Determinants of Dengue 2 Infection among Residents of Charters Towers, Queensland, Australia

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Dengue fever is caused by one of the four serotypes of the dengue virus and is transmitted by the urban mosquito Aedes aegypti. In 1993, the city of Charters Towers in the tropical north of Australia experienced an epidemic caused by the dengue 2 virus. A cross-sectional sample of 1,000 people was assessed for determinants of recent symptomatic dengue infection. After exclusion of people with prior exposure to dengue 2, a study group of 797 persons, including 196 patients with recent infection, were evaluated. Stepwise logistic regression analysis identified four determinants of infection: the presence of a case of dengue fever within two residential blocks (odds ratio (OR) = 3.61, 95% confidence interval (CI) 2.56–5.10), house screening (OR = 0.60, 95% CI 0.40–0.89), the presence of a water tank within two residential blocks (OR = 1.51, 95% CI 1.02–2.22), and the use of knockdown insecticide (OR = 1.75, 95% CI 1.22–2.51). Classification and Regression Tree analysis identified a group of 152 individuals in whom the prevalence of dengue infection was 50%. These people lived within two blocks of a suspected dengue fever case, did not have house screening, and used knockdown sprays. If dengue had not occurred within two residential blocks, there were no additional factors that significantly influenced the prevalence of dengue fever. Control of dengue epidemics should involve attempts to geographically contain the spread of infection, use of house screening, and the removal of mosquito breeding sites such as water tanks. Am J Epidemiol 1998; 148:1111-16.

Dengue fever is an acute self-limited infection characterized by fever, headache, rash, and muscular aches. It is caused by infection with any of the four serotypes of the dengue virus, and is transmitted from human to human in an epidemic manner by the bite of the mosquito Aedes aegypti (1). There are a number of factors—such as house screening, proximity to open sewers (2), insecticide use (3), and slum housing (4)—that have been identified as influencing an individual’s risk of being infected once an epidemic has started.

North Queensland, Australia, has been subject to dengue fever epidemics for over 100 years. To date, epidemics have been caused by the introduction of a single serotype of the dengue virus into an area where A. aegypti is known to exist. The most recent epidemic prior to this study was caused by dengue 2 in 1992-1993 (5, 6). Previous epidemics of dengue fever occurred in 1981 (dengue 1), 1954 (dengue 3), and 1942-1943 (dengue 2) (7). Since the completion of this study, there have been two additional epidemics of dengue fever—one caused by dengue 2 in the Torres Strait Islands between November 1996 and March 1997 (8) and the other caused by dengue 3 in Cairns, starting in December 1997. The Cairns epidemic was still ongoing as of October 1998.

While the public health impact of Flavivirus infection, especially of dengue fever, is undisputed, little is known of the factors that influence a person’s risk of infection with one of these viruses in an urban Australian environment. Part of the public health response to the threat of dengue fever in North Queensland has been to encourage people to reduce the opportunity for A. aegypti breeding around their homes and to reduce their exposure to the mosquito by the use of mosquito repellents and house screening.

A cross-sectional survey of 1,000 randomly selected people living in Charters Towers, a North Queensland provincial center, was conducted after the 1992–1993 epidemic. The main aim of this study was to assess current risk factors for and determinants of recent symptomatic dengue infection. Special importance
was attached to the evaluation of effects of household and behavioral factors, as these factors are the target of public health campaigns.

**MATERIALS AND METHODS**

**Study setting and study population**

Charters Towers is a city of approximately 10,000 people located in tropical North Queensland (latitude 20°5'S, longitude 146°16'E), 130 km west of the coastal city of Townsville. The average annual rainfall in Charters Towers is 658 mm, and the average maximum temperature is 30°C. The wet season occurs from November to March. The main industries in the region are gold mining and tourism. There are a number of boarding schools in the area, with a significant population of children from Papua New Guinea.

Many of the houses in Charters Towers are more than 50 years old, unscreened, and high-set, with wide verandas. Rainwater tanks are a popular form of water storage, and they are usually located next to the houses. Modern houses that are fully screened are located throughout the town. There are only a few areas where this is the predominant form of housing. Residential blocks are large, and many include a number of containers suitable for the proliferation of *A. aegypti*.

From March to June of 1993, the city was subject to an epidemic of dengue 2. There were 155 cases reported to health authorities.

This cross-sectional study enrolled 1,000 people from Charters Towers and was conducted from May to September of 1995, 2 years after the epidemic. To be eligible for inclusion in the study, a person was required to have resided in Charters Towers during the period of the epidemic and to have been a resident of North Queensland in 1981 (the latter requirement was related to a proposed study of the epidemic that occurred during that year). Children under 14 years of age were excluded.

Using a local telephone directory, every 10th telephone number was dialed, and the purpose of the study was explained to all respondents. Where possible, all eligible people in the same household were included. Recruitment for the study stopped when 1,000 people had been enrolled. The value of every individual's contribution, regardless of whether one believed that one had had dengue fever, was emphasized. After written informed consent was obtained, a standardized questionnaire was administered by a single investigator, and venesection was performed to obtain serum for later testing. Respondents were specifically asked about factors which might have influenced their exposure to infected mosquitoes, such as the presence of a suspected case of dengue in the household or within two residential blocks from the house, the presence of house screening, the presence of rainwater tanks on the property or within two residential blocks, and the presence of evaporative cooling units. In addition, the behavior of subjects during the epidemic with respect to mosquito avoidance—namely, the use of mosquito repellents, knockdown sprays, mosquito coils, and bed nets—was ascertained. The possibility of alterations in behavior due to publicity about the epidemic was assessed by inquiring about the protective measures respondents were currently using. A travel history was obtained, as was the person's recollection of symptoms experienced during the epidemic or on other occasions.

**Serologic testing**

Serum was analyzed for *Flavivirus* antibodies by means of the hemagglutination inhibition assay, as described by Clark and Cassals (9), using dengue 3 hemagglutinin and a serum dilution of 1:20, and by means of a commercial enzyme-linked immunosorbent assay (Panbio Proprietary Ltd., Brisbane, Queensland, Australia), which was performed according to the manufacturer's instructions. The choice of dengue 3 as the antigen in the hemagglutination inhibition assay was based on advice that this antigen might display more cross-reactivity than the other dengue antigens (J. Aaskov, Queensland University of Technology, personal communication, 1995). A subsequent study has demonstrated a high level of cross-reactivity among all four dengue serotypes in this assay (10). Serum that was positive in either test was analyzed for dengue 2 neutralizing antibodies using the plaque reduction neutralization test method described by Morens et al. (11). A 70 percent reduction in plaque numbers was used as the cutoff point.

**Statistical analysis**

A person was assumed to have had a dengue 2 infection during the 1993 epidemic if he or she could recall experiencing any symptom of illness at the time of the epidemic and his or her serum contained dengue 2 neutralizing antibodies. The rationale for this assumption was the low subclinical infection rate for dengue virus in adults (see Discussion), and it was designed to exclude people who had been infected during the 1942–1943 dengue 2 epidemic.

*Flavivirus* seropositivity was defined as a positive result on either the hemagglutination inhibition test or the enzyme-linked immunosorbent assay. If a person had antibodies to the *Flavivirus* group but did not fulfil the criteria for recent infection, he or she was assumed to have been infected with dengue or another flavivirus prior to 1993.

Bivariate and multivariate analyses of determinants of dengue 2 infection were based on a sample size of
797. People who had dengue 2 antibodies and were likely to have been infected in 1942–1943 (i.e., persons over 49 years of age who had been asymptomatic during the most recent epidemic) were considered immune, as were people who stated that they had had dengue fever at another time or place, and they were excluded from this analysis.

Classification and Regression Tree (CART) analysis was based on bivariate chi-squared tests. Logistic regression analysis was performed using forward and backward selection procedures. No significant interaction between determinants could be found.

RESULTS

Overall, of the 1,000 participants, 633 were female and 367 were male. Age ranged from 14 years to 88 years (mean = 48.8 years) and was found to be independent of sex. Antibodies to the Flavivirus group of viruses were present in the serum of 62.2 percent of participants, and 59.9 percent had serum that was positive in both the enzyme-linked immunosorbent assay and the hemagglutination inhibition test. Overall, 39.9 percent of the group’s serum samples had neutralizing antibodies to dengue 2, and 20 percent of the group fulfilled the criteria for a recent infection. Infection with dengue in a location other than Charters Towers was reported for 64 individuals, and the sera from 57 of these people contained Flavivirus antibodies. Overall, 203 individuals had potential prior dengue 2 exposure.

In the actual study group of 797 individuals, 24.6 percent were infected, with all age categories being equally represented. The age-specific infection rates were 27.1 percent (36/133) in persons under age 30 years, 21.4 percent (39/182) in those aged 30–39 years, 25.9 percent (53/205) in those aged 40–49 years, and 24.5 percent (68/277) in those aged 50 years or older.

A suspected case of dengue had occurred in the same household for 27 percent of the participants. A further 12.7 percent recalled the presence of neighborhood cases (within two residential blocks but not in their own house). House screening was present on the homes of 33.1 percent of participants, and in 90 percent of these situations the screening was judged by the respondent to be effective in excluding mosquitoes. Rainwater tanks were present on the property of 31.5 percent of participants, and 66.2 percent of the respondents had a tank either on their property or within two residential blocks. The presence of rainwater tanks was more common where houses were unscreened (71.9 percent) than where there was screening (54.9 percent) \( (p < 0.001) \). An evaporative cooling unit was present in the homes of 44.3 percent of respondents; most of these units were large roof-mounted units with water outlets that drained via the gutters of the house.

Use of mosquito repellents, knockdown sprays, bed nets, and mosquito coils was recorded for 29.9 percent, 57.5 percent, 6.1 percent, and 39.9 percent of the study population, respectively. The current use of these measures was 23.2 percent, 46.9 percent, 4.5 percent, and 26.5 percent, respectively. Use of repellents and knockdown sprays had increased in the group who had been ill during the epidemic. Respondents were asked what other measures they had used to minimize their risk of dengue fever. Many had used electric insect “zappers” and citronella candles. Nearly 60 percent had taken measures to reduce mosquito breeding by tipping water out of outdoor containers, cleaning bird baths, putting sand in receptacles that could gather water, or cleaning up their yards.

Bivariate associations between potential determinants and dengue 2 infection in the 797 people are displayed in Table 1. The presence of a case in the

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<th>TABLE 1. Bivariate analysis of the determinants of dengue 2 infection in susceptible individuals ( (n = 797) ), Charters Towers, Queensland, Australia, 1993</th>
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<td>Factor</td>
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<tr>
<td>Household case</td>
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<td>Neighbor case*</td>
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<td>Household or neighbor case</td>
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<tr>
<td>Travel to a tropical country</td>
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<tr>
<td>Presence of screening on house</td>
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<tr>
<td>Water tank on property or within two residential blocks</td>
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<td>Use of insect repellents</td>
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<td>Use of knockdown sprays</td>
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<td>Use of bed netting</td>
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<td>Use of mosquito coils</td>
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* Within two residential blocks.
same household or within two residential blocks and the presence of a rainwater tank within two residential blocks were both associated with increased risk of infection. Use of knockdown sprays or mosquito coils was also associated with higher risk. House screening and a history of travel to a tropical country were associated with lower risk. The use of knockdown sprays, mosquito coils, and bed nets was significantly more common in unscreened houses ($p < 0.001$ for each), although repellent use was similar in screened and unscreened homes.

The bivariate associations may have been distorted by potentially confounding effects. Consequently, a multivariate approach was used. Prevalence odds ratios resulting from stepwise logistic regression analysis are shown in table 2. The presence of suspected dengue fever in the same household or within two residential blocks proved to be the most important risk factor for recent dengue infection. House screening was independently associated with a reduced risk of symptomatic dengue infection, whereas having a rainwater tank on the property or within two residential blocks implied a significantly higher risk. The finding of a higher prevalence of infection among persons who used knockdown sprays remained significant in the logistic regression analysis. It is reasonable to interpret the use of these sprays as an indicator for the density of the mosquito population.

The CART analysis (figure 1) also demonstrated that the most important determinant of recent dengue infection was the absence or presence of a nearby dengue case—splitting up the study group into two subgroups with prevalences of 14 percent and 40 percent, respectively. If there were no dengue cases within two residential blocks, there were no additional factors that significantly influenced the prevalence of dengue fever. If dengue cases were occurring in the vicinity, house screening proved to be protective. Additional significant discrimination with respect to prevalence could be found for the presence of a nearby water tank and the use of knockdown sprays. Use of the sprays in connection with an unscreened house and a nearby dengue case characterized the subgroup ($n = 152$) with the highest prevalence (50 percent).

**DISCUSSION**

In this cross-sectional survey of people living in Charters Towers, Australia, we analyzed the determinants of recent dengue 2 infection. Our definition of infection was a recollection of experiencing symptoms during the period of the epidemic (approximately 4 months in the autumn of 1993) and the presence of dengue 2 neutralizing antibody. Previous studies have shown that most infections with dengue virus are symptomatic (12, 13), so it is reasonable to assume that most of the recent cases of dengue fever were included by our definition. Some people who had been exposed to dengue 2 in the past could have had incidental illness at the time of the epidemic and may have been accidentally included in our group of recently infected individuals, but this would be expected only to weaken any associations between determinants and illness that were found. We excluded all individuals who could have been immune to dengue 2 infection, but we did not exclude people who had been infected with other viruses from the *Flaviviridae* family. Infections caused by other flaviviruses such as Kunjin, Edge Hill, Stratford, and Murray Valley (the latter occasionally causing encephalitis) rarely cause clinically apparent infection but may contribute to overall *Flavivirus* seropositivity in the region. Prior infection with these viruses or with dengue 3 virus would be expected to result in seroconversion to the *Flavivirus* group of viruses in the hemagglutination inhibition test and the enzyme-linked immunosorbent assay, whereas the specific dengue 2 plaque reduction neutralization test should remain negative (14).

Four factors emerged in our study as significant determinants of dengue 2 infection in Charters Towers during 1993: the presence of a dengue case within two residential blocks, house screening, the presence of a water tank within two residential blocks, and the use of knockdown sprays. The choice of two residential blocks as the radius of influence was determined by the dispersal pattern of adult *A. aegypti* (15) and the likelihood that participants’ knowledge of cases and household attributes would extend no further than this.

The strength of the association between dengue 2 infection and the presence of nearby cases, as recalled by the study participants, reinforces observations that have been made concerning the epidemic spread of dengue fever outwards from an initial focus point (6).
The lack of any factors that significantly influenced the occurrence of infection in subjects who lived more than two residential blocks from a case of dengue strongly supports the use, during epidemics, of control measures that are concentrated in the area of the most intense viral transmission. No efforts were made in this study to determine how the diagnosis of dengue fever in family members or neighbors was made. We believe that many of the cases were self-diagnosed. However, such knowledge was highly predictive of increased risk for the participant. These findings support the use of control programs based on clinical rather than laboratory notification of disease, at least during an epidemic. The advantage of such a program would lie in the delivery of interventions at the time and place that the virus is being transmitted. The predictive value of clinical symptoms for the diagnosis of dengue fever in an individual patient has been low in other studies (16).

House screening emerged as a major determinant of dengue 2 infection. This was not surprising, and it was in agreement with findings from similar studies of risk factors for dengue infection (2–4). However, screening did not reduce prevalence to the same extent as living more than two blocks from someone with a suspected case of dengue fever. Prevalence among the participants who lived in a screened house with a case of dengue fever nearby was 27.7 percent, as compared with 14.3 percent in the group who, regardless of screening, did not live within two blocks of a suspected dengue case.

The increased risk of infection in the vicinity of water tanks is the first evidence that this kind of water container is important in dengue fever epidemics. Most of the water tanks in Charters Towers are made of iron and hold thousands of liters of water. Many residents made an effort to cover the opening to their water tank or put kerosene in it to discourage oviposition. The efficacy of these measures was not analyzed in this study. Water tanks have been identified as a breeding site for A. aegypti, and the local environmental health officer considered them a risk factor for dengue infection (L. Salinas, Charters Towers City Council, personal communication, 1995). The findings of this study support that view. The CART analysis indicated that only those people living in screened houses are at greater risk of infection if they live in the vicinity of a water tank. This would suggest that high mosquito densities overcome the protective effect of house screening. We are aware of only other study that demonstrated a higher independent risk with the presence of water containers (3); it was conducted in Mexico and involved containers with a capacity of 50–200 liters.

The only other factor associated with illness in this survey was the use of knockdown sprays. It was surprising that the use of knockdown sprays conferred a higher risk of infection on people exposed to infected...
mosquitoes (i.e., persons living in unscreened houses in areas where dengue transmission was occurring). Koopman et al. (3) have shown that the use of insecticides is associated with a lower risk of infection in areas where other factors predict high risk. They did find, however, that in areas of low risk, insecticide use was associated with infection. They also found that bed nets were associated with higher risk, and proposed that the use of bed nets was an indicator of higher mosquito density without having an effect on A. aegypti mosquitoes, which feed during the day (3). Similarly, in our study, the use of knockdown sprays may have been an indicator of mosquito density. The lack of efficacy, however, is difficult to explain. Insecticide resistance in the local population of A. aegypti mosquitoes should be investigated.

Charters Towers has, in common with many Queensland towns and older provincial coastal cities, a high proportion of older “Queenslander”-style dwellings which were originally built on stilts with wide-open verandas. Many of these houses have had their verandas closed in with wooden shutters. The installation of screens in such houses is a major undertaking. In Charters Towers, particularly, more modern dwellings, which are usually screened, are scattered throughout the town in the midst of the older dwellings. Only 13 percent of the dwellings in this study were both screened and not in close proximity to a water tank. In 1992, a dengue 2 outbreak in Townsville, 130 km away, started in a suburb with predominantly older-style homes, and transmission in that suburb was intense. The present study highlights the risks associated with this style of housing. While house screening and residence away from water tanks confers a lower risk of dengue infection overall, these measures may be less effective where intense viral transmission is occurring.

The proportion of the population infected during a dengue epidemic is unlikely to be linearly related to the proportion of houses with screening or without water tanks. A mathematical model of epidemic transmission (3) demonstrates how a small reduction in the basic reproduction number (the number of people infected by one person) can cause a large reduction in the size of the epidemic. A reproduction number of 1.25, for instance, is estimated to cause an epidemic that would affect 40 percent of the population. If the reproduction number falls below 1, however, the epidemic should stop. The prevention of dengue epidemics by early case detection and by prevention of virus transmission to the mosquito population should be the main priority of public health professionals. In Charters Towers, a program designed to reduce the potential for major epidemics by increasing the proportion of houses with screening and by decreasing the number of water tanks should also be undertaken.

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REFERENCES