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THE DENGUE AND DENGUE HEMORRHAGIC FEVER EPIDEMIC IN PUERTO RICO, 1994–1995

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Abstract. From June 1, 1994 to May 31, 1995 a total of 24,700 cases of dengue (7.01/1,000 population) were reported to the laboratory-based surveillance system in Puerto Rico (1991–1994, annual average: 2.55/1,000). Dengue virus 2 predominated. The earliest indicator of epidemic activity was the virus isolation rate in May 1994 (14.0% versus 5.7% average). The male-to-female ratio among cases was 1:1.1; 65.4% were younger than 30 years (the 10 to 19 year age group had the highest incidence, 11.8/1,000). At least 5,687 cases (23.0%) showed a hemorrhagic manifestation; 4,662 (18.9%) were hospitalized, and 40 died (0.2%; 10 laboratory-positive). Two cases documented by laboratory were transmitted by unusual routes—intrapartum and through a bone marrow transplant. Among 2,004 hospitalized cases reported by infection control nurses, 139 (6.9%) fulfilled the criteria for dengue hemorrhagic fever (DHF) and another 13 cases (0.6%) had dengue shock syndrome. This epidemic produced the largest number of hospitalizations, DHF cases, and deaths from any dengue epidemic in Puerto Rico. Severity did not change throughout the year. Surveillance capabilities were maintained by temporary, simplified reporting methods, none of which could be recommended as the single method of choice for surveillance; each must be used (on site, or as a service available from a reference laboratory) at the right time in the epidemic cycle. The utility of comparisons of current and previous data underscores the value of long-term surveillance. Our analysis was unable to document whether significantly increased transmission occurred more often in cities where the water supply was rationed or where the local landfill was closed.

INTRODUCTION

Dengue is an acute disease caused by four dengue virus serotypes (DEN-1, DEN-2, DEN-3, and DEN-4). The principal vector is *Aedes aegypti*, a mosquito with worldwide distribution in tropical and many subtropical areas. All serotypes produce a similar illness (characterized by fever, intense headache, myalgias, arthralgias, rash, nausea and vomiting) and induce life-long immunity that is specific to the infecting serotype. A small proportion of infected persons may develop the severe form of disease, dengue hemorrhagic fever (DHF), which is characterized by fever, thrombocytopenia, hemorrhagic manifestations, and excessive capillary permeability that may lead to shock (dengue shock syndrome [DSS]) and death.[1,2] With early diagnosis and proper management, the case-fatality rate (CFR) of DHF is generally under 1%, but the CFR may be over 10% once shock develops.[3]

Dengue transmission requires the simultaneous presence of three factors—susceptible humans, a competent mosquito vector, and dengue virus. Variations in any of these may promote or hinder disease activity, but these microdeterminants are in turn affected by large social changes (e.g., migration, urbanization) interacting in different degrees at each locality.[4,5] Puerto Rico experienced dengue epidemics in 1963 and 1969, but it was not until 1975 that the first case of DHF was documented.[6] In spite of further epidemics, multiple cases of DHF and deaths caused by dengue did not occur until 1986.[7] Three dengue serotypes (DEN-1, -2, -4) circulated from 1985 to 1997, with DEN-1 predominating for 3 years before the epidemic. The disease showed a seasonal pattern, with minimal occurrence from March to June and peaks in activity from September to November (Figure 1). The annual incidence of reported disease increased steadily from 1987 to 1992, markedly decreased in 1993, and then increased to epidemic levels in 1994.

Two events may have increased the number of potential mosquito-production sites in Puerto Rico in 1994, and may therefore have promoted dengue transmission: the closure of many municipal sanitary landfills and widespread water rationing. In April, 32 (52%) of all 61 sanitary landfills were closed due to the implementation of new regulations promulgated by the United States Environmental Protection Agency (EPA), and stricter rules and higher fees were established for depositing old tires and large refuse items, such as kitchen appliances, in the remaining landfills.[8,9] This resulted in increased illegal dumping of such materials in vacant lots and along roadways. The interruptions in water service due to drought conditions were extensive and prolonged, occurring from May to October 1994. During this period, residents of the affected areas stored water in a wide variety of containers both inside and outside their homes and businesses.

We describe here the dengue and DHF epidemic that occurred in Puerto Rico from mid-1994 through early 1995, highlighting the occurrence of severe disease and the surveillance mechanisms that allowed us to monitor disease activity.

METHODS

Surveillance. The Dengue Branch, Division of Vector-Borne Infectious Diseases, Centers for Disease Control and Prevention (CDC), receives diagnostic specimens from government clinics, public and private hospitals and laboratories, and physicians' offices throughout Puerto Rico. These specimens are sent directly, or collected locally and delivered by personnel of the Puerto Rico Department of Health (PRDH). To evaluate the severity of reported cases, the dengue case-investigation form includes information on patient symptoms, date of onset of illness, and date of sample collection. In addition, infection control nurses (ICNs) at all 57 general acute-care hospitals are asked to complete and sub-

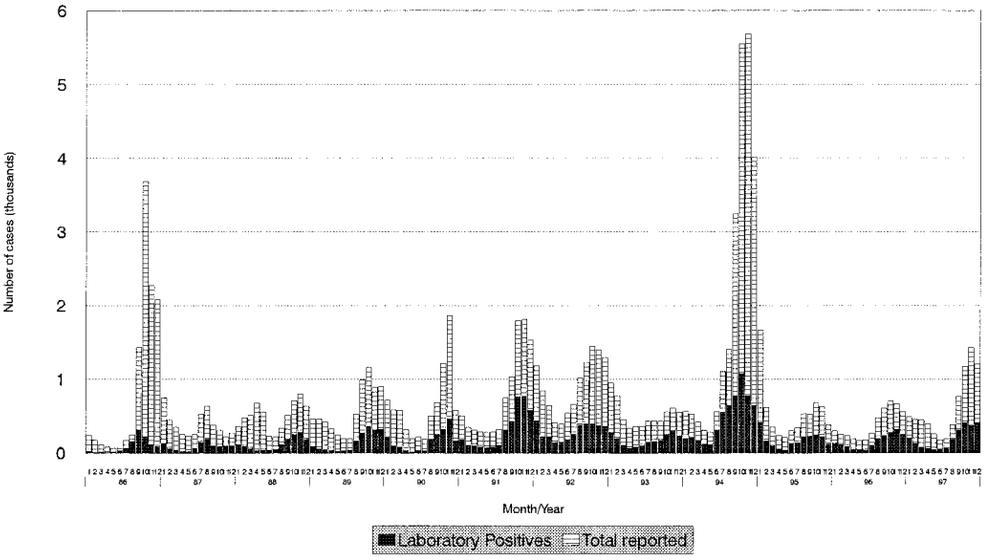

FIGURE 1. Laboratory diagnosis of dengue cases (by month of onset) Puerto Rico, 1986–1997.

mit a 40-item report of demographic and clinical information on all patients admitted with a diagnosis (or consideration) of dengue fever. The ICNs provide the data voluntarily; therefore, some ICNs at large public hospitals do not participate routinely. Data are stored and analyzed at CDC using Epi-Info software.[10] For the analysis of temporal trends, cases are assigned to the date of onset of symptoms. Data for the 3 years before the epidemic were used as a baseline comparison. From 1990 to 1994, the annual dengue incidence curve always reached a nadir in May. Therefore, the baseline years went from June 1 to May 31 for 1991–1992, 1992–1993, and 1993–1994. The epidemic year went from the month of initial increase in incidence (June 1994) to the end of May 1995, although the incidence curve returned to baseline in April 1995. We used 12 months of data for the epidemic (rather than the 10 months of elevated incidence) so that comparisons of rates among years would be valid.

Hospital bed-occupancy ratio. To monitor hospital occupancy at the peak of the epidemic (reporting weeks 41–50, October 12–December 14, 1994), ICNs were asked to respond to weekly telephone calls inquiring about the number of hospital beds in the previous day's census that were occupied by patients with an admission diagnosis of thrombocytopenia or suspected dengue or DHF. A mean bed-occupancy ratio per hospital per week was calculated by taking the total number of reported occupied beds, divided by the hospital's bed capacity, multiplied by the number of weeks that the ICN had responded to our call. This was multiplied by 100 to express the ratio as a percent, i.e., ratio = (100 × total beds reported occupied)/(total hospital beds × number of weeks that calls were answered by ICNs).

Case definitions. From September 1, 1994 to March 31, 1995 the volume of samples submitted to the CDC Dengue Branch greatly surpassed the laboratory's capacity to receive, log in, test, and report results. Therefore, it was necessary to assign priority testing to more severe cases and to cases reported from municipalities that had not previously reported disease. As a result, an analysis of only laboratory-positive samples would not be an accurate representation of disease activity during this period. Therefore, unless otherwise specified, this description will focus on *reported* cases of dengue, that is, any patient for whom a diagnostic sample for dengue, ordered by a physician, was received at the CDC Dengue Branch. A reported case of DHF is any case for which a clinical report was sent by ICNs, and which fulfilled the criteria in the clinical case definition established by the World Health Organization, and clarified by the Pan American Health Organization, as follows: 1) fever, or history of recent fever; 2) any hemorrhagic manifestation; 3) thrombocytopenia (100,000/mm^3 or less); and 4) plasma leakage caused by increased capillary permeability, as documented by hemoconcentration (hematocrit increased by 20% or more from baseline, or decreased 20% or more after hydration) or other objective evidence of capillary permeability, such as hypoalbuminemia, hypoproteinemia, or pleural or abdominal effusions (documented by x-ray, ultrasound, or computerized axial tomography). Dengue shock syndrome was defined by the above criteria plus hypotension or narrow pulse pressure ($\leq$ 20 mm Hg).[1,2] Hemoconcentration was calculated as the ratio of the difference of maximum and minimal hematocrit values, divided by the minimal value. In consideration of the reference values used in local hospitals, hypoalbuminemia was defined as a serum albumin less than 3 g/dL.

Laboratory diagnoses. 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.[11,12] 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).[13] IgG antibody determinations were made using an IgG-ELISA.[14] Because the measurement of IgM antibody may fail to diagnose about

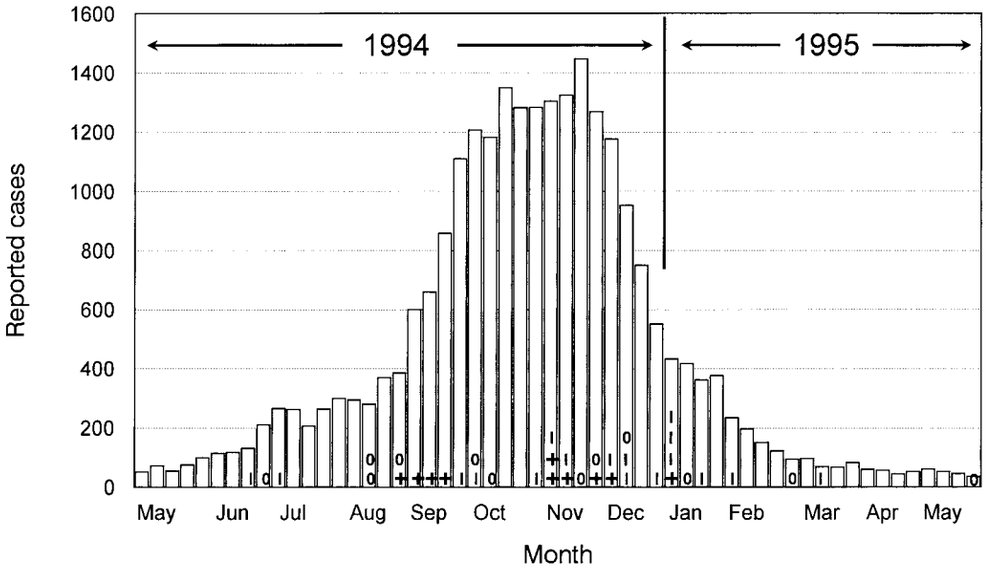

FIGURE 2. Reported cases of dengue and fatal cases, by week of onset of illness, Puerto Rico, 1994–1995. + = one laboratory-positive fatal case; 0 = one laboratory-negative fatal case; I = one indeterminate fatal case (or with no sample submitted).

5% of secondary dengue infections,[15] 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.

Laboratory case definitions. Confirmation of a current dengue infection was based on the following criteria: 1) dengue virus isolation from serum or autopsy tissue samples; or, 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.[16,17]

Probable dengue cases were those individuals who submitted a single serum sample that was IgM positive, or had an antibody titer by IgG-ELISA $\geq$ 163,840. These cases were considered probable because the persons might have had dengue in the preceding 3 months (significantly elevated IgM may be detectable for 90 days or longer), and the symptoms at the time of blood collection might have been due to an illness other than dengue.[15] Unless otherwise stated, probable and confirmed cases were considered together as laboratory-diagnosed or laboratory-positive cases. In specimens collected 6 or more days after onset of symptoms, the absence of IgM was considered to rule out the diagnosis of dengue, and the case was considered negative. Samples not processed because of the laboratory 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.

Ecologic risk factor analyses. The list of municipal sanitary landfills closed in April 1994 was provided by the Puerto Rico Solid Waste Management Authority. The list of municipalities that suffered interruptions in potable water service was provided by the Office of Corporative Communications of the Puerto Rico Aqueduct and Sewer Authority. The interruptions, alternating 16-hour shut-offs with 32 hours of service, started on May 7 in the eastern portion of the San Juan metropolitan area. As drought conditions worsened, interruptions for up to 36 hours, affecting more municipalities of the San Juan metropolitan area, were in effect from August 9 to September 20, when rationing was discontinued. Municipalities in the southern, eastern, and central areas of the island experienced similar, progressively longer interruptions of service from May 31 to October 25. To examine the effect of landfill closure and water rationing on a municipality's reported dengue incidence, we compared the incidence in 1994–1995 to the average in 1991–1993, examining the 95% confidence interval for the difference in reported cases, and the ratio of incidence rates in those two periods.[18]

RESULTS

The earliest indicator of exceptional disease activity was the high positivity rate for virus cultures in May 1994 (26 of 186, 14.0%) compared to the average for the same month in the years 1991–1993 (31 of 548, 5.7%, relative risk 2.71, 95% confidence interval 1.51–4.86). In the 3 previous years, the predominant dengue virus among the total 1,314 isolations was DEN-1 (640, 48.7%), followed by DEN-2 (401, 30.5%) and DEN-4 (273, 20.8%). During the epidemic, DEN-2 was the predominant serotype isolated (602, 62.1%), followed by DEN-4 (207, 21.4%) and DEN-1 (160, 16.5%). Dengue virus 2 was of the Group III genotype (Jamaica), as in previous years (CDC, unpublished data).[19] The number of dengue cases reported to the laboratory-based surveillance system in Puerto Rico from June 1, 1994 to May 31, 1995 was 24,700 (7.01/1,000 population) compared with an average of 8,992 cases (2.55/1,000) annually from 1991–1992 to 1993–1994. The week of onset for the largest number of reported cases (1,447) was the next to last week of November (Figure 2).

After unusually low dengue transmission in 1993–1994,

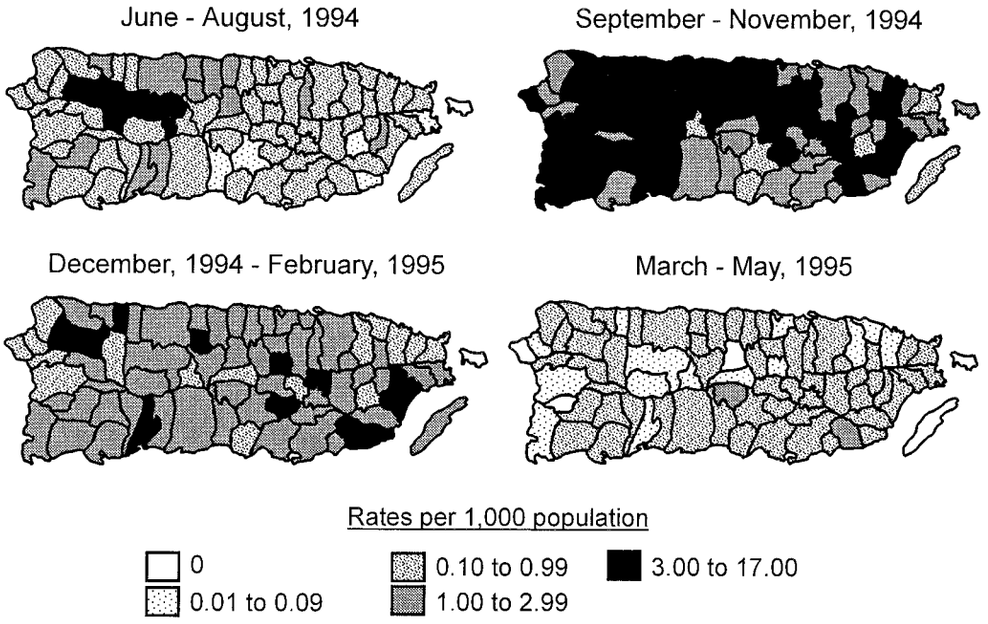

FIGURE 3. Reported dengue cases, Puerto Rico; 1994–1995, quarterly municipal rates per 1,000 population.

epidemic dengue activity was reported at the end of June 1994 in the municipality of Lares, in the mountainous west-central area of the island (Figure 3). In July and August, San Sebastián and Utuado (adjoining Lares) and municipalities in the northwest region were also affected. From September to November, the entire western half and the central eastern portion of the island became involved. From December 1994 to February 1995, 61 (78%) municipalities showed high reporting rates (1/1,000 or more), while from March to May, only 2 municipalities had such rates. The highest municipal rates of reported disease had decreased progressively in the previous 3 years (1991–1992, 41.2; 1992–1993, 13.5; 1993–1994, 8.4), while the highest municipal rate during the epidemic was 22.7/1,000. The median municipal rates in the 3 previous years (2.4, 2.5, and 1.3, respectively) were markedly lower than in 1994–1995 (6.7/1,000). An elevated incidence of reported dengue in 1994 (compared to the average for 1991–1993) was more frequent (although not statistically significantly different) among municipalities with water rationing (25 of 27, 92.6 %) than those without it (40 of 51, 78.4%, relative risk [RR] = 1.18, 95% confidence interval [CI] = 0.99–1.41), and almost as frequent where the local landfill was closed (25 of 29, 86.2%) than in municipalities where it was not closed (40 of 49, 81.6%, RR = 1.06, 95% CI = 0.87–1.29).

During the epidemic, the male-to-female ratio among reported cases was balanced (1:1.1); 65.4% of patients were younger than 30 years of age (median 21 years); the 15 to 19 year age-group had the highest incidence, 11.8/1,000) (Figure 4); 5,687 cases (23.0%) showed at least one hemorrhagic manifestation, and 4,662 (18.9%) were reported as hospitalized. Of the 24,700 cases reported in the epidemic year, 11,363 (46.0%) were tested; among those tested, 5,564 (49.0%) were positive, 1,928 (17.0%) were negative, and 3,871 (34.1%) were indeterminate. The positivity rate was slightly higher than usual, probably because the samples were selected more rigorously than in previous years. Of the 969 virus-positive patients, IgG results were available for 936 (96.6%). Among them, 173 (18.5%) had primary infections and 763 (81.5%) had secondary infections. The geographic distribution of incidence rates for laboratory-diagnosed dengue cases showed a similar distribution to reported cases of disease during the epidemic, and the rates for positives, as expected, were one-third to one-half the rates for reported cases.

The large volume of incoming samples delayed data entry, so that epidemiologic analysis, even of reported cases, could not be kept current. In addition, there was interest in monitoring the bed availability in hospitals. From October 12 to December 14, 1994 the hospital bed occupancy for patients with dengue or dengue-like illness, as reported weekly by ICNs, was used to monitor the progress of the epidemic. Through this system we first noted that disease incidence was increasing in the southwest corner of the island, when a 124-bed institution in San Germán reported 14 hospitalized cases at the time of our initial call. The average total number of beds occupied by suspected dengue cases reported per week was 232, with an average of 53 hospitals reporting every week (Figure 5). Reported bed occupancy reached a maximum during the second half of November. The marked drop for the week of November 22 corresponds to the week of the Thanksgiving holiday, when only 41 hospitals reported. In spite of the large number of hospitalized cases reported, most bed-occupancy ratios were under 10% (median 2.8%, range 0.2% to 47.2%), with markedly uneven geographic distribution. Consistent with the regular surveillance system, the hospitals with the highest ratios were in those municipalities with the highest reported rates of disease. The hospitals with the lowest ratios were tertiary-care institutions, indicating that most hospitalizations were managed without requiring intensive-care facilities. Private hospitals

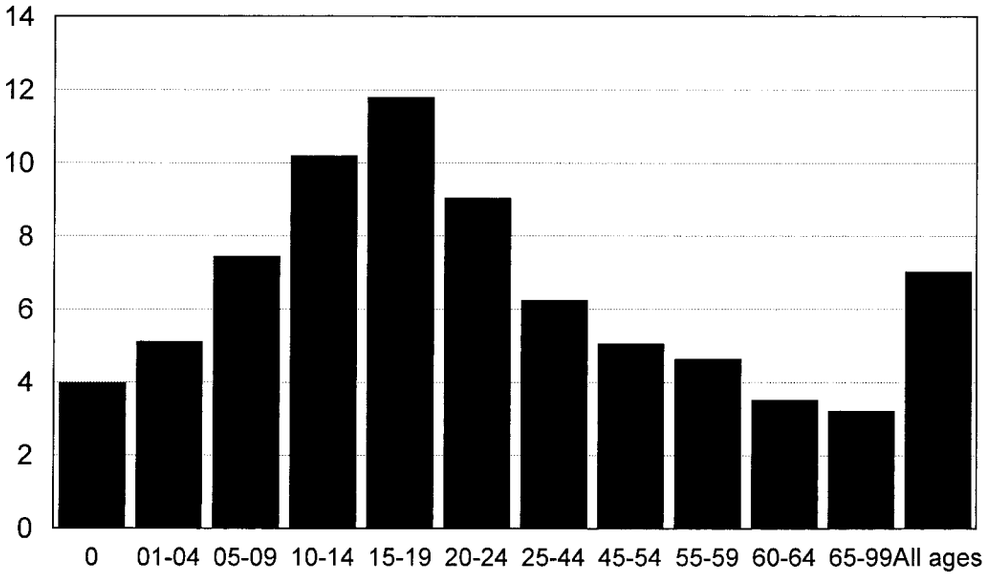

FIGURE 4. Incidence rates of reported dengue, by age-group (years), Puerto Rico, 1994–1995 epidemic.

showed a higher mean occupancy ratio (5.4%) than public hospitals (3.5%; $P < 0.04$, Kruskal-Wallis H test).

ICNs provided 2,004 reports of hospitalized cases, of which 139 (6.9%) fulfilled the four clinical criteria for dengue hemorrhagic fever established by the World Health Organization (45 laboratory-positive, 8 negative, 52 indeterminate, and 34 without diagnostic samples). From the ICN reports, an additional 13 cases (0.6%; 5 laboratory-positive, 3 negative, 2 indeterminate, and 3 without diagnostic samples) fulfilled the criteria for DSS. Among the thousands of laboratory-positive cases documented during the epidemic, two were transmitted by unusual routes—intrapartum, and through a bone marrow transplant. Intrapartum transmission was suggested in the case of an infant born on October 13, who developed irritability on October 19, and whose diagnostic sample (obtained October 20) was positive for DEN-2 by polymerase chain reaction. His mother had onset of a dengue-like illness the day before cesarean delivery, and a diagnostic sample taken on October 18 was positive for anti-dengue IgM antibodies; mother and child recovered. As the IgM result suggested, her illness was due to dengue, so delivery would have occurred during the viremic period. The child's first symptoms developed 6 days after birth—the usual incubation period for dengue is 4–7 days[20]—which suggests that exposure occurred around the time of birth. The other unusual route of transmission observed was a bone marrow transplant, performed on November 10. The recipient, a 6-year-old child, developed fever on November 14

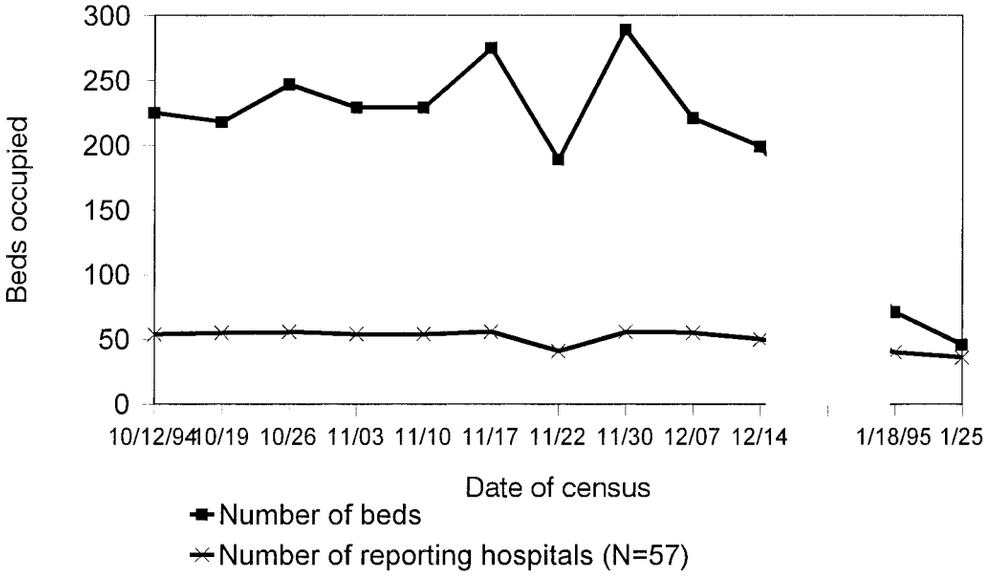

FIGURE 5. Beds occupied with cases of thrombocytopenia or suspected dengue or dengue hemorrhagic fever (DHF), Centers for Disease Control and Prevention and Puerto Rico Department of Health active telephone surveillance, Puerto Rico, October 1994–January 1995.

and died on November 21 (Figueroa M, unpublished data). Dengue virus 4 was isolated from blood, ascitic fluid, and postmortem tissue samples. The donor developed fever and headache 2 days after the marrow was harvested (November 9). A diagnostic sample from the donor obtained on December 2 was positive for anti-dengue IgM antibodies, and titration in the same test against separate dengue antigens indicated that DEN-4 was the most likely infecting serotype.

There was no indication that disease severity changed throughout the course of the epidemic. The monthly ratio of severe cases (fulfilling three or more criteria for DHF) to reported hospitalized cases did not show a significant change from the mean (3.03% when excluding laboratory-negative cases, or 3.93% if only using laboratory-positives), similar to the means and trends of previous years.[21] Suspected dengue-related deaths were reported for all months (Figure 2) except April, and the death-to-suspected-case ratios ranged from 0 to 0.57% (May), with a mean of 0.12%. Laboratory-positive fatal cases were documented only during the central months of the epidemic.

Forty fatal cases with suspected dengue were reported in the epidemic year. Twelve were found to be negative, 9 were indeterminate, and no sample was submitted for the other 9 (8 of them had dengue listed as a cause of death in the death certificate). The remaining 10 had positive diagnostic samples for dengue (3 males, 7 females; mean age 37 years, range 0–79; 1 DEN-2, 1 DEN-4). In spite of the number of hospitalized cases and reported suspected dengue-related deaths, the epidemic did not affect the overall mortality rate in Puerto Rico (1993: 7.9/1,000 population; 1994: 7.7; 1995: 8.1). The increase of 1,752 deaths in 1995 compared to 1994 was distributed among all major causes of death, with the notable exception of fatalities related to human immunodeficiency virus, which showed a decline.[22,23]

As in the 1977 dengue epidemic in Puerto Rico, influenza, a disease with similar symptoms, was also documented to be circulating with higher than normal intensity.[24] The number of influenza-like illnesses reported to the PRDH in December 1994 was 68% higher than in December 1993 (27,063 cases compared to 16,089, respectively). Serologic testing of paired serum samples from 12 dengue-negative patients (10 of whom reported nasal congestion), residing in seven municipalities throughout the island, showed that 6 had a four-fold or greater rise in antibody titers. Four influenza B (Panama) infections were diagnosed in residents of Bayamón (north coast, San Juan metropolitan area, 2 cases), Coamo (south-central foothills), and Humacao (east coast), and two influenza A (H3N2) infections were diagnosed in residents of Humacao and Moca (north western mountains) (CDC, unpublished data). These influenza virus types were also seen in the South Atlantic region of the United States in 1994–1995.[25] The PRDH also reported an increased number of cases of meningococcal disease in the first semester of 1995 (8, compared to 7 for all of 1994).[26]

DISCUSSION

The 1994–1995 dengue epidemic in Puerto Rico was probably the most severe in the island's history. A larger number of cases (over 27,000) was reported in the DEN-3 epidemic of 1963–1964, but the number represents reports of clinically diagnosed patients.[27,28] The data for 1994–1995 consist of cases for which diagnostic samples were submitted, and therefore do not include the large number of clinically-diagnosed patients for whom samples were not sent to CDC. Although cases of influenza or meningococcal disease may have been included in the reports of suspected dengue, the 1994–1995 epidemic produced, without question, the largest number of hospitalizations, DHF cases, and deaths from any dengue epidemic in Puerto Rico. A 34% rate of indeterminates among the cases tested for dengue diagnosis should not be seen as indicative of gross clinical or laboratory misdiagnosis, but was due to the large number of single, acute-phase samples, when an elevation of IgM titers could not be demonstrated.

The costs of control efforts for the PRDH included over $400,000 in materials and equipment for truck-mounted, ultra-low volume spraying of malathion against *Ae. aegypti* and against a concurrent emergence of nuisance mosquitoes in salt marsh areas of the north coast. There were also unspecified costs associated with multiple press releases and conferences, nearly 23,000 home visits and 36 clean-up campaigns in the most affected areas, a large number of lectures, municipal anti-dengue days, and the distribution of 272,678 copies of educational leaflets.[29] The direct costs of hospitalization in 1994 alone have been estimated at more than $12 million, and another calculation assigned a value of 1,492 disability-adjusted life years to the economic impact of dengue in Puerto Rico in the calendar year 1994.[30,31] Other costs have not been calculated, but are not trivial. For example, the 1994 dengue epidemic was reported as one of the principal events affecting the tourism industry in the decade from 1987 to 1996.[32]

What was the cause of the epidemic? Was it the accumulation of susceptibles from the low incidence year in 1993, the reassumption of predominance by DEN-2 after years of DEN-1, water rationing, or closure of landfills? Many publications have recently proposed an increase in dengue incidence because of environmental changes. Our analysis was unable to document that significantly increased transmission occurred more often in cities where the water supply was rationed or the local landfill was closed. We did not conduct household interviews to ascertain water shutoffs or storage practices, mosquito indices, or disease occurrence. Recent studies in Venezuela, that carried out house inspections, have showed correlations between unreliable water supply and poor trash collection, and elevated *Ae. aegypti* larval indices.[33,34] In endemic and epidemic dengue situations, many factors act concurrently upon incidence. Identifying the most forceful determinant of dengue incidence would require a comparative study, or an observational study with more controlled data than we are able to collect in our surveillance system. In contrast, our finding of constant disease severity throughout the epidemic (as opposed to recent reports from Australia and Cuba, but not French Polynesia) is probably due to our surveillance system's prolonged history, with stable data sources and case definitions, and our ability to provide a laboratory-based diagnosis for large numbers of cases.[35–37] It is therefore less subject to reporting bias (for example, less frequent dengue reporting at the beginning of an epidemic, or preferential reporting of the most severe cases as the epidemic progresses).

Our surveillance system continued to be useful under the stress of the epidemic due to its adaptability. Its most expensive components, virus isolation and long-term operation, were most useful in predicting an epidemic and characterizing it in the early stages. As the number of cases mounted, laboratory diagnosis of the problem was less necessary. At the peak of the epidemic, even individual case reporting became onerous, and weekly calls to hospitals served to quickly determine the disease's progress. None of these components could be recommended as the single method of choice for surveillance; each must be used (on site, or as a service available from a reference laboratory) at the right time in the epidemic cycle. The inordinate increase in cases during the epidemic resulted in the diagnostic laboratory's receiving four times the volume of samples as in the previous year. Samples were selected for dengue testing according to priority criteria devised for such situations, criteria that had been widely circulated to healthcare providers since May 1992. Surveillance capabilities were initially maintained by the creation of an additional database for unprocessed samples (facilitating data entry by the absence of laboratory-related variables). As this mechanism, in turn, quickly became overwhelmed, a weekly call to hospital ICNs proved to be an alternative to follow both the progress of the epidemic (in terms of hospitalized cases) and the hospital-bed availability across the island. The PRDH-CDC laboratory-based surveillance system, as it adapted to the changing incidence of disease in 1994–1995, provided early indicators for important characteristics of the epidemic. The high positivity rate of virus cultures in May 1994, followed in June by the premature increase in dengue incidence (the Lares outbreak, 2 months earlier than the usual pattern), were clear signals of especially high disease activity. The identification of DEN-2 as the predominant serotype after three years of DEN-1 predominance was also an early warning of an extensive, severe epidemic.[38–40] We could predict there would be a large number of hospital admissions because of the early increase in reports from hospital ICNs. Similarly, an unusual number of deaths with a positive dengue laboratory diagnosis could be predicted when, by September, reports exceeded the previous annual record of three in 1986. Warning signals such as these early indicators of unusual disease activity are at times received with skepticism (rejected as premature or alarmist) by the public and professionals in health care institutions, who must progress through the classic sequence of the ''grief reaction'' (denial, anger, depression, bargaining) before reaching acceptance.[41] Public health officials need to be prepared in using the most effective strategies for announcing potentially menacing events to medical practitioners, policy makers, and even the news media.[42] Dengue announcements should serve to mobilize resources and agencies and to motivate and educate community members to take action to control *Aedes aegypti,* the mosquito vector of dengue and DHF. The reliability and predictive capability of the Puerto Rico system were made possible by the comparison of the early data for 1994–1995 with data for previous non-epidemic years. The utility of these comparisons underscores the value of laboratory-based dengue surveillance as a long-term activity, not just one conducted near the time of epidemics.[43]

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