. Mosquito cell cultures and specific monoclonal antibodies in surveillance for dengue viruses. *Am J Trop Med Hyg* 33: 158-165.
6. Burke DS, Nisalak A, Ussery MA, 1982. Antibody capture immunoassay detection of Japanese encephalitis virus immunoglobulin M and G antibodies in cerebrospinal fluid. *J Clin Microbiol* 15: 1034-1042.
7. Chungue E, Marché G, Pichart R, Boutin JP, Roux J, 1989. Comparison of immunoglobulin G enzyme-linked immunosorbent assay (IgG-ELISA) and hemagglutination inhibition (HI) test for the detection of dengue antibodies. Prevalence of dengue IgG-ELISA antibodies in Tahiti. *Trans R Soc Trop Med Hyg* 83: 708-711.
8. Ruechusatsawat K, Morita K, Tanaka M, Vongcheree S, Rojanasuphot S, Warachit P, Kanai K, Thongtradol P, Nimnakorn P, Kanungkid S, Igarashi A, 1994. Daily observation antibody levels among dengue patients detected by enzyme-linked immunosorbent assay (ELISA). *Japan J Trop Med Hyg* 22: 9-12.
9. Hall WC, Crowell TP, Watts DM, Barros VLR, Kruger H, Pinheiro F, Peters CJ, 1991. Demonstration of yellow fever and dengue antigens in formalin-fixed paraffin-embedded human liver by immunohistochemical analysis. *Am J Trop Med Hyg* 45: 408-417.

10. CDC, 1997. Case definitions for infectious conditions under public health surveillance. *MMWR* 46 (No. RR-10): 45–46.
11. Sanders EJ, Rigau-Pérez JG, Smits HL, Deseda CC, Vorndam AV, Aye T, Spiegel RA, Weyant RS, Bragg SL, 1999. Leptospirosis in dengue-negative patients, after a hurricane in Puerto Rico, 1996. *Am J Trop Med Hyg* 61: 399–404.
12. CDC, 1997. Summary of notifiable diseases, United States, 1997. *MMWR* 46 (No. 54): 4, 6.
13. Rymzo WT, Jr., Cline BL, Kemp GE, Sather GE, Craven PC, 1976. Dengue outbreaks in Guánica-Ensenada and Villalba, Puerto Rico, 1972–1973. *Am J Trop Med Hyg* 25: 136–145.
14. Gubler DJ, Novak RJ, Vergne E, Colón NA, Vélez M, Fowler J, 1985. *Aedes (Gymnometopa) mediovitatus* (Diptera: Culicidae), a potential maintenance vector of dengue viruses in Puerto Rico. *J Med Entomol* 22: 469–475.
15. Morrison AC, Getis A, Santiago M, Rigau-Pérez JG, Reiter P, 1998. Exploratory space-time analysis of reported dengue cases during an outbreak in Florida, Puerto Rico, 1991–1992. *Am J Trop Med Hyg* 58: 287–298.
16. Meltzer MI, Rigau-Pérez JG, Clark GG, Reiter P, Gubler DJ, 1998. Using disability-adjusted life years to assess the economic impact of dengue in Puerto Rico:1984–1994. *Am J Trop Med Hyg* 59: 265–271.
17. Cifuentes E, 1997. Abundante la lluvia y mínimo el calor en el 1996. *El Nuevo Día* (San Juan), 1 March 1997: 26.
18. Cifuentes E, 1998. Trajo El Niño en el 97 pocas nubes y mucho sol. *El Nuevo Día* (San Juan), 2 January 1998: 20.