Epidemic Dengue and Dengue Hemorrhagic Fever at the Texas–Mexico Border: Results of a Household-based Seroepidemiologic Survey, December 2005

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Abstract. A dengue-2 epidemic causing dengue hemorrhagic fever (DHF) occurred in the contiguous border cities of Matamoros, Tamaulipas (Mexico), and Brownsville, TX, in 2005. In December, we conducted a household-based epidemiologic survey to determine the incidence and seroprevalence of dengue infection among Matamoros and Brownsville residents and to identify risk factors associated with infection. Antibodies to dengue were measured in 273 individuals. The estimated incidence of recent dengue infection was 32% and 4% among Matamoros and Brownsville participants, respectively. The estimated prevalence of past dengue infection was 77% and 39% among Matamoros and Brownsville participants, respectively. The Breteau index was 28 in Matamoros and 16 in Brownsville, reflecting an abundant winter population of Aedes mosquitoes. Discarded waste tires and buckets were the two largest categories of infested containers found in both cities. Our results underscore the risk for epidemic dengue and DHF in the Texas-Mexico border region.

INTRODUCTION

Dengue is an acute infection caused by the four dengue virus serotypes (DENV-1, DENV-2, DENV-3, and DENV-4) and transmitted by Aedes species mosquitoes. Most DENV infections cause no symptoms or mild illness, but any of the four serotypes can cause dengue fever or the potentially fatal clinical syndrome of dengue hemorrhagic fever (DHF). Although the mechanisms for the development of DHF and severe disease manifestations are not fully understood, a major risk factor for DHF is secondary infection with another serotype.1–3 Viral strain and host factors also may influence the development of DHF and severe disease manifestations.4–7

In the fall of 2005, Texas health officials reported a 31-year old woman from Cameron County, in southern Texas, with autochthonously acquired DHF.8 This was only the second case of locally acquired DHF ever reported in Texas and the Mexican state of Tamaulipas, which has a population of 3.2 million (Figure 1). In 2005, 7,062 dengue cases were reported in Tamaulipas, including 1,832 (26%) cases classified as DHF. DENV-2 was the predominant serotype in Tamaulipas (i.e., 27 of 28 viral isolates were DENV-2, 1 was DENV-1; Panorama Epidemiológico del Dengue y Dengue Hemorrágico, http://www.cenade.gob.mx/dengue/panorama/Panoramasemana52.pdf) The DENV-2 virus was a southeast Asia strain previously associated with DHF in the Americas.4,10

In December 2005, ~2 months after the Tamaulipas dengue epidemic peaked, we conducted a household-based seroepidemiologic survey in the contiguous border cities of Matamoros, Tamaulipas (population 462,157), and Brownsville, TX (population 167,493). The objectives were to determine the incidence of recent dengue infection among Matamoros and Brownsville residents and the seroprevalence of antibodies to dengue. We measured the presence of Aedes species mosquitoes and identified the containers serving as immature mosquito habitats in both cities. We further sought to identify risk factors for dengue infection in each city.

MATERIALS AND METHODS

Survey. We used a two-stage cluster survey design similar to that used by the World Health Organization (WHO) Expanded Program on Immunization to obtain a representative sample of households from Brownsville and Matamoros.11 Thirty census tracts from 2000 census data were systematically selected from each city after ordering by income to
achieve adequate representation of the burden of disease across all socioeconomic levels. We mapped each selected census tract, and in each tract chose a random start point and random direction for sampling and enrolled the first four households encountered with willing participants.

Binational teams, each consisting of a nurse or physician, an entomologist, and a bilingual interviewer, conducted the survey. At each participating household, all residents present who were at least 5 years of age were asked to provide a blood sample and to respond to a short questionnaire, which included information on sociodemographics, travel history, and mosquito avoidance practices. A questionnaire for the head of household solicited general household information including additional sociodemographic data, the presence of air conditioning, whether windows and doors had screens, and knowledge of dengue prevention. Lot size and distance to next residence were recorded.

Entomology. Yards and patios of participating residences were inspected for evidence of *Aedes aegypti* and *Aedes albopictus* larval and pupal habitats. Larvae and pupae were collected and sent to the Texas Department of State Health Services for speciation. We calculated the Breteau index (the number of infested containers per 100 residences inspected) for each city. The mean lot size was smaller in Matamoros (307 m²) than in Brownsville (1070 m²; *P* < 0.05), reflecting its more dense urban environment. Forty-six percent of participants from Brownsville had air conditioning; in contrast, most (85%) homes surveyed in Matamoros had air conditioning (*P* < 0.05). Nearly two thirds of homes (65% in Matamoros and 61% in Brownsville) had screens on windows and doors, per the residents’ report. The mean lot size was smaller in Matamoros (307 m²) than in Brownsville (1070 m²; *P* < 0.05), reflecting its more dense urban environment. Forty-six percent of participants from each city reported having crossed the US–Mexico border in the preceding 3 months. Few Matamoros residents (13%) or Brownsville residents (21%) reported using insect repellent “often” or “always” when outdoors in the 3 months before the survey.

Laboratory. Serum samples were tested for IgM antibodies to dengue using an IgM antibody-capture enzyme-linked immunosorbent assay (MAC-ELISA). A quantitative IgG ELISA was performed to detect IgG antibodies. Serum samples that tested positive for IgM antibodies were tested by a duplex microsphere-based immunologic assay to rule out cross-reactivity with IgM antibodies to other flaviviruses: West Nile virus (WNV) and St. Louis encephalitis virus (SLEV). ELISA format microneutralization testing was performed on samples that tested positive for IgG antibody titers ≤ 1:2,560 to test for neutralizing IgG antibodies to DENV serotypes and to WNV and SLE. Those with IgG titers > 1:2,560 were excluded from microneutralization testing because of greater potential for cross-reactivity among the flaviviruses.

Serologic evidence of recent dengue infection was defined by IgM antibodies ≥ 0.2 optical density (OD) or the presence of high-titered IgG antibodies > 1:40,960, consistent with a recent secondary infection. Evidence of any past dengue infection either recent or remote, was defined by the presence of IgM antibodies to dengue (≥ 0.2 OD) or IgG antibodies ≥ 1:40.

Analysis. Data were weighted to reflect probability of selection, taking into account the population and number of households per census tract and size of household. Analysis was performed using SAS v.9.1 (SAS Institute, Cary, NC) software. Frequencies and crude and adjusted odds ratios (ORs) and their 95% confidence intervals (CIs) were calculated. Variables found to be associated with dengue infection on univariate analysis (*P* ≤ 0.10), as well as covariates age, sex, and socioeconomic status (SES) as measured by census tract income data from the 2000 US and Mexico census, were included in the multivariate logistic regression models.

Ethical review. The investigation protocol was reviewed by the Human Subjects Coordinator at the National Center for Infectious Diseases, Centers for Disease Control and Prevention, and by the *Centro Nacional de Vigilancia Epidemiológica y Control de Enfermedades* of Mexico and determined to be an outbreak study and public health response that did not require further human subjects review. Blood samples (∼4 mL) were collected from consenting participants. Informed consent of a parent or guardian was obtained before taking blood from a minor.

**RESULTS**

**Survey.** From December 5 through 10, 2005, 240 households in Matamoros were visited. Adult residents were home in 143 households; 111 (78%) households agreed to participate in the survey. From the 111 participating households, 132 serum samples were collected. From December 12 through 15, 2005, 346 households in Brownsville were visited. Adult residents were home in 161 households; 118 (73%) households agreed to participate in the survey, and 141 serum samples were collected.

One third (29%) of homes surveyed in Matamoros had air conditioning; in contrast, most (85%) homes surveyed in Brownsville had air conditioning (*P* < 0.05). Nearly two thirds of homes (65% in Matamoros and 61% in Brownsville) had screens on windows and doors, per the residents’ report. The mean lot size was smaller in Matamoros (307 m²) than in Brownsville (1070 m²; *P* < 0.05), reflecting its more dense urban environment. Forty-six percent of participants from each city reported having crossed the US–Mexico border in the preceding 3 months. Few Matamoros residents (13%) or Brownsville residents (21%) reported using insect repellent “often” or “always” when outdoors in the 3 months before the survey.

**Entomology.** During the residential surveys in Matamoros, we found larvae and pupae of *Ae. aegypti* mosquitoes; we did not find *Ae. albopictus*. In contrast, both *Ae. aegypti* and *Ae. albopictus* immature forms were collected in Brownsville. The Breteau index was 28 in Matamoros (*Ae. aegypti* only) and 16 (combined *Aedes* species) in Brownsville. Tires represented one third (32%) of the infested containers identified in Matamoros and a quarter (26%) of the infested containers identified in Brownsville, making up the largest single category of infested container in either site (Figure 2). Buckets were the second leading category of infested container for both cities.
Dengue serology. One third (32%) of Matamoros residents had serologic evidence of recent dengue infection, as did 4% of Brownsville residents (Table 1). Approximately one half (25 of 42) of the recent dengue infections in Matamoros were associated with high IgG antibody titers and thus seemed to be secondary infections. One third (2 of 6) of the recent dengue infections in Brownsville seemed to be secondary infections. Most (77%) Matamoros residents had serologic evidence of past dengue infection, as did 39% of Brownsville residents. Through microneutralization testing, we detected IgG antibodies to all four DENV serotypes among Matamoros residents and antibodies to DENV-1 and DENV-3 among Brownsville residents. No antibodies to WNV or SLEV were detected.

Few participants from 5 to 14 years old were enrolled from either city (Table 2). Among Matamoros residents at least 15 years old, the prevalence of past dengue infection varied between 71% and 78%. In contrast, the seroprevalence in Brownsville varied from a low of 14% among those 45–64 years old to 56% among those 25–44 years old.

Risk factor analysis—Matamoros. In Matamoros, those living with a head of household who cited source reduction methods (e.g., “cleaning up patios”) as important in dengue control were six times more likely to have serologic evidence of recent dengue infection than those living with heads of household who did not identify source reduction as useful in controlling dengue (Table 3). Those without air conditioning in the house were seven times more likely to have serologic evidence of past dengue infection than those with air conditioning (Table 3). Those who reported no or infrequent insect repellent use were twice as likely to have serologic evidence of past dengue infection than Matamoros residents who reported using repellent always or often.

Risk factor analysis—Brownsville. Among Brownsville residents, those with smaller lot size (less than the median size among those surveyed) were 15 times more likely to have serologic evidence of recent dengue infection than those Brownsville residents with lot sizes greater than the median (Table 3). Those residents born outside of the United States were three times more likely to have serologic evidence of past infection than Brownsville residents who were native to the United States (Table 3).

Autochthonous dengue—Brownsville. Twenty-four Brownsville survey participants were born in the United States and reported never having traveled outside the United States. Of these 24 people, 6 (25%; 95% CI, 12–45%) were seropositive for antibodies to dengue, indicating past infection. One person had IgM antibodies only, four had IgG antibodies only, and 18 had IgG titers > 1:40,960.

| TABLE 2 | Serology results for seroepidemiologic survey by age and sex, Matamoros and Brownsville—December 2005 |
| Matamoros | Brownsville |
| Age group (years) | N | Recent infection* (%) | Past infection† (%) | N | Recent infection* (%) | Past infection† (%) |
| 5–14 | 3 | 69.4 | 69.4 | 1 | 0 | 0 |
| 15–24 | 22 | 33.9 | 76.7 | 22 | 0 | 16.7 |
| 25–44 | 66 | 36.0 | 77.6 | 56 | 1.4 | 56.2 |
| 45–64 | 32 | 20.2 | 76.4 | 44 | 6.9 | 13.5 |
| ≥ 65 | 8 | 37.1 | 71.2 | 16 | 10.0 | 42.8 |
| Sex§ | | | | | | |
| Male | 45 | 35.3 | 81.1 | 34 | 7.5 | 22.1 |
| Female | 85 | 25.7 | 73.9 | 104 | 2.4 | 43.4 |

* The estimated incidence (point estimate) and [95% CI] of recent dengue infection, defined by the presence of either dengue IgM ≥ 0.2 OD or dengue IgG > 1:40,960.
† The estimated prevalence (point estimate) and [95% CI] of any past dengue infection (either recent or remote), defined by the presence of either dengue IgM ≥ 0.2 OD or dengue IgG titer ≥ 1:40.
§ Missing data from two Matamoros participants and three Brownsville participants.
tibodies only, and one person had both IgG and IgM antibodies. Their ages ranged from 24 to 85 years and all had lived in Brownsville for at least the past 20 years. Seropositive and seronegative residents had similar durations of residence in Brownsville (mean, 40 versus 31 years, \( P > 0.2 \)).

**DISCUSSION**

In the sister border cities of Brownsville, TX, and Matamoros, Mexico, the burden of dengue infection was higher for Mexico than for Texas residents as measured both by the incidence of recent dengue infections during the 2005 epidemic and the prevalence of past dengue infection. However, the 2005 epidemic in Brownsville was markedly larger than initially recognized, and a substantial proportion of the Brownsville population has been infected with DENV. We found an abundant winter population of vector mosquitoes on both sides of the border that could support dengue transmission. Our findings underscore the risk of dengue fever and the potentially growing threat of DHF along the Texas–Mexico border area.

Previous investigators have proposed that various infrastructure factors, such as the widespread use of air conditioning, limit dengue transmission in Texas by reducing human contact with disease vectors.\(^{17}\) Our data are consistent with this hypothesis. In Matamoros, where dengue incidence and seroprevalence were both significantly higher in Matamoros than in Brownsville, residential lot sizes are smaller and air conditioning was less available than in Brownsville. Both small lot size and lack of air conditioning could potentially increase human contact with the peridomestic *Aedes* mosquito. Furthermore, we found that lack of air conditioning was a risk factor for past dengue infection among Matamoros residents, and smaller lot size was a risk factor for recent dengue infection among Brownsville residents.

Our survey findings also indicated that the 2005 dengue epidemic infected many more South Texas residents than the few that were reported to Texas health officials. Although only a small proportion of the population was affected, in absolute terms when extrapolated to the Brownsville population (167,493), 4% (95% CI, 1–6%) represents from 1,675 to 10,050 residents with recent dengue infections. The 39% (95% CI, 28–50%) seroprevalence of antibodies to dengue that we observed among Brownsville residents is consistent with findings from a 2004 Brownsville serosurvey.\(^{13}\) These data indicate that, despite living conditions at home that include the availability of air conditioning, substantial numbers of Brownsville residents acquired dengue infection. Many residents likely acquired infection while across the border in Mexico, where dengue is endemic. Almost one half of Brownsville residents surveyed reported crossing the Texas–Mexico border in the 3 months preceding the survey. However, evidence of autochthonous transmission also indicates that dengue may now be endemic in Brownsville. Therefore, infections could have been acquired in the United States.

The current epidemiology of dengue and DHF in south Texas reflects changes that have already occurred in Mexico.\(^{19,21}\) Since 1995, when all four dengue virus serotypes were first identified in Mexico and in the border state of Tamaulipas, an increasing percentage of reported dengue cases in both Mexico and Tamaulipas have been DHF.\(^{20,22}\) The percentage of DHF cases in Tamaulipas increased from 3.7% between 2000 and 2004 to 25.9% in 2005 and 23.4% in 2006 (Boletín Epidemiológico, http://www.dgepi.salud.gob.mx/boletin). All four serotypes have circulated locally in South Texas,\(^{23–25}\) and locally (US) acquired DHF has been recently reported.\(^{8,9}\) Furthermore, additional case finding efforts in late 2005 in Cameron County, TX, suggest that more DHF cases occurred in 2005 in south Texas than initially recognized.\(^{8}\)

Our finding that source reduction awareness was associated with dengue incidence in Matamoros was unexpected. We had hypothesized that knowledge of source reduction as an important component in the control of dengue would be associated with lower dengue infection risk. Our finding of a positive association between knowledge of dengue control and perception of dengue risk is consistent with interviews in a national serosurvey conducted in the late 2000s.\(^{10,20,22}\) Of all four serotypes recognized, the most frequently reported were dengue virus serotypes 1 and 2.\(^{8,9}\) However, in small lot size and lack of air conditioning could potentially increase human contact with the peridomestic *Aedes* mosquito. Furthermore, we found that lack of air conditioning was a risk factor for past dengue infection among Matamoros residents, and smaller lot size was a risk factor for recent dengue infection among Brownsville residents.

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Our finding that source reduction awareness was associated with dengue incidence in Matamoros was unexpected. We had hypothesized that knowledge of source reduction as an important component in the control of dengue would be associated with lower dengue infection risk. Our finding of a positive association between prevention knowledge and dengue infection could reflect increased awareness after infection or after educational campaigns in high-risk areas. Our data suggest the possibility of prevention messages being communicated, but not in a timely enough manner to prevent dengue infections. Also, knowledge of source reduction as important to control dengue does not necessarily mean preventive actions were taken. Our cross-sectional study design makes these results difficult to interpret: we do not know if aware-
ness of source reduction to prevent dengue preceded infection or vice versa.

Lack of air conditioning and not using insect repellent were both found to be associated with dengue infection in Matamoros. This protective effect of air conditioning is consistent with a 1999 study in the Laredo/Nuevo Laredo border area.\textsuperscript{17} We found that insect repellents were used “often or always” by 13% of Matamoros participants and had a protective effect against dengue infection. These data suggest an unexpected prevention opportunity, because earlier focus group data from border regions had suggested that repellent use would be very limited in Mexico (E. Zielinski-Gutierrez, unpublished data).

Discarded waste tires made up the single largest category of infested containers found in either city. In the subtropical climate of the region, the water holding capacity of tires, their insulating qualities that protect against weather extremes, and their dark color make tires an ideal oviposition habitat for \textit{Aedes} mosquitoes.

The only factor found to be associated with recent dengue infection in Brownsville was smaller lot size. This finding could reflect denser concentration of people or could be related to socioeconomic factors.\textsuperscript{18,26} Past dengue infection among Brownsville residents was associated with birth outside the United States, as expected given the high level of dengue transmission in Mexico.

**Limitations.** Short winter days limited available daylight hours in which to do surveying. Low temperatures may have hampered our ability to fully detect all mosquito larvae and pupae on premises. The mosquito populations detected during December may not have reflected those during the peak dengue transmission period. Small sample size limited our ability to detect statistically significant associations. Last, there may be recall bias in that data were collected retrospectively.

**Conclusions.** Dengue and, more recently, DHF are growing public health problems in the Texas–Mexico border area. The entomologic, serologic, and virologic conditions in South Texas could support the continued development of locally (US) acquired DHF: Abundant \textit{Aedes} species mosquitoes were detected in December on both sides of the subtropical Texas–Mexico border. Because nearly 40% of Brownsville residents have been infected with DENV, a substantial proportion of the population is likely to be at increased risk for DHF should they acquire a second DENV infection, especially one with a virulent strain.\textsuperscript{27}

We recommend strengthening dengue surveillance in the region to include more virologic testing. Actively monitoring for circulating DENV serotypes may provide early warning of outbreaks. Clinicians practicing in South Texas and the general public should be aware of the possibility of DHF and dengue fever in the region. Clinicians should be trained in recognizing and managing DHF. Last, prevention measures including repellent use and source reduction efforts involving waste tire disposal and proper storage of buckets should be encouraged by public health officials along both sides of the border.

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