

DISTRIBUTION OF DENGUE AND JAPANESE ENCEPHALITIS AMONG CHILDREN IN RURAL AND SUBURBAN THAI VILLAGES

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Abstract. In the rainy season of 1989, IgG and IgM antibodies against dengue and Japanese encephalitis viruses (measured by enzyme-linked immunoassay [ELISA]) in serum from all primary-school children in two areas of central Thailand were sampled in order to choose a study site for more detailed epidemiological and entomological analysis. Students in three schools in the largely non-agricultural, suburban community of Bang Bua Thong, Nontaburi Province were sampled in late June and July. Of 1,477 children, 33/1,000 had recent dengue infection and 7/1,000 had recent JE infection. The rate of dengue infection in each village influenced the rate in schools, in that the rate of the school could be predicted from the proportion of students coming from each village. This result suggested that most transmission occurred in the residential environment; otherwise, the rate in each village going to a single school would be identical. Serum samples were taken in late August in the agricultural community of Hua Samrong, Chachoengsao Province. Of 748 students in two schools, 95/1,000 had signs of recent dengue infection and 32/1,000 had signs of recent JE infection. Two of 12 villages had significantly less flavivirus infection than some other villages and three villages had significantly more flavivirus infection. The children from one village had a dengue infection rate of 256 per 1,000, which was higher than the national average for the worst year (1987) previously recorded in Thailand. Within Hua Samrong, there was evidence for significant dengue transmission in one of the schools and concentrated transmission in small areas of two of the villages. The younger age group (3–8 years old) had significantly higher risk of infection by either flavivirus than older children. Elevated homes with wooden floors had significantly higher risk of dengue in the largest village. The observations from 1989 describe the epidemiological situation in rapidly developing, rural villages. This stage of development is probably being repeated throughout Southeast Asia as formerly isolated, rural villages become connected by transportation and economy to urban centers. What appears to be a single dengue outbreak based on passive surveillance conducted on a regional basis may actually be a variety of epidemiological situations. The practical implication of this conclusion is that application of a combination of vaccination and vector control should be targeted to higher risk areas in order to increase the likelihood of regional dengue virus eradication.

INTRODUCTION

Some of the highest transmission rates in the world for flaviviruses, including the four serotypes of dengue virus and Japanese encephalitis (JE) virus, are found in Thailand.^{1–3} Public health and clinical interventions can reduce damage from these viruses, but there is a need to target such efforts to areas where transmission is most intense. Thailand's national communicable disease reporting system³ furnishes valuable data on clinically diagnosed dengue and encephalitis among the more than 61 million of its inhabitants. However, most clinically diagnosed dengue is dengue hemorrhagic fever (DHF), so that milder dengue (indistinguishable from many other fevers) goes unreported.^{4–6} The public health reporting system also misses many cases of Japanese encephalitis virus transmission because of misdiagnosis of the cause of aseptic meningitis and because of the large proportion of asymptomatic infections. As a result of these limitations, passive surveillance of dengue and Japanese encephalitis by the Thai public health system is only sensitive to larger scale regional and seasonal trends of virus transmission.^{7, 8}

Active surveillance of flaviviruses attempts to identify every case of transmission, providing data that can be associated with specific risk factors and exact geographic distribution. The hemagglutination inhibition assay (HAI) has been used to assess transmission of dengue in a number of studies, including empirical criteria for distinction of primary from secondary infections.⁹ More recently, enzyme-linked immunosorbent assays (ELISA) have been used to

measure IgG and IgM antibodies separately against dengue and Japanese encephalitis viruses.¹⁰

As a prelude to starting a detailed study of the interaction of vector populations and dengue transmission, in 1989 we undertook a pilot study using active serological (ELISA) surveillance of dengue and Japanese encephalitis to locate a promising field site. The study took place in 1989, but the results are still relevant as they provide a rare look at the transmission of these viruses during that period. Relationships of transmission to local lifestyles, vector populations, and housing types compared to subsequent public health records indicated a relationship between urban development and dengue transmission which may be repeated throughout Southeast Asia.

MATERIALS AND METHODS

Study locations. Study locations were chosen as potential sites for a longitudinal study of dengue transmission. Each location needed to have reasonably high rates of dengue transmission (indicated by public health statistics on DHF and dengue shock syndrome or DSS), a primary-school student population that was representative of the geographic area (i.e., all children in the school came from the area and a large majority of children in the area went to the school), and good relationships with local governments and schools. Primary-school children were considered the ideal sentinel population for dengue in central Thailand. Most infections occurred in this age group because the majority of adults are immune to further dengue virus infection. Furthermore, we

required a location that was close to our central laboratory in Bangkok so that live mosquitoes could be analyzed for virus. Following a review of dengue transmission in the region, we met with provincial governors, provincial directors of public health, and school officials. One of the sources of children for the preliminary 1989 serosurveys were schools in Bang Bua Thong County, Nontaburi Province. Children's blood was sampled in June and July, the serology therefore reflecting dengue infections from May–June. The other source of children was Plaeng Yao County, Chachoengsao Province, which was sampled on August 24, reflecting dengue infections from July–August. Although conclusions are weakened by the one-month difference in sampling times, the authors feel that valid comparisons can be made since both periods are in the peak season of transmission. A more serious concern is the lack of replication over a number of years needed to establish that the data were not exceptional at one site or the other in 1989. Further study would be desirable, but the 1989 study conclusions can at least be viewed as introducing hypotheses, confirming epidemiological patterns observed in other studies, and establishing a baseline for further work.

Children sampled in Chachoengsao Province attended either Hua Samrong or Ao Chang Lai Primary Schools located in Hua Samrong Subdistrict, Plaeng Yao County. Students came from a total population of 10,000 divided into 12 villages. Only Village 1 (small villages in Thailand are commonly designated by number rather than by name) had the appearance of a small town, with rows of shops, the presence of government buildings (including Hua Samrong School), and relatively dense housing. The other villages were smaller, had few shops, and were interspersed with land dedicated to agricultural activity (e.g., mango and custard apple orchards, pastures, small vegetable plots, and rice fields). There were three basic types of dwellings: one-story dwellings made from local materials; elevated houses built from sawn lumber; and one-story cement and cinderblock houses. None of the villages had running water or community trash pick-up. Although the study area was rural in the sense that it was focused on agriculture, residents had a great deal of contact with the provincial capital, Chachoengsao (20 km distant), Bangkok (100 km distant), and other urban centers. Three villages were chosen for more concentrated study, selected so that approximately half of the students attended Hua Samrong School and half attended Ao Chang Lai School. Village 8 was the largest, with 147 school-age children and numerous road connections to other areas. Village 9 had only 65 school children and was the least densely populated of the three villages. Although roads through Village 9 connected different areas, most traffic was local. Village 6, with 54 children, was the smallest and most isolated village. It was completely surrounded by rice fields and had only a single road. Most residents of Village 6 had to store large quantities of water obtained from nearby Ao Chang Lai School because local wells were slightly saline.

The study site in Nontaburi Province differed greatly from the one in Chachoengsao. Located only about 30 km northwest of Bangkok, many residents commuted to Bangkok to work. The majority of students attended a large primary school in the town of Bang Bua Thong, which included middle-class housing developments, government buildings, an

extensive shopping area, and dense housing with running water. Other students attended one of two small schools in outlying areas.

Study participants and samples. Sera were taken from all children in kindergarten through sixth grade (4–13 years old) who were present on the day of sampling (and therefore without acute illness), who were willing to participate, and who had given (through their parents or guardians) written informed consent. The study protocol was approved by the Ethical Review Sub-Committee of the Ministry of Public Health, Thailand, and Institutional Review Boards convened by the Walter Reed Army Institute of Research and the Office of the U.S. Army Surgeon General.

We recorded the school, classroom, home address, age, and gender of each child at the time of sampling. All samples were collected in heparinized capillary tubes from finger sticks. In addition, a serosurvey of preschool children was conducted in Chachoengsao (Village 8) in early November, 1989, recruiting volunteers by asking at each house.

Serology. IgM antibodies to dengue virus (any of the four serotypes, not distinguished by the serological test) and Japanese encephalitis virus were measured in all specimens by antibody capture enzyme immunoassay (EIA).¹⁰ It was necessary to measure antibodies against both viruses, because dengue and Japanese encephalitis occur in the area of the study. Test results were expressed in EIA units (U) established by in-house reference standards. Recent (occurring in the previous two months) flavivirus infection was diagnosed for any individual with an IgM result > 40 U.^{9–11} In most instances, these infections could be classified further as due to dengue virus or Japanese encephalitis virus, depending on the relative amounts of virus-specific IgM. A serological ratio of IgM antibody against dengue virus to IgM antibody against Japanese encephalitis virus > 1.1 defined dengue infection (DEN). A ratio < 1.1 and > 0.91 was considered to be the result of infection with an unknown flavivirus. Finally, a ratio ≤ 0.91 defined a Japanese encephalitis virus infection (JE). The use of IgM prevalence defined by the in-house test to estimate flavivirus infection rates was independently validated using paired specimens taken 2.5 months apart from children elsewhere in Thailand. In the validation study, there was 80% concordance between seroconversions defined by a four-fold rise or fall in hemagglutination-inhibiting antibodies to the four types of dengue virus or Japanese encephalitis virus and recent infections defined by IgM ≥ 40 U in the last serum specimen (Innis BL, unpublished data). The rate defined by IgM prevalence was lower, presumably reflecting the more transient elevation of IgM compared to the total immunoglobulin quantitated by the hemagglutination-inhibition test, especially among those with secondary flavivirus infections. There is good evidence to support the use of the ratio of the anti-dengue virus IgM to the anti-Japanese encephalitis virus IgM that was defined by the in-house test to discriminate between the infecting virus species where the two viruses are sympatric.¹⁰

Preparation of site maps. Results from the villages under concentrated study in Hua Samrong were plotted on maps using a global information program (ATLAS Graphics, Strategic Mapping, Inc., San Pedro, CA). The maps were prepared from aerial photographs examined under a dissecting microscope in order to determine the exact location of every

TABLE 1

Exposure of primary-school students in Nontaburi Province to flavivirus, compared by school attended. Adjusted values include the addition of unknown flavivirus cases in proportion to known dengue (DEN) and Japanese encephalitis (JE) serologies

School	n	Serological results as rate per thousand (95% CI)				Adjusted	
		No flavivirus	DEN	JE	Unknown flavivirus	DEN	JE
1	1,000	953 (940–966)	32 (21–43)	2 (0–5)	13 (6–20)	42 (30–54)	3 (0–6)
2	197	980 (960–1,000)	10 (0–24)	0	10 (0–24)	20 (0–40)	0
3	280	971 (951–991)	11 (0–23)	18 (2–34)	0	11 (0–23)	18 (2–34)
Total	1,477	960 (950–970)	25 (17–33)	5 (1–9)	10 (5–15)	33 (24–42)	7 (3–11)

house, addresses of the houses were confirmed by site visits. Apparent areas of concentrated dengue transmission were determined from plots of DEN-positive and DEN-negative children, not including those with undetermined flavivirus infection.

Analysis. Trends by school, classroom, age, and gender were evaluated by tabulating the data (CROSSTABS procedure, SPSS PC+, SPSS, Inc., Chicago, IL). Adjusted dengue and Japanese encephalitis rates were calculated by adding cases of unknown flavivirus infection in proportion to DEN and JE cases. In addition, 95% confidence limits of percentages (applied as rate per thousand) were calculated so that pair-wise comparisons could be made.¹² Addresses for the areas of concentrated transmission (determined from maps) were extracted from the database and a chi-square test performed to determine whether significantly more children had been infected in the area of concentration than outside of it.

Surveys of larval *Aedes* mosquitoes were conducted near the schools and in Village 8 in Chachoengsao Province, as previously described.¹³ Briefly, every water-filled container in each house was examined and scored as either having or not having *Aedes* larvae. Results were mapped as number of positive containers per house and compared to the spatial distribution of homes having children with recent dengue infection. The number of residents per house and various aspects of house construction were compared between the areas of Village 8 with higher and lower concentrations of dengue infection.

RESULTS

Serological results from Nontaburi showed that there had been moderate levels of flavivirus transmission during the previous two to three months. The adjusted rate among all Nontaburi students was 33 DEN per thousand and 7 JE per thousand. School 1 had significantly more DEN than School 3, but there were no other differences between schools (Table 1). Using 95% confidence limits of the percentages, there were no statistically significant differences between adjusted infection rates of girls (DEN 34/1,000, JE 11/1,000, $n = 695$) and boys (DEN 31/1,000, JE 4/1,000, $n = 692$), age groups (3–8 years: DEN 41/1,000, JE 4/1,000, $n = 688$; 9–15 years: DEN 26/1,000, JE 9/100, $n = 788$), or villages (Table 2) in the Nontaburi schools.

Variation in DEN and JE between schools was closely related to variation between villages that contributed children to the schools. There was a close linear correlation between the number of flavivirus infections in each school and the number calculated from the rate in each village providing children to that school. The regression was calculated with the number of children in the school who were DEN, JE, or flavivirus positive as the dependent variable. The predicted number of children (calculated from the rate in each village and the number of village children in each school) was the independent variable. The result of the regression analysis showed that the profile of villages feeding into each school was highly correlated to each school's infection rate, with $r^2 > 0.99$ for each of the schools. In contrast, there was no significant difference in transmission between classrooms, as might have been expected if there had been a clustering of transmission occurring within schools.

In Chachoengsao, 127/1,000 children were DEN, JE, or flavivirus positive. As in Nontaburi, there were no significant differences between adjusted rates of boys (DEN 100/1,000, JE 33/1,000, $n = 385$) and girls (DEN 77/1,000, JE 33/1,000, $n = 363$) in Chachoengsao, though the unadjusted DEN rate for boys (88/1,000) was twice that for girls (44/1,000). The younger age group (3–8 years) had more flavivirus infections, as shown by a significantly lower rate of uninfected children in the lower age group (834/1,000, $n = 349$, CI = 795–873) than in the older age group (907/1,000, $n = 399$, CI = 879–935). There were great differences in rates of flavivirus infection between the two schools in Chachoengsao (Table 3). Ao Chang Lai School had more than three times the adjusted dengue rate as Hua Samrong School, but only a quarter of the rate of JE. Differences between villages were less apparent than those between schools; however, two villages (Villages 2 and 3) had less flavivirus infection than some other villages and three villages (Villages 4, 6, and 9) had significantly more flavivirus infection (Table 4). Village 9 had the greatest rate of dengue infection (adjusted value of 256/1,000), which was significantly higher than in most other villages.

Examination of the distribution of cases within three of the villages and at the schools suggested that both were important sites of dengue transmission. Figures 1–3 plot the distribution of DEN-positive and DEN-negative children in Villages 6, 8, and 9. In Villages 6 and 8, the areas with the most dengue were significantly different from the areas with

TABLE 2

Exposure of primary-school students in Nontaburi Province to flavivirus compared by village of residence. Other villages were those with less than 15 students. Adjusted values include addition of unknown flavivirus cases in proportion to known dengue and Japanese encephalitis serologies

Village	n	Serological results as rate per thousand (95% CI)					
		No flavivirus	DEN	JE	Unknown flavivirus	Adjusted	
						DEN	JE
Town	240	954 (927-981)	38 (14-62)	4 (0-12)	4 (0-12)	42 (17-67)	4 (0-120)
1	211	976 (955-997)	14 (0-30)	0	9 (0-22)	23 (3-43)	0
2	24	946 (916-976)	36 (12-60)	0	18 (1-35)	54 (24-84)	0
3	326	979 (963-995)	0	9 (0-19)	12 (0-24)	0	21 (5-37)
4	149	987 (969-1,000)	13 (0-32)	0	0	13 (0-31)	0
5	72	903 (835-971)	83 (19-147)	0	14 (0-41)	97 (29-165)	0
6	169	947 (913-981)	36 (8-64)	6 (0-18)	12 (0-28)	46 (14-78)	8 (0-21)
13	44	909 (824-994)	45 (0-106)	23 (0-67)	23 (0-67)	60 (0-130)	31 (0-82)
Other*	35	943 (866-1,000)	29 (0-85)	29 (0-85)	0	29 (0-85)	29 (0-85)

* Villages with < 15 students.

less dengue (Table 5), suggesting that there were areas of concentrated transmission within those two villages.

Data from Village 8 showed that transmission within schools might have also been important. Approximately half of the children in Village 8 attended Hua Samrong School (78 children, 3 with dengue exposure) and half attended Ao Chang Lai School (69 children, 5 with dengue exposure). Within the area of concentration in Village 8 (where transmission probably occurred at home) four of the cases were among preschool children and two were from students at Hua Samrong School, the school with the lower rate of dengue. In contrast, five of six cases outside of the area of concentration were from students attending Ao Chang Lai School, the school with a high rate of dengue, suggesting that they acquired their infection at school.

Aedes larvae were present in and near the schools in Chachoengsao. At Hua Samrong School, there were 29 positive sites in homes or in outbuildings within 20 m of classrooms. Twenty-three of the sites were water jars, six were cement basins in bathrooms, and one was a dish used to provide water for chickens. In the school itself, three of 29 classrooms contained flower vases with *Aedes* larvae. Ao

Chang Lai School had a greater number of larvae, with a total of 50 positive sites near classrooms. These consisted of 46 water jars, two piles of coconut shells, one plastic bottle, and one plastic bucket. Thirty-nine (78%) of the positive sites were concentrated near the four classrooms used for kindergarten and first grade. Two of 18 classrooms had a total of seven flower vases with larvae.

Surveys of homes in Village 8 showed that construction characteristics differed in the area of concentrated dengue transmission. First, the mean elevation of the floor above the ground was greater in the area with more dengue (Table 6). Second, proportionately more floors were made of wood and fewer were made of cement (Table 7). Finally, proportionately more walls were made of wood and fewer were made of masonry (Table 7), though this trend was only marginally significant statistically. Gaps in the walls, composition of the roofs, nature of window coverings, and frontage length of the houses were the same in the two areas. It is noteworthy that none of the houses in the village had screens. The mean number of positive containers per house was essentially the same in both areas, but visual inspection of a map plotting distribution of containers with *Aedes* larvae indicated a

TABLE 3

Exposure of primary-school students in Chachoengsao Province to flavivirus compared by school. Children were sampled on 24 August, 1989. Adjusted values include addition of unknown flavivirus cases in proportion to known dengue and Japanese encephalitis serologies

School	n	Serological results as rate per thousand (95% CI)					
		No flavivirus	DEN	JE	Unknown flavivirus	Adjusted	
						DEN	JE
Hua Samrong	462	909 (883-935)	39 (21-57)	32 (16-48)	19 (7-31)	49 (29-69)	41 (23-59)
Ao Chang Lai	286	815 (770-860)	112 (75-149)	7 (0-17)	66 (37-95)	174 (130-218)	11 (0-23)
Total	748	873 (849-897)	67 (49-85)	23 (12-34)	37 (23-51)	95 (74-116)	32 (19-45)

TABLE 4

Exposure of primary-school students in Chachoengsao Province to flavivirus compared by village. Children were sampled on 24 August, 1989. Adjusted values include addition of unknown flavivirus cases in proportion to known dengue and Japanese encephalitis serologies

Village	n	Serological results as rate per thousand (95% CI)				Adjusted	
		No flavivirus	DEN	JE	Unknown flavivirus	DEN	JE
1	109	862 (797-927)	73 (24-122)	46 (7-85)	18 (0-43)	84 (32-136)	53 (11-95)
2	84	940 (889-991)	36 (0-76)	12 (0-35)	12 (0-35)	45 (1-89)	15 (0-41)
3	56	964 (915-1,000)	18 (0-53)	18 (0-53)	0	18 (0-53)	18 (0-53)
4	46	891 (801-901)	87 (6-168)	0	22 (0-64)	109 (19-199)	0
5	48	875 (781-969)	42 (0-99)	21 (0-62)	63 (0-132)	84 (6-162)	42 (0-99)
6	54	741 (624-858)	130 (40-220)	0	130 (40-220)	26 (0-68)	0
7	118	924 (876-972)	34 (1-67)	42 (6-78)	0	34 (1-67)	42 (6-78)
8	147	871 (817-925)	54 (17-91)	14 (0-33)	61 (22-100)	48 (13-83)	35 (5-65)
9	65	723 (614-832)	185 (91-279)	15 (0-45)	77 (12-142)	256 (150-362)	21 (0-56)
10	14	857 (674-1,000)	71 (0-206)	71 (0-206)	0	71 (0-206)	71 (0-206)
11	1	1,000	0	0	0	0	0
12	2	1,000	0	0	0	0	0
Other*	4	1,000	0	0	0	0	0

* Villages with < 15 students.

slightly higher density of larval sites on the side of the village with more dengue. Furthermore, the area of concentrated dengue transmission was located adjacent to the main transportation route.

DISCUSSION

Widespread, endemic transmission of dengue is a relatively recent development in central Thailand. Historical data are necessarily based on severe illness (usually assumed to be DHF if serious enough for hospitalization), because only the most severe cases are reported through the public health system. Ungchusak and Kunasol¹⁴ divided the early history of dengue hemorrhagic fever in Thailand into three

phases between 1958 and 1987, with rural transmission starting in 1978. They claimed that by 1985, 80% of transmission took place in rural areas. Public health statistics document an increase in the proportion of rural, symptomatic dengue (mostly DHF) from 43% in 1987 to 51% in 1995.³ Wellmer⁷ attributed the extension of dengue infection to increases in public transportation and provincial population, specifically mentioning Chachoengsao Province as a place likely to experience large increases. Since 1990, the rate of dengue in Bangkok has actually decreased relative to other sites in Thailand.³ Throughout the history of dengue in Thailand, the disease has occurred in outbreaks separated by two to four years. In the year of the current study, 1989, the total number of DHF cases (a small proportion of total seropositive chil-

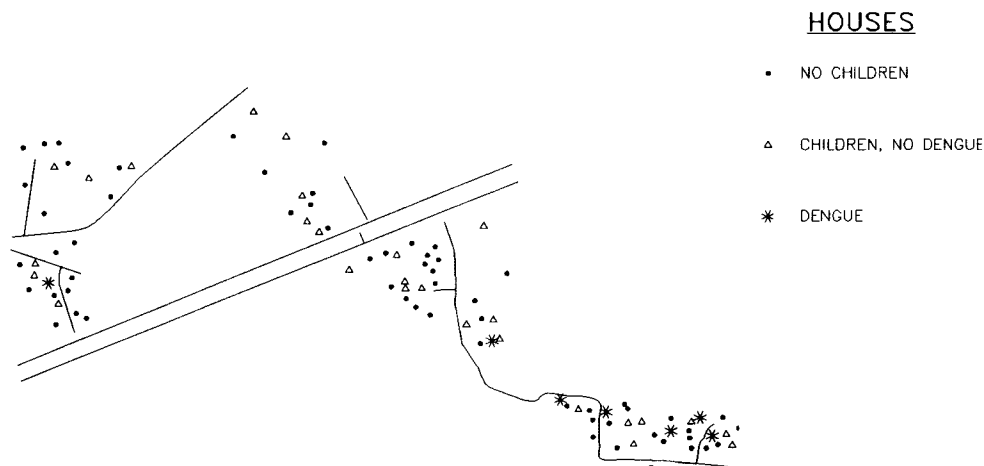


FIGURE 1. Distribution of children (4-13 years old) in Village 6 with and without serological indications of recent dengue infection.



FIGURE 2. Distribution of children (all ages to 13 years old) in Village 8 with and without serological indications of recent dengue infection.

dren in any given year) in Thailand was 69,204 (380 per 100,000 children < 15 years old), compared to outbreak years of 1985 with 80,076 (390 per 100,000 children), 1987 with 174,285 (819 per 100,000 children), and 1990 with 113,855 cases (420 per 100,000 children).^{3,8}

Comparisons of the results in Nontaburi and Chachoengsao are difficult because of the two-month difference in sampling. The peak rate of symptomatic dengue usually occurs in the latter half of summer, though there has been considerable variation from 1989–1998 (Table 8). This variation is an example of the important epidemiological differences that can occur locally, despite what appears to be a consistent national trend for peak transmission in July.³

Results from Nontaburi revealed few details about epidemiology in Bang Bua Thong County. Considering that 87% of dengue infections in children are asymptomatic,⁵ the observed rate of 33 DEN per 1,000 children can be roughly

translated to 4 symptomatic cases per 1,000. This rate suggests that transmission in 1989 in Bang Bua Thong County was at least moderately high relative to historical rates (5/1,000) of symptomatic dengue during the epidemic year of 1987 in Nontaburi (Epidemiology Section, Department of Health, Nontaburi Province, “Situation of Dengue in Nontaburi Province, January 1987 to July 1989”) and throughout Thailand (8/1,000).³ Our results also suggested that dengue was transmitted mainly in homes rather than in schools in Nontaburi during the first half of the rainy season.

Sampling in late August in Chachoengsao probably captured data on a greater proportion of total infections than the earlier sampling in Nontaburi. Therefore, the data from Chachoengsao may show more epidemiological details. The probable difference in infection between males and females suggests a behavioral difference that causes boys to be bitten by mosquitoes in different areas of the community. Other

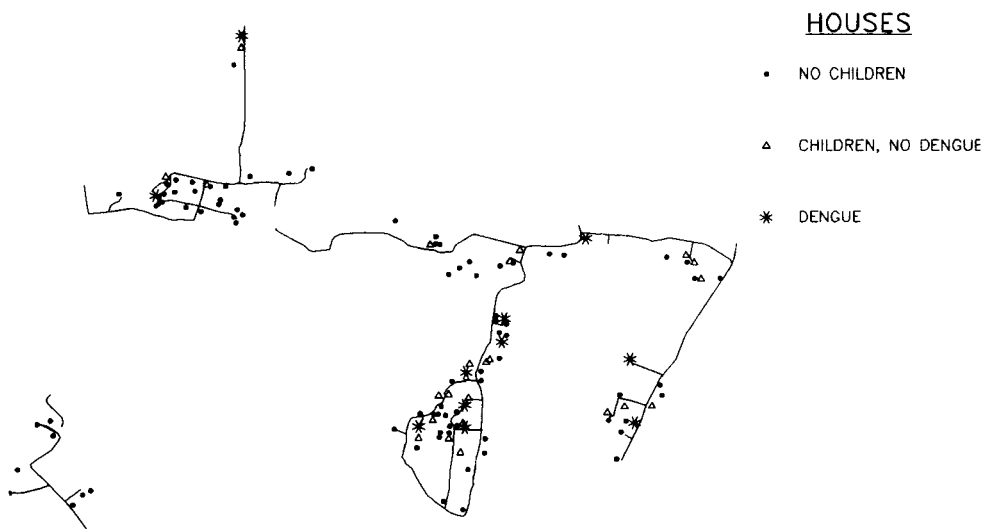


FIGURE 3. Distribution of children (4–13 years old) in Village 9 with and without serological indications of recent dengue infection.

TABLE 5

Occurrence of recent dengue infection in primary-school students from three villages in Chachoengsao. Preschool children were sampled in Village 8 only. Number of students varies from Table 8 because of students with unknown addresses

Village No.	Area of concentration	No. (%) with dengue	No. (%) with no dengue	Those with dengue: age in yrs (school)*
6	In†	5 (26)	14 (74)	6 (A), 8 (A), 9 (A), 9 (A), 9 (A)
6	Out	2 (7)	28 (93)	6 (A), 6 (A)
8	In‡	6 (12)	46 (88)	1 (P), 2 (P), 4 (P), 5 (P), 7 (H), 8 (H)
8	Out	6 (4)	143 (96)	6 (H), 7 (A), 8 (A), 8 (A), 8 (A), 10 (A)
9	In§	5 (18)	23 (82)	6 (A), 7 (A), 8 (A), 9 (A), 9 (A)
9	Out	7 (19)	29 (81)	6 (A), 7 (A), 7 (A), 7 (A), 8 (A), 9 (A), 11 (A)

* P = preschool, A = Ao Chang Lai, H = Hua Samrong.

† Chi-square for in versus out, with or without dengue = 3.67, df = 1, P = 0.055.

‡ Chi-square = 3.87, df = 1, P = 0.049.

§ Chi-square = 0.026, df = 1, P = 0.87.

studies have found that either males¹⁵ or females^{15,16} may be predominately infected, depending on the local situation.

In other studies, association of dengue with age has depended on a number of aspects of their particular focus. Where dengue does not occur yearly, older age groups have the highest rates of infection. For example, Kaplan and others¹⁶ found that Mexican adults 40 to 59 years old had the highest infection rates as determined by a nationwide 1980 survey using HAI assay. Waterman and others¹⁷ also reported high infection rates in older children and adults 10 to 29 years old in Puerto Rico during 1982. In endemic areas, younger children tend to suffer the highest rates of infection and the most illness. Russell and others⁴ observed that 17–44% of children 2–10 years old on Samui Island, Thailand, had HAI titers indicative of recent exposure. Summarizing public health statistics, Ungchusak and Kunasol¹⁴ showed that children under the age of 15 had the highest rates of DHF during the 1987 outbreak in Thailand. Up to 1997, the age distribution of symptomatic dengue has increased, though the age group 5–9 years old always had the highest rate.³ Public health statistics from Nontaburi and Chachoengsao reflect this trend, though the difference in age groups was most pronounced in Chachoengsao prior to 1996 (Table 8). The results of our study in Chachoengsao indicated that the area was an endemic focus in 1989, with the younger age group having the higher rate of infection.

The most interesting aspect of dengue transmission in Chachoengsao was the appearance of specific foci of transmission in two of the villages and in one of the schools. The density of vector mosquitoes may have been one of the factors causing the concentration of transmission since the school with more dengue had more larval sites and the part of Village 8 with more dengue had marginally more larval sites than the remainder of the village. Although the area of concentrated dengue transmission in the village was asso-

ciated with a higher concentration of wooden elevated houses, direct association between this construction type and transmission is unclear.

A number of studies have detected clustering of dengue cases within communities. Schools are a logical focus for transmission in endemic areas, since asymptomatic, viremic children associate with other children in a setting that often includes the vector.^{6,18} Among homes, transmission can be clustered within households,^{17,19} within groups of houses in neighborhoods,^{20,21} or in particular neighborhoods within cities.²² The correlates associated with clustering of dengue infection included larval abundance of *Aedes aegypti* and generally lower socioeconomic conditions^{17,22} or greater abundance of adult vector mosquitoes.²¹ The extreme variation of DEN rates in Chachoengsao villages is another indication of how transmission can be more concentrated in one area and less concentrated in nearby areas. The rate of 256 DEN per 1,000 in Village 9 would translate to approximately 33 symptomatic cases per 1,000, compared to a national rate of only 8 cases per 1,000 for the entire year of 1987, the worst epidemic Thailand had experienced up to 1997.³

The data from this study represent serological snapshots

TABLE 7

Qualitative characteristics of houses in relation to whether house was located inside area of concentrated transmission of dengue or outside area of concentrated transmission in Village 8

Category	Characteristic	No. (%) per category		P of differences within category*
		Outside	Inside	
Floor	Cement	68 (39.5)	3 (11.1)	0.021
	Wood	99 (57.6)	24 (88.9)	
	Dirt	4 (2.3)	0	
	Other	1 (0.6)	0	
Wall gaps	No gaps	126 (72.4)	18 (66.7)	0.54
	With gaps	48 (27.6)	9 (33.3)	
Walls	Wood	86 (49.7)	21 (77.8)	0.10
	Bamboo	7 (4.0)	1 (3.7)	
	Mat	1 (0.6)	0	
	Masonry	67 (38.7)	3 (11.1)	
	Thatch	10 (5.8)	2 (7.4)	
	Metal	2 (1.2)	0	
Roof	Cement tile	87 (50.3)	14 (51.9)	0.57
	Thatch	7 (4.0)	0	
	Metal	79 (45.7)	13 (48.1)	
Windows	Solid	70 (40.9)	12 (44.4)	0.88
	Glass	59 (34.6)	8 (29.6)	
	Open	42 (24.6)	7 (25.9)	

* Determined by chi-square test.

TABLE 6

Quantitative characteristics of houses in relation to whether house was located inside area of concentrated transmission of dengue or outside area of concentrated transmission in Village 8

Characteristics	Mean ± SD		P*
	Outside	Inside	
Frontage length (meters)	9.0 ± 2.7	9.2 ± 2.7	0.750
Floor elevation (meters)	1.0 ± 0.9	1.5 ± 0.8	0.007
Positive containers/house	4.3 ± 5.5	3.9 ± 2.9	0.609

* Determined by unpaired t-test.

TABLE 8
Symptomatic dengue recorded by the Ministry of Public Health, Thailand, in Nontaburi and Chachoengsao Provinces

Year	Total Cases	Peak Month (%*)	Percentage of cases for year			
			May-June	July-August	Age 5-9	Age 10-14
Nontaburi						
1989	813	Aug (20)	11	34	34	29
1990	499	Aug (14)	20	28	35	31
1991	187	Jan (17)	7	22	50	28
1992	222	Oct (19)	8	24	36	26
1993	314	Nov (14)	14	19	27	35
1994	356	Sep (17)	13	28	28	31
1995	282	Aug (25)	10	40	31	27
1996	284	Nov (20)	10	24	31	27
1997	2,101	Sep (23)	3	20	26	27
1998	1,618	Jan (18)	8	17	24	26
Chachoengsao						
1989	873	Jun (23)	29	39	39	30
1990	760	Jun (29)	34	42	42	26
1991	109	Jul (18)	18	30	46	25
1992	626	Sep (32)	24	37	35	37
1993	350	Jul (18)	20	36	45	28
1994	325	Jul (27)	14	50	42	22
1995	450	Aug (24)	17	38	38	27
1996	498	Jul (22)	28	37	38	32
1997	1,344	Aug (28)	15	45	29	31
1998	545	Mar (14)	19	23	31	29

* Percentage of cases for the peak month compared to total for the year.

of dengue and Japanese encephalitis virus transmission approximately twelve years ago. Since that time, Bang Bua Thong has become more closely associated with Bangkok and Hua Samrong has become less rural. The sequential change of communities in Thailand is probably representative of development throughout Southeast Asia. Completely isolated, rural communities have little risk of dengue, but become susceptible once transportation systems connect them to sources of the major vector, *Aedes aegypti*. Rural communities have the greatest risk of dengue transmission when they are at the stage where transportation is good but local services are absent. Hua Samrong in 1989 was a good example of a community with this high risk because people working in nearby cities could constantly reintroduce dengue virus and the vector could reach a maximum number of people due to the lack of running water and trash pick-up. Suburban areas like Bang Bua Thong probably could have been expected to see a decrease in transmission as city services improved. Large cities like Bangkok finally achieve a decrease in transmission when economics allow widespread distribution of services, reducing vector populations. The significant rates of Japanese encephalitis infection observed on the outskirts of Bangkok and in Chachoengsao indicate that this zoonotic disease continues to infect the human population, despite the availability of a vaccine. Public health statistics which only report symptomatic Japanese encephalitis are almost blind to the threat, having reported only two cases of the disease in Nontaburi and two cases in Chachoengsao from 1994 through 1999 (Ministry of Public Health, Thailand, unpublished data). More current serosurveys would be welcome additions to the literature, possibly documenting some of the generalizations suggested by a comparison of our older data to public health statistics.

The capability of assessing risk of dengue transmission within a community would be very useful in controlling this

disease. Concentration of mosquito abatement assets in high-risk areas could conceivably stop an outbreak before it had a chance to start. Numerous studies^{17,21-27} suggest what would seem to be a self-evident connection between vector density and intensity of transmission. However, there is currently strong opinion that the correlation is weak^{28,29} and that transmission will proceed when the vector is scarce.³⁰ Probably both sides of the argument are true, depending on the specific situation of vector density, vector competence, and human population immunity. Our study suggests that patterns of transmission can be different in communities that are located close to each other, creating a situation where epidemiologically distinct outbreaks occur simultaneously. This distinction may be most evident during times when transmission is at a relatively low level. Despite the potential for exceptions, the safest general assumption is that schools and poorer neighborhoods should be given priority for dengue vector control.

Hopefully, a tetravalent dengue vaccine will be available in the near future. Like vector control, this important tool should be targeted to foci of greatest transmission, regardless of the ability of local residents to purchase the vaccine. By preferentially applying vaccination and vector control to concentrated foci and by protecting dengue-free areas with barriers of preventive treatment, there is a real and very favorable possibility that the disease could be eliminated regionally. Relying on distribution of vaccine according to economic resources would probably result in inconsistent prevention, as seems to be demonstrated by the high prevalence of antibody to JE demonstrated in this study despite the availability of an effective vaccine.

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