VECTOR DENSITIES THAT POTENTIATE DENGUE OUTBREAKS IN A BRAZILIAN CITY

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Abstract. To identify the critical vector density that potentiates dengue outbreaks in an endemic site and to identify obstacles to anti-dengue activities, we correlated a series of dengue outbreaks in a Brazilian city with the intensity of its anti-vector source-reduction activities. The proportion of houses infested by vector mosquitoes correlated inversely with intensity of anti-mosquito interventions, and the vector population developed independently of rainfall. Local periods of drought promoted vector abundance in two ways: residents stored water in which vector mosquitoes could breed, and cholera outbreaks due to contaminated water diverted local health workers from routine anti-vector activities. One dengue outbreak became apparent to authorities more than two months after it commenced but would have been identified almost immediately had dengue-like disease in indicator hospitals been monitored. Active surveillance, therefore, offers a window of opportunity for promptly executed anti-dengue interventions. Source-reduction measures that suppress vector infestations to less than 1% of houses effectively avert outbreaks of dengue.

INTRODUCTION

South America was, until recently, virtually free of dengue because the main vector mosquito, Aedes aegypti, had been eliminated from the continent. This remarkably successful anti-vector campaign, designed to prevent urban yellow fever, was adopted by the Pan American Health Organization (then known as the Pan American Sanitary Bureau) in 1947.1 The goal was attained within two decades,2,3 but was lost two decades later4 This mosquito reinvaded during the 1980s and soon was followed by another potential vector of dengue, Aedes albopictus.5,6

Although only a few isolated cases of dengue had ever been recorded in Brazil,7 outbreaks of dengue serotypes 1 and 4 struck the Brazilian Amazon region in 1981–1982.8 Soon thereafter, in 1986 and 1987, dengue 1 struck several large Brazilian cities.9,10 Dengue 2 became endemic in 1990, followed by the first Brazilian deaths due to dengue hemorrhagic fever.11 Indeed, dengue soon became established in at least 21 of the 26 Brazilian states.12 The Brazilian health authorities responded to the emergence of this disease by adopting an anti-vector strategy based mainly on a source-reduction strategy similar to that which previously had eliminated yellow fever.13

The success of the original anti-yellow fever source-reduction effort owed much to the ability of South American health authorities to reach virtually every residence in their jurisdictions. In the original intervention, personnel of the various central governments discovered and destroyed all local sources of vector mosquitoes. Although other interventions against dengue that relied on a similar “top-down” structure have not always been sustained,15–17 some have succeeded.18 Results have not been definitive for less rigorous “bottom-up”19 efforts that relied on voluntary community participation.19 The relationship between the intensity of Ae. aegypti source-reduction efforts and the intensity of dengue transmission has not been evaluated rigorously.

It may be that routine anti-dengue source-reduction efforts effectively suppress transmission and that outbreaks more frequently follow lapses in this routine than weather-related events. Accordingly, we correlated a series of dengue outbreaks occurring in a Brazilian city with intensity of corresponding anti-vector source-reduction activities. In particular, we compared dengue incidence since 1986 in Fortaleza, Brazil with the amount of rainfall and with changes in the intensity of the centrally directed anti-dengue activities in this city.

MATERIALS AND METHODS

Description of study site. This series of observations was conducted in and around Fortaleza, the capital of Ceará State, located in northeastern Brazil. This city lies on the Atlantic coast (3°43'02"S and 38°32'35"W), extends over 336 km² of land, and is located about 16 m above sea level. The temperature is stable throughout the year, with a mean of about 27°C, a mean maximum of 30°C, a mean minimum of 24°C, an absolute maximum of 33°C, and an absolute minimum of 21°C. Precipitation mainly occurs between January and June, with an annual mean of 1,787.1 mm (minimum = 979.7 mm, maximum = 2,905.3 mm). Little, if any, rain falls at other times of the year. In 1998, Fortaleza had 2,175,000 inhabitants (6,473/km²) with a mean of six persons per house. During this study, public sources of potable water were available to only 74% of the population and the sewer system to 21%. Many local residents live in poverty. In 1991, for example, 97% of the residents earned less than $1,000 per month and 41% earned less than $250. Almost one-third of the population lived in substandard housing, scattered among 85 of the city’s 133 neighborhoods. The presence of extensive beaches renders Fortaleza one of the most important tourist sites in northeastern Brazil, particularly during the months of January and July.19

Program administration and source-reduction methods. Methods for monitoring and suppressing Ae. aegypti infestations in Fortaleza were developed by the National Health Foundation (NHF), a federal agency that is responsible for protecting residents of Brazil from vector-borne disease.4,20,21 The Ceará branch of the NHF modified these guidelines to reflect local conditions and administers the Fortaleza program vertically. The city was divided into blocks, in which all local residences were marked with a unique...
number. Blocks were grouped to form neighborhoods. Each neighborhood was visited by a team of government field workers once every three months, the expected duration of the residual action for the larvicide used. Teams inspected every house in a neighborhood to determine whether larval *Ae. aegypti* were present. Source-reduction measures were conducted after adult householders gave informed consent. Where feasible, these efforts emphasized removal of the containers in which vector mosquitoes were found. Other containers were treated with Abate® (American Home Products, Parsippany, NJ) (temephos) as a larvicide. During outbreaks, specialized teams delivered malathion as an adulticidal ultralow volume aerosol throughout each affected neighborhood. The activities of each team were scheduled and rigorously monitored by means of maps organized in a geographic information system. The outcome of each visit was recorded in detail on a special form and deposited in the central administrative office of the Ceará branch of the NHF.

Our effort to evaluate anti-dengue activities in Fortaleza was approved by the Council of the Department of Community Health at the Federal University of Ceará. All of the public health activities described are under the control of the National Health Council of the Ministry of Health, the Ceará State Health Council, and the Municipal Health Council of Fortaleza. At each of these three levels, ethical review was conducted by panels composed half of government representatives and half of community representatives.

**Clinical and vector monitoring methods.** The frequency of dengue in Fortaleza was determined by examining the public records of the Ceará branch of the NHF and the Municipal Health Office of Fortaleza City. Physicians were required to report each such diagnosis to the national NHF office before 1994 and to the municipal office thereafter. At the time that the dengue cases were reported, an Epidemiological Surveillance Team visited the health facility to verify each diagnosis and to conduct a preliminary epidemiologic investigation. When more than one case was recognized in a neighborhood, the team systematically contacted each appropriate local facility to encourage reporting. Reporting was further improved by general announcements on television, over the radio, and in specially convened meetings of health providers. All laboratory tests, including serology, were recorded systematically for the Ceará State laboratory. The clinical definition of dengue specified either an acute febrile illness with headache, retro-orbital pain, muscle pain, joint pain, or exanthema,22 or, during a recognized epidemic, an otherwise unexplained acute fever.

To evaluate the sensitivity of the dengue case-reporting system, we reviewed each clinical diagnosis rendered on an outpatient at São José Hospital in the months immediately preceding recognition of the 1994 dengue outbreak. As the sole infectious disease hospital in Ceará, the São José Hospital was an ideal indicator institution.

Vector surveillance data were derived from the public files of the Ceará State branch of the NHF. For data collection, the 350,000 houses in Fortaleza City were divided administratively into 133 neighborhoods. Teams of field workers visited each neighborhood at three-month intervals to identify any larval *Ae. aegypti* mosquitoes that may have been developing in each house. The degree of coverage achieved by the program was expressed as the proportion of neighborhoods visited. The nature of this program remained constant over the period of the study except when other priorities diverted public health resources, as noted.

The density of vector mosquitoes found during each three-month cycle of work was expressed as a house index (HI), representing the proportion of inspected houses that contained one or more larval *Ae. aegypti*. During periods for which no infestation data are available, because monitoring and suppression activities had been abandoned, we carried forward the HI of the preceding cycle as a conservative estimator of vector abundance; more households undoubtedly became infested when vector suppression visits did not occur. From 1986 to 1994, the same teams that were responsible for monitoring the density of larval mosquitoes in houses also were required to destroy any breeding sites they discovered. Thus, the HI was based upon 100% of houses visited. Beginning in 1995, however, separate teams performed the monitoring and the vector-suppression functions. The HI during this period was based on a random survey of 10% of the houses in each block of the entire city. Rainfall data are derived from the publicly available records of the Fundação Cearense de Meteorologia e Recursos Hídricos (FUNCEME), the agency of Ceará State that is responsible for meteorologic observations and forecasts.

**RESULTS**

**Vector density and source-reduction.** First, we correlated prevalence of vector infestation with intensity of source-reduction efforts. The proportion of Fortaleza houses infested by *Ae. aegypti* was recorded systematically for the first time early in 1986, in response to a recognition of similar infestations elsewhere in Brazil. Previous monitoring in the city had been restricted to periodic surveys of the port facilities, airport, highways, and cemeteries. Virtually every surveyed neighborhood was infested during the first few months of 1986. Although the HI exceeded 30% in almost half of infested neighborhoods (Figure 1), monitoring was discontinued until September, when it was extended to the entire city. Beginning in September, with the initiation of source-reduction methods, the HI decreased to about 4% for several months and then to less than 1% over several years. Infestations increased when the source-reduction program was interrupted during much of 1989 through 1991; the fragmentary information available suggests that the HI increased to 1.4% in certain neighborhoods and to 3.7% in others. Coverage increased once again in early 1991 and remained in effect until 1993; the HI decreased to less than 1% during this period. When anti-vector activities were discontinued again between July and September of 1993, the HI increased to 7% by December. All anti-dengue activities (suppression as well as monitoring) then were suspended until April 1994. Interventions resumed by May 1994 and, in general, remained at effective levels of coverage until October 1997, thereby holding the index below 1% during most of 1994 and 1995 and at approximately 1–2% during most of 1996 and 1997. Between November 1997 and February 1998, anti-vector activities were restricted, with coverage reduced to 40% of the neighborhoods, and the HI increased to about 5% at the beginning of 1998. Sixty percent of breeding sites
the proportion of neighborhoods visited by vector suppression teams compared with the proportion of houses infested by vector mosquitoes, the proportion of neighborhoods visited by vector suppression teams (coverage), and the amount of precipitation.

identified in 1997–1998, were large containers used to store the household supply of potable water, and these exceptionally productive sites were widely distributed in the community. The remainder included disused automobile tires, chamber pots, and a variety of food and beverage containers. In summary, _Ae. aegypti_ abundance expanded episodically during four periods between 1986 and 1998, with each substantial increase following a relaxation in the intensity of anti-vector, source-reduction activities. The proportion of houses infested by _Ae. aegypti_ larvae correlates inversely with the intensity of anti-vector intervention efforts.

Dengue incidence. We then determined whether the risk of dengue similarly correlates with the intensity of anti-vector intervention efforts. Fortaleza had its first in a series of recognized dengue outbreaks in 1986 (Figure 1). Subsequent outbreaks struck in 1989, 1994, and 1998. Each outbreak followed a period of relaxed monitoring and source-reduction activity and a consequent increase in the abundance of vector mosquitoes. Each of the four recognized dengue outbreaks occurred when more than 1% of the households were infested by larval _Ae. aegypti_.

Effect of rainfall. To consider the possibility that dengue outbreaks result from anomalous patterns of precipitation, we analyzed the relationships linking rainfall, the abundance of vector mosquitoes, the degree of source-reduction coverage, and the occurrence of dengue during the 13-year period of observation. Although rainfall was relatively constant during 1986 through 1992, virtually all rain in 1993 and 1994 fell between January and July, with about twice as much rain in 1994 as in 1993 (Figure 1). The _Ae. aegypti_ HI during the middle of the 1993 dry season was eight times greater than during the preceding 1993 rainy season. The 1994 outbreak began before the rainy season had commenced; increased vector abundance at this time correlated with household storage of water during the drought and with an interruption of vector suppression efforts. Although precipitation exceeded the average during 1995 through 1997, the HI was virtually nil at this time, and no outbreaks were recorded. Another outbreak of dengue accompanied the 1998 drought. Heavy rainfall does not correlate with an elevated HI and dengue incidence if vector suppression efforts remain vigorous. When suppression activities are interrupted, however, periods of drought may serve to potentiate dengue outbreaks.

**Concurrent cholera outbreak.** We next determined whether a 1993 failure in the supply of potable water in Fortaleza might have promoted dengue transmission indirectly by initiating the first local cholera outbreak of the century. Although larval _Ae. aegypti_ house indices remained nil during 1993, when the first of the two observed episodes of cholera transmission occurred, they increased sharply one year later, coincident with the second cholera outbreak (Figure 2). The 1994 outbreak of dengue followed some six months later, by which time the HI had increased from less than 1% to nearly 7%. In neighborhoods where vector infestations were most intense, the HI increased to between 10% and 30% (median = 15.4%). Interestingly, only 17% of the houses in Fortaleza were inspected for vector mosquitoes during 1993, in contrast to 52% of the households visited during 1992. Cholera outbreaks apparently potentiate dengue outbreaks by diverting local health workers from their routine anti-vector activities.

**Recognition of dengue outbreaks.** To evaluate the sensitivity of the local system for reporting cases of dengue, we determined whether nonspecific clinical diagnoses of fever might be disproportionately frequent immediately prior to dengue outbreaks. Toward this end, we analyzed the incidence of diagnosed rubella and acute, nonspecific febrile viral disease in the outpatient records of the São José Infectious Disease Hospital during the five-month period (from January to May) preceding official recognition of the 1994 dengue outbreak. The incidence of dengue-like disease increased several-fold during late February and early March and continued to increase steeply in subsequent weeks (Figure 3). However, the dengue outbreak was recognized by the public health passive surveillance system only at the beginning of May. If the sudden increase in dengue-like disease at São José Hospital indeed reflected unidentified cases of dengue, it is notable that passive detection identified the outbreak more than two months (10 weeks) late. Thus, a dengue monitoring system based on activated passive surveillance for dengue-like disease at tertiary health services appears to offer an increased opportunity for timely interventions.

**Dengue serotypes.** Two dengue serotypes proliferated in one or another of the four dengue outbreaks that occurred in Fortaleza during our 13-year study period. Those in 1986
and in 1989–1990 were caused by dengue virus type 1. Dengue type 2 first appeared in Fortaleza in 1994, and the first deaths from dengue hemorrhagic fever (DHF) were recorded. The fourth local outbreak in 1998 included both dengue serotypes.

**Frequency of fatal DHF.** To determine when during the course of an outbreak severe dengue-related disease may occur, we compared dengue incidence with deaths due to DHF during the 1994 outbreak. Soon after the epidemic was announced by authorities, a university autopsy service recorded a succession of deaths associated with acute febrile illnesses (Figure 3). Although clinical diagnoses initially failed to relate these deaths to the dengue epidemic, their proximity in time suggested the occurrence of DHF. As a consequence, the official surveillance system established an emergency activated passive surveillance investigation in the city’s hospitals. Ultimately, during May and June, 10 deaths were attributed to dengue. These episodes of dengue-related mortality coincided with the peak intensity of the dengue outbreak. They occurred some two months after the beginning of an abrupt surge in dengue-like disease that appeared to represent a series of early and unidentified dengue cases. Dengue-related deaths may ensue many weeks after outbreaks commence.

**DISCUSSION**

Dengue outbreaks appear to occur in Fortaleza when anti-vector source-reduction efforts cease. The first of the four episodes of intense transmission recorded there commenced 30 years after the original Brazil-wide effort to extirpate *Ae. aegypti* had succeeded. The mosquito recolonized Brazil, but anti-vector efforts had not yet resumed. The second outbreak began after the federal government withdrew financial support for anti-mosquito interventions in Fortaleza. A third was associated with a local water shortage that caused residents to store potable water and diverted health resources to the resulting anti-cholera effort. The last followed an interruption of federally funded anti-vector activities due to a severe economic crisis. Dengue outbreaks did not appear to be related to population immunity; they never occurred when house indices were held below 1%, no matter whether the population was immunologically completely naive, as in 1986, or had prior experience with multiple serotypes, as in 1998. Whenever source-reduction activities were relaxed, the proportion of households infested with larval *Ae. aegypti* mosquitoes increased to well over 1%, and dengue outbreaks did ensue.

Our observation that dengue epidemics seem to occur solely after anti-vector efforts have been abandoned implies that such interventions can be effective. Although anti-dengue interventions may include adulticidal as well as anti-larval components, insecticidal aerosols are applied mainly after an outbreak of mosquito-borne disease has already been demonstrated. Therefore, physical and larvicidal source-reduction measures constitute the main mode of preventive anti-vector intervention. The Fortaleza experience demonstrates the public health benefits of a source-reduction program because dengue remains suppressed as long as the breeding sites of the vector mosquitoes are scarce.

Traditional passive systems of dengue surveillance are notoriously insensitive. A “passive” dengue surveillance program is here defined as one that seeks to detect outbreaks solely by recording reported clinical diagnoses. When designated clinical facilities are routinely asked for reports of any dengue-like illness, the system is said to be “activated.” Other available information, including entomologic data, also may inform such a strategy. Indeed, the passive Fortaleza surveillance system failed to detect the outbreak that struck the city in 1994 in time to signal an intervention. This massive threat to human health was recognized only after disease incidence had attained nearly maximum levels. However, the authorities might have anticipated a dengue outbreak because 1) anti-vector coverage had been reduced, 2) the *Ae. aegypti* HI had increased even before the rainy season began, 3) increasing quantities of potable water were stored in homes, and 4) clinical diagnoses of various acute febrile conditions had increased. A synthesis of these various points of information could have alerted the local health authorities to the developing hazard and might have saved human lives by advancing the beginning of anti-epidemic activities by about two months. Deaths attributed to DHF began to occur only one week after the outbreak eventually was declared. Such diagnostic delays occur frequently where the health care delivery system has had little recent experience with dengue. Indeed, erroneous clinical diagnoses of “rubella” and of certain other acute febrile illnesses have persisted for months during epidemics that later were rec-
recognized as dengue.\textsuperscript{24–27} An activated system of dengue surveillance in sentinel hospitals may provide sufficient sensitivity to serve as the basis for rapid initiation of interventions in response to outbreaks. It may be that a sudden increase in the incidence of dengue-like disease can usefully signal a dengue epidemic, even where laboratory capabilities are lacking. A central health authority would collate information on physician-diagnosed cases of dengue-like illness and would then enlist the assistance of a diagnostic reference laboratory to confirm dengue virus as the etiologic agent and to identify the serotype. In this manner, routine clinical surveillance for unusual increases in diagnoses of nonspecific dengue-like disease, in combination with virologic testing, might provide a basis for recognizing and truncating dengue outbreaks before they escalate.

The ratio of diagnosed DHF cases to reported dengue cases in the 1994 Fortaleza outbreak was minuscule, much smaller than the ratios reported for the 1981–1982 Cuban outbreak\textsuperscript{28} or for the outbreaks that repeatedly strike Southeast Asia.\textsuperscript{29,30} Serology on actively surveyed, randomly chosen Fortaleza residents indicates that in 1994, 37% of the population experienced a secondary (or anamnestic) response.\textsuperscript{31} Thus, about 700,000 people apparently had been exposed to dengue 1 infection during previous epidemics and may have been at risk of DHF during the 1994 dengue 2 outbreak. Despite the magnitude of prior exposure, only about 100 Fortaleza residents developed DHF symptoms,\textsuperscript{32–34} and only 10 died. No explanation is available for the relative infrequency of DHF during dengue outbreaks in Brazil.

The 1994 dengue epidemic coincided with a collapse of the public water supply due to a prolonged drought. As a result, many people drank unsafe water and stored water for domestic use. Cholera transmission increased. The water crisis intensified during the last two months of 1993, when an alternative source of brackish, virtually undrinkable water was substituted. Emergency measures stimulated by the resulting cholera outbreak tended to divert all available health resources to the more immediate threat and thus promoted the epidemic of dengue that followed. This cholera epidemic effectively competed for dengue resources because the personnel who normally conduct the residential anti-dengue activities were used to distribute both chemicals for chlorinating stored water and rehydration fluids for those with cholera. Cholera and dengue control activities were never integrated, although with a different form of organization they might have been.

The series of dengue outbreaks in Fortaleza provided an opportunity for judging the usefulness of the threshold values for transmission indices that had been estimated for Brazil. Yellow fever outbreaks in Brazil were considered as imminent when the HI approached 5%, and this experiential value was extended to include dengue during the mid-1980s.\textsuperscript{3,11} The Fortaleza experience, however, argues that the critical HI value for dengue should be reduced to 1%.\textsuperscript{20,22} The four dengue outbreaks in Fortaleza occurred when the HI values were 4%, 3%, 7%, and 5%, respectively. Therefore, our observations in Fortaleza confirm that a dengue outbreak is unlikely when vector mosquitoes infest less than 1% of the houses.

Various indices have been devised for recording the density of dengue vector mosquitoes. Although estimates of larval density based on the HI may be less reliable than are pupal indices\textsuperscript{35} or on Breteau or other container indices, this simple method is readily conducted by operational personnel. Our observations were sufficiently numerous that any error associated with this method would be averaged out. Indeed, our results are coherent and provide an HI value that may be useful as an operational threshold for preventing outbreaks in other South American cities.

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REFERENCES