EXPLORATORY SPACE-TIME ANALYSIS OF REPORTED DENGUE CASES DURING AN OUTBREAK IN FLORIDA, PUERTO RICO, 1991–1992

AMY C. MORRISON, ARTHUR GETIS, MARILYN SANTIAGO, JOSE G. RIGAU-PEREZ, AND PAUL REITER

Dengue Branch, Centers for Disease Control and Prevention, San Juan, Puerto Rico; Department of Geography, San Diego State University, San Diego, California; Water Resources Division, Caribbean District, United States Geological Survey, Guaynabo

Abstract. The spatial and temporal distributions of dengue cases reported during a 1991–1992 outbreak in Florida, Puerto Rico (population = 8,689), were studied by using a Geographic Information System. A total of 377 dengue cases were identified from a laboratory-based dengue surveillance system and georeferenced by their residential addresses on digital zoning and U.S. Geological Survey topographic maps. Weekly case maps were generated for the period between June and December 1991, when 94.2% of the dengue cases were reported. The temporal evolution of the epidemic was rapid, affecting a wide geographic area within seven weeks of the first reported cases of the season. Dengue cases were reported in 217 houses; of these 56 (25.8%) had between two and six reported cases. K-function analysis was used to characterize the spatial clustering patterns for all reported dengue cases (laboratory-positive and indeterminate) and laboratory-positive cases alone, while the Barton and David and Knox tests were used to characterize spatio-temporal attributes of dengue cases reported during the 1991–1992 outbreak. For both sets of data significant case clustering was identified within individual households over short periods of time (three days or less), but in general, the cases had spatial pattern characteristics much like the population pattern as a whole. The rapid temporal and spatial progress of the disease within the community suggests that control measures should be applied to the entire municipality, rather than to the areas immediately surrounding houses of reported cases. The potential for incorporating Geographic Information System technologies into a dengue surveillance system and the limitations of using surveillance data for spatial studies are discussed.

Dengue fever, a viral disease transmitted by the mosquito Aedes (Stegomyia) aegypti (L.), can spread rapidly in explosive epidemics.1 Since no vaccine or chemotherapy is available, prevention and control of the disease are dependent on vector control measures such as source reduction (to eliminate larval habitats) or ultra-low volume spraying (to kill adult mosquitoes). During outbreaks, emergency measures are often centered on reported dengue cases, a practice that assumes that female Ae. aegypti rarely travel further than 50–100 m during their lifetime.2 Recent studies of oviposition, however, have indicated that dispersal is driven by the search for oviposition sites,3,4 and that in Puerto Rico much greater distances are involved.5 The relative contribution of mosquitoes, persons, or both to the dispersal of dengue viruses within a community is poorly understood. Several investigators have reported on clusters of cases inside the same or adjacent houses and descriptions of the focal nature of the disease are relatively common,1, 6–8 but there are no previous studies on the spatial-temporal patterns of the disease.

The Geographic Information System (GIS), a computer system that can store, assemble, manipulate and analyze geographically referenced information, offers a new approach to geographic studies of disease patterns. In a GIS environment, geographically referenced point data sets can be analyzed by considering the distance between each point and all other points, facilitating the use of a variety of methods that describe and analyze point patterns9–11 and disease clustering in time and space.12–14 We report here on the application of these methods to surveillance data obtained during an outbreak of dengue in the municipality of Florida, Puerto Rico in 1991–1992. In addition, we discuss the potential for incorporating GIS technologies into a dengue surveillance system and the limitations of using surveillance data for spatial studies.

MATERIALS AND METHODS

Study area. The municipality of Florida (area = 26 km²; population = 8,689) is a small rural community15 located in the hills of north central Puerto Rico (Figure 1). In 1991, this community had the highest reported incidence of dengue (15.7/1,000) in Puerto Rico.16 Dengue-2 was the predominant serotype.16 The municipality consists of nine well-defined urbanizations (neighborhoods or housing developments), two public housing projects, and seven rural neighborhoods. Some of these areas are separated by steep, eroded karst limestone hills (= 250 m), which probably act as a natural barrier for Ae. aegypti.

The community was originally selected for an entomologic study because it is spatially separated from other population centers. Dengue reporting in Florida during this period was probably better than in other areas on the island because it had a readily accessible government health center (Centro de Diagnostico y Tratamiento). Community awareness of dengue during the epidemic was high because of the large number of cases and the occurrence of four highly publicized cases of dengue hemorrhagic fever (DHF), one of which was fatal.16

Data sources. Data surveillance database. Data were obtained from a laboratory-based surveillance system of the San Juan Laboratories, Dengue Branch, National Center for Infectious Diseases, Centers for Disease Control and Prevention (CDC).17 Blood samples from clinically suspected dengue cases are submitted to CDC from government clinics, public and private hospitals, and physicians’ offices throughout Puerto Rico, along with a standardized dengue case information sheet (DCI). The DCI requests data on the home address, age, sex, and date of onset of symptoms of the patients. It also contains a checklist to indicate the symptoms and signs reported by the patient or elicited in the evaluation. The surveillance information used in this retrospective study is presented by date of onset of symptoms or...
Serum specimens were tested for anti-dengue immunoglobulin M (IgM) by the IgM antibody-capture ELISA method (MAC-ELISA), adapted from the method developed by Burke and others \(^1\) and Gubler and others. \(^2\) Specimens with borderline results by MAC-ELISA were further evaluated with hemagglutination-inhibition (HI) testing (adapted to microtiter) \(^3\) or after October 1991, by IgG-ELISA. \(^4\) Serum specimens collected fewer than six days from the onset of illness were also processed in C6/36 mosquito cell cultures for virus isolation. \(^5,\) Dengue viruses were identified by using serotype-specific monoclonal antibodies in an indirect fluorescent antibody test on virus-infected cell cultures. \(^5\)

Dengue cases were classified as confirmed, probable, or indeterminate. For this report, probable (clinically compatible illness with a positive IgM result or very high IgG titer \(> 1:163,840\), ELISA; \(> 1:1,280\), HI) and confirmed (virus isolation or four-fold or greater change in anti-dengue antibody titer in paired serum samples) are considered together as laboratory-diagnosed cases. \(^5\) Single specimens negative for virus and for IgM were considered indeterminate, if collected five days or less from the onset of illness. The absence of IgM was considered a negative dengue diagnosis in specimens collected at six or more days after the onset of symptoms and are not considered in this study. Because the positivity rate (number of laboratory positive cases divided by laboratory-positive plus negative dengue diagnoses) was greater than 80% in Florida (Rigau-Perez JG, unpublished data), at least this proportion of the indeterminate specimens are judged to be true dengue cases, and thus were included in the spatial pattern analysis. We recognize, however, that some of these indeterminate cases probably are not dengue, and therefore may adversely affect the interpretation of the geographic clustering patterns observed. Therefore, all spatial pattern analyses described in this study were carried out for two groups of cases: a combination of laboratory-positive cases and indeterminate cases (hereafter called all cases), and laboratory-positive cases.

The clinical spectrum of dengue includes a large percent of asymptomatic or mild disease, so surveillance data under-reports infected individuals. We therefore assumed that the dengue cases reported to the CDC surveillance system represented a random (unbiased) spatial sample of all infected individuals. This assumption is reasonable if the spatial and temporal distributions of undetected cases (asymptomatic) did not differ significantly from detected cases (symptomatic). As mentioned above, characteristics of the 1991–1992...
Florida outbreak suggest that dengue reporting during this period was probably better than in other areas on the island.

**Base maps.** Digital maps were either created in ARC/INFO software or converted to that format. U.S. Geological Survey (USGS) digital topographic quadrangles (1:20,000) form layers containing roads, municipality boundaries, hydrography, and topography. These were used to create map coverages for the municipality of Florida. The position of individual housing lots was obtained from digital zoning maps (1:2,000) prepared by the Puerto Rico Planning Board from existing zoning maps of the area. The original zoning maps were developed from aerial photographs with revisions based on field checks. Four zoning maps (Florida tiles 6 [1980], 10 [1988], 11 [1980], and 14 [1984]) were available. These only covered a portion of the populated areas in Florida and did not show all individual lots in the downtown area. All lots were located in the field, and the line work was added to show their positions. In urbanized areas, lot sizes were measured with a measuring wheel (Model master [model mm45]; Rolatape Corp., Spokane, WA); in less developed regions, the number of houses was counted between two intersections and the lot locations were estimated. This formed a polygon coverage (Florida lot coverage), containing 2,989 lots, that was used for statistical analyses (Figure 1).

Each lot observed on zoning maps was assigned to an appropriate U.S. Census Topologically Integrated Geographic Encoding and Referencing (TIGER) block, based on house counts made in the field and on physical boundaries. Basic demographic information, including number of people by sex and age-group and housing (number of occupied and vacant housing units), was linked to each TIGER block by a unique census tract and block number. For each block, the average number of persons per housing unit was estimated and used to assign a population density estimate (persons/house) to each lot in Florida. Although this method masks some inter-house variation, it provides an adequate characterization of the location of the population within the community.

**Dengue case georeferencing.** The residential address of each reported dengue case was noted in the DCI form, located in the field, and recorded on a base map (paper copy). When the address was incomplete, absent, or incorrect (a number or location that did not exist), an effort was made to locate the patient’s residence with the aid of local health workers, community leaders, and store owners. In most cases, the patient’s address was represented by the centroid of a lot polygon on the appropriate base map. In rural areas, where lot sizes were not available, the position of the center of the house was measured directly from a known intersection on a zoning or USGS topographic map, by using the measuring wheel. The geographic coordinates of each residential address were converted into ARC/INFO format by an electronic digitizing tablet (#AC41; Altek Corp., Silver Springs, MD) or by digitizing the position directly on a base map located on the computer screen. Each case location was linked to the case information by a unique CDC case identification number. The database used in the spatial analysis included no personal identifiers and case maps presented in this paper do not identify individual houses. The georeferenced dengue case data set was then used to generate weekly maps of cases by date of onset of symptoms for the period between June and December 1991 and for spatial analysis of the cases reported for the entire transmission season (June 1991 to May 1992).

**Spatial pattern analysis.** The spatial resolution of the statistical analysis described below is the individual house (lot level). To identify possible spatial clusters of reported dengue cases, K-functions for the pattern of all cases and laboratory-positive were calculated and contrasted with a K-function for the distribution of the population of Florida. The K-functions were calculated from the distances between all pairs of cases and all pairs of persons per household (weighted points), at a series of distances d ranging from 5 to 100 m. The K-functions are represented by a plot of distance (x axis) by values of K(d) (y axis). We assume that all members of the Florida community were susceptible to dengue. Although some members of the community were immune to dengue-2 virus at the time of the epidemic, the absence of previous dengue activity (lowest municipal incidence rates in Puerto Rico during the previous five years) allows us to assume that this number was low. A direct comparison of the K-functions representing susceptible individuals with the K-function for dengue cases allows identification of clustering patterns of the disease over and above the clustering of the entire population. If both cases and population were randomly distributed in Florida, K(d) would equal d, and the plot would be a straight line with a positive slope and a y-intercept of zero. Since both cases and population are far more clustered in Florida than random, their K-functions will lie above the line representing spatial randomness. In addition, this approach was extended to determine whether differences in the spatial pattern of the disease exist by age or sex.

The Knox test was used to identify whether spatial patterns of dengue cases varied by temporal cluster. For this approach, a temporal cluster includes the successive cases that are separated by less than the average time interval between all successive cases. The spatial coordinate centroids of each temporal cluster are identified and compared. When there is little difference in the centroids of each temporal cluster, the implication is that there is no major change in the spatial pattern of cases. The test cannot distinguish between a temporal cluster that is clumped around a central point from another cluster that is widely dispersed around the same point, nor is it affected by size (number of cases) differences in the temporal clusters. This test was used to identify temporal changes in pattern of all cases and cases grouped by sex and age. For age, two different group types were studied: ≤ 15 years and >15 years.

The Knox test was used to identify time-space clusters of cases. This method tests for possible interaction between the distance and time separating cases, that is, whether the number of case pairs found in a particular time-space window (e.g., case pair separated by 35 m and five days) are significantly different from the number of cases expected in the same window given the total number of cases, considering the period over which the epidemic took place and the extent of the spatial distribution of all the cases. Only preplanned comparisons, based on a specific hypothesis, should be tested. For this study, the critical time periods tested were...
based on the gonotrophic cycle length of *Ae. aegypti* and the spatial clustering patterns identified by K-function analysis.

To identify whether local hot spots of dengue cases exist within the broad pattern of cases, a local K-function analysis was performed. Here the focus is on each individual case, one at a time. We searched for significantly more cases within a specified distance from each case than would be expected by chance, controlling for the local population distribution. If a series of nearby cases had in their immediate neighborhood significant numbers of nearby cases, that group of cases was considered a spatial cluster.

**RESULTS**

During 1991 and 1992, a total of 466 dengue cases were reported in Florida. Of these, 377 (80.9%) laboratory-positive and indeterminate cases were located and plotted, 40 (8.6%) were confirmed as negative for dengue fever, 37 (7.9%) had misclassified addresses (located outside Florida), and 12 (2.6%) had missing DCI forms or could not be located with the address data available. Thus, we were able to georeference 97% (377 of 389) of the reported cases. Of these, 294 occurred during the June 1991 to May 1992 transmission season (16 per 1,000 population), a 30-fold increase in reported dengue incidence over the previous two years. Of the 294 cases studied, 47.3% were laboratory-positive and 52.7% had an indeterminate diagnosis. Slightly more (53.7%, 158 of 294) reported cases were female. The age distribution was positively skewed toward the younger age groups. About half (151 of 294) were ≤ 15 years old, 30.6% (90 of 294) were between 16 and 30 years of age, and 18.0% were more than 30 years of age.

Almost all of the reported cases during the 1991-1992 transmission season occurred between June 21, 1991 and January 4, 1992 (94.2%) (Figure 2). Weekly plots of dengue cases by their date of onset of symptoms for this period showed a rapid progression of the disease through the community. The first reported case in 1991 was a 16-year-old male with date of onset on June 21 (Figure 3A). No cases were reported until five weeks later, when three new cases were observed in two of 18 areas (see week 6, Figures 2 and 3A). Week 7 of the outbreak had only one case. In week 8 (August 4–10, 1991) dengue incidence increased to 15 cases in six neighborhoods distributed over a wide geographic area (Figure 3B). For the following seven weeks, transmission remained high (11–18 cases per week) and the disease spread to an additional nine neighborhoods (Figure 2). Focal transmission continued in the affected neighborhoods. Incidence was highest in the week 16 (September 29–October 5), when 39 cases were reported (Figure 3C). Transmission decreased for the rest of 1991. Of the 18 areas affected, eight had ≥ 10 reported dengue cases. In areas with ≥ 10 reported cases overall, cases were generally detected each week after virus introduction, with the exception of a few neighborhoods, where no transmission was detected for 1–3-week periods. The more heavily affected neighborhoods were larger and more heavily populated than neighborhoods where transmission was sporadic.

The weekly plots showed a definite clustering of cases inside individual houses (Figure 4). For the June 1991–May 1992 transmission season, dengue was reported in 217 houses, of which 56 (25.8%) had between two and six reported cases. A large portion (45.2%) occurred within five days of the subsequent cases within the same house, and 8.4% occurred within 6–10 days of each other (Figure 5). In contrast, only 20.2% of within-house cases were separated by 11–30 days.

**Spatial pattern analysis.** The K-function describes the apparent clustering of the population of Florida (Figure 6). As distance increased from each of the 2,989 lots contained within Florida, the population increased rapidly over short distances (to 100 m) (Figure 1), well above the curve representing randomness (Figure 6). The slope of the K-function for all cases of dengue was similar to that of the population beyond 10 m, but at less than 10 m, the height of the case curve was much greater than the population curve. Since the minimum distance separating adjacent lots in Florida is 7 m, the higher K(d) values observed at 5 and 10 m imply that significant clustering of dengue cases occurred within households. Beyond the household, however, the distribution of cases was similar to the distribution of the population. The K-function for laboratory-positive cases was...
Figure 3. Map of residential address locations of reported dengue cases in three regions of Florida, Puerto Rico. A, week 1 (June 16–22, 1991) and week 6 (July 21–27, 1991), no cases were reported in Areas II or III; B, week 8 (August 4–10, 1991); C, week 16 (September 29–October 5, 1991).

similar, but slightly more clustered than for all cases (Figure 6). For the laboratory-positive cases, clustering extends up to 15 m compared with 10 m in the combined group.

In a series of comparisons using the K-function, we looked for possible patterns by sex, age, and reporting status of the patient. When K-functions were stratified by sex, the observed clustering patterns were contradictory. For all cases, females clustered more than males (Figure 7A). In contrast, for laboratory-positive cases, more dengue in males is observed within 15 m of each other than for females; beyond 15 m the patterns of no clustering were nearly identical.

No distinctive clustering was observed by age group for all cases. For laboratory-positive cases, dengue in children (≤ 15 years) appeared to be more clustered over longer distances than for all of the cases (Figure 8A), to a distance of approximately 60 m.

Between June 1991 and May 1992, the Barton and David test identified 23 temporal clusters of all dengue cases. An hypothesis of no difference among the centroids was not rejected ($Z = 0.344, P > 0.05$), suggesting that the spatial patterns for the temporal clusters were not significantly different. In addition, the test found no differences between male and female case patterns or between the two age groups. The Barton and David test on laboratory-positive cases also showed no significant change in the pattern of cases over time.

Based on the results of the K-function analysis, the Knox test allowed us to use a working hypothesis that the spatial distance between all cases is no greater than 5 m (with the
household). Since a female *Ae. aegypti* mosquito begins oviposition approximately three days after taking her first blood meal, this number was used to define the time-space window tested. Since the majority of oviposition occurs outdoors, we expect that mosquitoes would need to leave houses where they are blood feeding at least every three days to lay their eggs. For the 1991–1992 transmission season, 29 case pairs occurred within 5 m and three days of each other, compared with an expectation of 5.43 case pairs, given the 40,470 pairs of possible interactions. Thus, significantly more cases occurred within the 5-m, three-day time-space window than would be expected by chance \((P < 0.0001)\). Because the gonotrophic cycle of *Ae. aegypti* lasts for several days, another time-space window was explored. Significant clustering was also observed at 35 m and five days. These results were similar for laboratory-positive cases.

Figure 9 shows the local K-functions for two representative case locations (Figure 9A and B) and a special dengue case site (Figure 9C) taken from all cases. A commonly observed pattern for a case occurring in a house with multiple cases shows a distinct cluster up to 5 m and the next closest case between 25 and 30 m away (Figure 9A). Overall, the case curve beyond 5 m has a slope similar to the population distribution surrounding the given household. In contrast, for another case from a household having no other cases within it, the nearest case during the epidemic was 35 m away (Figure 9B). Again, the case slope is similar to the population distribution slope, but no case clustering is evident. We were able to identify only one of 294 cases (Figure 9C) that had a K-function value greater than two standard deviations from the mean at 100 m. This single location showed clustering over the population between 65 and 100 m but would not
qualify for hot-spot status simply because, in any normal distribution, a few reasonable outliers would be expected. This implies that the only hot spots were those households where multiple cases were reported.

DISCUSSION

This study characterized the spatial and temporal patterns of reported dengue cases in one municipality (Florida) in Puerto Rico, over a single transmission season (June 1991-May 1992). The most interesting characteristics of this outbreak were the rapid spread of the disease throughout the entire municipality and the apparent clustering of cases at short distances over short periods of time. The pattern of reported dengue cases in Florida was a result of the rapid dissemination of the virus by mosquitoes, humans, or both; or alternatively, an artifact of biases in the dengue surveillance data.

The first dengue case reported (June 21) was laboratory positive, but appeared to be an isolated or sporadic case. The previously reported case occurred seven months earlier and was the sole laboratory-diagnosed case in 1990. Five weeks after this case, the outbreak began: cases were then detected in each of 23 subsequent weeks. The geographic spread occurred early in the course of the outbreak. Between July 21 (week 6) and August 11 (week 9), the number of neighborhoods affected increased from two to seven. At this stage of the outbreak, six of the eight areas with ≥10 reported cases already had cases. This observation was consistent with the results of the Barton and David test, which detected
no change in the overall pattern of cases. Since cases were so widespread throughout the course of the epidemic, the centroids of the temporal clusters varied little.

There are several plausible explanations for the nearly simultaneous appearance of dengue cases throughout the municipality of Florida. First, the pattern may be a direct result of the insensitivity of the dengue surveillance system, especially early in the course of an epidemic. A characteristic lag phase, ranging from a few weeks to several months, when few cases are reported because of physicians’ low levels of suspicion has been reported previously. Second, dengue virus could be introduced into the community many times during the transmission season or a few viremic individuals could spread the virus to houses infested with *Ae. aegypti*. Many of Florida’s citizens are highly mobile, working and traveling outside of the municipality and visiting relatives and friends within the community itself. Finally, it is less likely that the expansion of cases into different neighborhoods is due to mosquito dispersal. Although *Ae. aegypti* may be capable of movement over distances measurable in hundreds of meters, the natural barriers between these neighborhoods and the fact that only a small number of mosquitoes survive the extrinsic incubation period preclude the simultaneous appearance of cases in geographically separated neighborhoods. Apparently, the role of *Ae. aegypti* in the dispersal of virus within neighborhoods is significant.

The rapid spread of dengue virus was most apparent at the level of an individual house. Clustering of both laboratory confirmed and reported dengue cases inside houses has been described previously. Halstead and others noted that the onset dates of family members hospitalized with DHF were often separated by only a few days. Waterman
and others\(^8\) demonstrated statistically significant household clustering, but their study did not assess the time-space relationship between these cases. In our study, we were able to demonstrate clustering of dengue cases inside houses and at short time intervals (three days). Histologic studies\(^{37,38}\) and field observations\(^{39,40}\) have demonstrated that \textit{Ae. aegypti} commonly blood feeds multiple times during a single gonotrophic cycle. The epidemiologic implications of this behavior include the occurrence of clusters of dengue patients in the same household with a similar date of onset of illness\(^1\), \(^8\) and the rapid and often explosive spread of dengue,\(^1\) both of which occurred in Florida. The high degree of household clustering could also occur if \textit{Ae. aegypti} abundance is high, that is, time-space clusters may also be a result of different individuals being infected by different mosquitoes in the same house. Results of entomologic studies in Florida during August 1991 indicated that the average number of female \textit{Ae. aegypti} per bedroom per person was 2.3,\(^{41}\) and the risk of dengue infection increased with increasing mosquito density.\(^16\) Since the daily survival rate of \textit{Ae. aegypti} has been estimated at 66–86\%,\(^{42}\) the probability of more than one infected mosquito surviving the 8–12-day extrinsic incubation period within a single house is low. In addition to the high number of mosquitoes required to support transmission, those mosquitoes would need to remain in the same house for 2–3 gonotrophic cycles to infect multiple members of a household. For this reason, multiple feeding behavior remains as the simplest explanation for household clustering of dengue cases.

Serial plots of dengue cases demonstrated temporal clus-

---

**Figure 5.** Temporal distribution of reported dengue cases occurring in the same households. Triangles represent the date of onset of symptoms of a reported case; each horizontal line represents a single residence containing $\geq$ 2 reported cases; consecutive days are for the June 1991–May 1992 transmission season in Florida, Puerto Rico.

**Figure 6.** K-function for the location of laboratory-positive and reported (laboratory-positive and indeterminate) dengue cases and weighted (persons per household) lots for the June 1991–May 1992 transmission season in Florida, Puerto Rico. K(d) was calculated for 5-m intervals.
FIGURE 7. K-functions for male and female dengue cases reported from Florida, Puerto Rico between June 1991 and May 1992. A, all reported dengue cases (laboratory-positive and indeterminate); B, laboratory-positive cases only.

FIGURE 8. K-functions for the patterns of reported dengue cases ≤15 and >15 years of age in Florida, Puerto Rico (June 1991–May 1992). A, all reported dengue cases (laboratory-positive and indeterminate); B, laboratory-positive cases only.

FIGURE 9. Local K-functions for three representative case locations in Florida, Puerto Rico. A, household with multiple cases showing clustering up to 5 m and the next closest cases 25 and 30 m away; B, household with a single case and the nearest case 35 m away; C, household with clustering over the population between 65 and 100 m.

ters, but generally, spatial clusters beyond the household were not evident. In nearly all instances, the K-function analysis revealed a spatial pattern of cases that mirrored the pattern of the population distribution beyond about 10–15 m or adjacent houses. In addition, no hot spots were identified outside of household clustering.

The absence of wider level clustering (i.e., town block) using K-function analysis could have resulted from the insensitivity of the surveillance data or might reflect highly efficient virus dispersal mechanisms. Factors contributing to the insensitivity of the surveillance data include 1) the occurrence of asymptomatic disease,16 and 2) technologic and logistic limitations in virologic and serologic techniques for detecting dengue result in a high percentage of indeterminate laboratory results. This latter factor is most likely responsible for the high percentage of indeterminate laboratory cases. As was mentioned earlier, indeterminate laboratory results were included in our analysis because we believe that for Florida a large percentage of these cases represent dengue.

For the June 1991–May 1992 transmission season, spatial patterns of laboratory-positive cases and all reported cases were consistent, except that laboratory-positive cases were slightly more clustered than the combined group. This illustrates some possible differences in the spatio-temporal patterns each type of sample. There was a large temporal difference in the confirmation rate; the percentage of dengue cases that had positive laboratory results decreased towards the end of the outbreak. Over-reporting often occurs later in the course of an epidemic43 because of increased awareness of the disease; at the same time, confirmation rates may have decreased because of increased confidence in clinical diagnoses by physicians who do not request additional tests, such as a paired serum sample, to confirm the diagnosis. The diff-
ference in K-function patterns may result from the non-dengue cases included in the indeterminate group.

Given the data limitations described above and the high probability that we are underestimating wider level clustering, the observation that beyond the individual household the case pattern follows that of the population suggests widespread movement (i.e., between neighborhoods) of virus within the community. If dispersal of Ae. aegypti is driven by oviposition, as suggested by Reiter and others, one would expect periods of 1–3 days of blood feeding, possibly in the same house, followed by oviposition that often extends for several days. We postulated that clustering would therefore extend to nearby houses after a period consistent with the gonotrophic cycle of the mosquito. Ae. aegypti would need a minimum period of five days to blood feed, develop eggs, complete oviposition, and then blood feed again. We examined this hypothesis using the Knox test in an exploratory mode and observed a secondary peak at 35 m and five days. Since many additional parameters influence mosquito dispersal, e.g., availability of oviposition sites, it is not possible to make further evaluations of the significance of mosquito movement.

The exploratory spatial analysis applied in this study enabled us to make direct comparisons of clustering patterns in different risk-groups. Unfortunately, when examining sex differences, K-functions were not consistent depending on whether all cases or only laboratory positive cases were examined. Thus, no conclusions can be made from this analysis. The apparent clustering of children at distances up to 60 m in the laboratory-positive group is of some interest. Although we can only speculate as to the reasons for these differences, further investigation of children’s movements could confirm or negate the following hypothesis: case clustering occurs at distances consistent with the location of children’s playmates. Definitive interpretation of this kind would require accurate sex- and age-specific population estimates to confirm that these patterns are not an artifact of differences in the distribution of different sex or age groups.

One of the objectives of this project was to evaluate the practical potential for incorporating GIS into the current dengue surveillance program. Some of the observations made during this study have been made previously using less sophisticated techniques than GIS. However, the ability to do spatial statistical analyses are greatly enhanced if the data are incorporated into a GIS. Furthermore, adding a geographic component to the current system would be useful for identifying hot-spots of dengue transmission. The GIS allows for exploratory spatial analysis to be conducted at regular intervals. Small areas could be studied retrospectively so that affected individuals could be questioned in detail on their movement patterns. Also, when an outbreak is identified, additional entomological and serological data can be collected efficiently. Possible dispersal patterns of Ae. aegypti can be directly compared with those of dengue cases.

An address georeferencing system and accurate base maps at a 1:2,000 would be required for an effective GIS. Unfortunately, neither are readily available in Puerto Rico and many other endemic areas. Zoning maps available at a 1:2,000 scale are not up to date, contain geographic errors because of the methodology used to create them, and are unavailable in rural zones. In addition, the address system in Puerto Rico is constantly changing and incomplete for many areas on the island. Development of an address georeferencing system for the island would be a monumental task. The alternative to address georeferencing that we used in this study was extremely labor-intensive. The address of each case was located and verified in the field. We estimate that time required to georeferencing each case in this study was approximately 3.4 person-hr. However, once this effort is expended, as a research tool, the potential applications of exploratory spatial analysis would be significant.

In conclusion, significant dengue case clustering was identified at very short distances (most likely within households) over short time periods (three days or less), but, in general the cases had spatial pattern characteristics similar to the population pattern as a whole. Wider level clustering could not be identified. Our results suggest that focal spraying and other area-limited responses would be ineffective because of the explosive nature of the disease. Targeting control measures against houses where cases are reported will do little to prevent new cases because so many individuals in a wide geographic area are likely to be infected by the time these control measures are implemented. Thus, the Ae. aegypti control measure adopted (i.e., source reduction, adulticiding) should be implemented at the municipality level at least as soon as cases are detected. Although a dengue surveillance data base managed within a GIS could add many useful elements to the surveillance system, it would only be practical if a reliable address georeferencing system were to be instituted for the island.

Acknowledgments: We thank Alec Bost (San Diego State University) for preparing some of the maps; Dr. Vance Vornmad, Ivette Gomez, Edgardo Vergne, Noemi Rosado, and Luz Nereida Acosta for conducting the serologic and virologic testing of dengue samples at CDC; and Maria Rivera for data entry. We gratefully acknowledge the advice and support of Dr. Gary Clark (Chief, CDC Dengue Branch). The input of Hernan Horta, Alfredo Casta-Velez, and Ramon Barea of the Puerto Rico Health Department was greatly appreciated.

Financial support: This work was supported in part by a cooperative agreement between the U.S. Geological Survey and the Puerto Rico Department of Health, and San Diego State University. Amy C. Morrison was supported in part by a National Centers for Infectious Disease, CDC/American Society for Microbiology Postdoctoral Research Fellowship.

Disclaimer: This article reports the results of research only. Use of trade names is for identification only and does not imply endorsement by the Public Health Service, the U.S. Department of Health and Human Services, or the U.S. Geological Survey.

Authors’ addresses: Amy C. Morrison, Department of Entomology, 1 Shields Avenue, 367 Briggs Hall, University of California at Davis, Davis, CA 95616, Arthur Getis, Department of Geography, San Diego State University, San Diego, CA 92182, Marilyn Santiago, Water Resources Division, Caribbean District, U.S. Geological Survey, GSA Center 651 Federal Drive, Suite 400-15, Guaynabo, PR 00965, Jose Rigau and Paul Reiter, Dengue Branch, Centers for Disease Control and Prevention, 2 Calle Casia, San Juan, PR 00921-3200.

Reprint requests: Paul Reiter, Dengue Branch, Centers for Disease Control and Prevention, 2 Calle Casia, San Juan, PR 00921-3200.

REFERENCES


33. Barton DE, David FN, 1962. Randomization basis for multi-


