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Changing epidemiology of dengue hemorrhagic fever in Thailand

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SUMMARY

Dengue haemorrhagic fever (DHF) and dengue shock syndrome (DSS) are reportable diseases, the third most common causes for hospitalization of children in Thailand. Data collected from the Ministry of Public Health were analysed for trends. Rates of DHF increased in Thailand until 1987 when the largest epidemic ever, 325/100000 population, was recorded. Whereas the disease used to be confined to large cities, the rate is now higher in rural (102·2 per 100000) than urban areas (95·4 per 100000 in 1997). The age of highest incidence has increased, and the age group most severely affected is now those 5–9 years old (679/100000 in 1997). The case fatality rate has decreased with improved treatment and is now only 0·28%.

INTRODUCTION

Epidemics of dengue fever were first reported from the coast and later from the inland in Southeast Asia in the 19th century [1]. The first description of an outbreak of dengue haemorrhagic fever (DHF) was reported from the Philippines in 1953, followed by an outbreak in Thailand in 1958 [2]. Dengue haemorrhagic fever and dengue shock syndrome (DSS) are serious complications of dengue infection that occur primarily in children. In Thailand DHF occurred first only in Bangkok, but soon spread to the suburbs and other municipal areas [3, 4]. Dengue, DHF and DSS are now endemic in Southeast Asia. During the last decade dengue infection with its complications has increased globally [5–7]. Imported cases of dengue have been reported from Europe and the USA. The spread of DHF and DSS has resulted in its being considered as one of the emerging infectious diseases [8]. It has been thought of as a primarily urban disease.

Because DHF is so common in Thailand, Thai medical students are thoroughly trained to recognize and treat the disease and practically all cases of DHF and DSS are hospitalized. DHF and DSS occur primarily in children who have previously acquired antibody to another serotype of the four dengue viruses, and in infants who still have maternal antibody [7, 10–12].

The main vector, *Aedes aegypti*, a domestic mosquito, is thought to have been introduced to Asia from Africa [1, 13]. *Aedes albopictus*, a mosquito present in the vegetation, particularly in forested areas, may also serve as a vector [13]. *Ae. aegypti* was almost eradicated in the Americas with control of yellow fever, but has now returned [7, 14]. This makes future epidemics of dengue and its complications a possibility even in the United States.

The purpose of this communication is to describe the changes in the epidemiological pattern of DHF in Thailand.

METHODS

Reporting

A system for reporting communicable diseases including DHF/DSS was instituted in Thailand in 1972,

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and was considered fully installed in 1974. The case reports contain information on age, sex, day of onset, the address (locality) where the case occurred, separating municipalities (cities and suburbs) and 'other' (mostly rural) areas. A clerk is responsible for reviewing all in- and out-patient records and reports to the provincial health office, which delivers the reports to the Division of Epidemiology of the Ministry of Public Health. These reports are now forwarded electronically. The surveillance system is directed by supervisory teams from the five Regional Epidemiological Centres to ensure complete and accurate reporting. The Thai data have been computerized, and the current report is based on the data bank of DHF and DSS available at the Ministry of Public Health, Bangkok. The dengue haemorrhagic fever category included both DDS and DHF from 1972–81, and are presented here together. After 1982 DHF and DSS were reported as separate entities, but not consistently from all areas of the country. Beginning in 1989 dengue fever was also reported, but is not included in this report. In 1993, 11·6% of DHF reports originated from central (tertiary) hospitals, 32% from general hospitals, 50·5% from community hospitals, 3·6% from municipal hospitals in Bangkok, 1·4% from private hospitals and 0·7% from official clinics and health centres. Thai hospitals provide both in- and out-patient care, but by necessity practically all DHF cases are hospitalized.

Diagnosis

Most DHF cases are diagnosed by clinical and haematological observations based on WHO criteria [9]. It is logistically impossible to verify the diagnosis serologically during epidemics, when hospitals quickly fill up with DHF cases requiring intensive monitoring of the fluid balance. Serological testing is done only in the beginning of epidemics and in doubtful cases.

Laboratory methods

In a proportion of cases, particularly in the dry season (December–April), antibody studies are carried out. Sera are collected on special filter papers and tested by ELISA [15] and haemagglutination-inhibition (HI) [16] techniques. The National Laboratory receives 6000–8000 serum samples annually, primarily from physicians unsure of the diagnosis. Thus in 1994, 68·4% of the sera were antibody positive, 13% negative, and 18·6% were uninterpretable for technical reasons.

Typing of dengue viruses is carried out at the Virus Research Institute, Department of Medical Sciences, the Thai National Institute of Health and at the Armed Forces Research Institute of Medical Sciences (AFRIMS) in Bangkok. These institutions collaborate and share information with the Ministry of Public Health. AFRIMS laboratory provides isolation and typing of the virus from patients at the nearby Children's hospital and from Aedes mosquitoes. Thus, the predominant virus types are known for Bangkok for each season, but not for the rest of the country.

RESULTS

Secular trends

Figure 1 shows the rate of DHF/DSS in children $<$ 15 years old, 1974–97. Major epidemics occurred at 2-year intervals in the 1970s, whereafter the intervals between major epidemics became longer, but incidence increased. The largest epidemic ever was recorded in 1987 with 174285 cases for an incidence of 325/100000 per total population, and 819/100000 in children $<$ 15 years of age. There were 1007 deaths reported.

Only for Bangkok is there sufficient knowledge about which of the four dengue serotypes was predominant in different years. Serotype 2 has been the most frequent isolate, present in all years. Serotype 2 was predominant in 1980–1, but serotype 1 was also present. In 1987, the year of the highest incidence, serotypes 2 and 3 predominated. Between 1989–91 serotypes 1 and 2 were isolated in almost the same proportion. Serotype 4 was rarely found, it was present in 1984–5 and again in 1992.

Seasonality

The incidence during the cold months of December and January is low and starts to increase during the dry hot months of April–June (Fig. 2). Epidemics usually peak 2–4 weeks after the arrival of the rains, which may begin anytime between June–September with considerable local variation. The rainy season is usually over in October, but can last into November. Whereas epidemics coincide with the rainy season, the magnitude of the epidemics appears not to be related to rainfall.

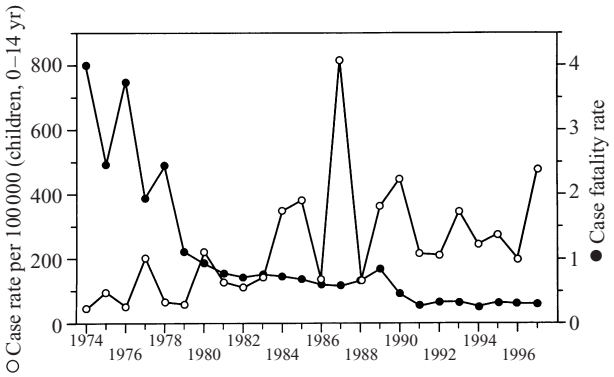

Fig. 1. Rates of dengue haemorrhagic fever/100000 children < 15 years old (○), and case fatality rate (●), Thailand, 1974–97.

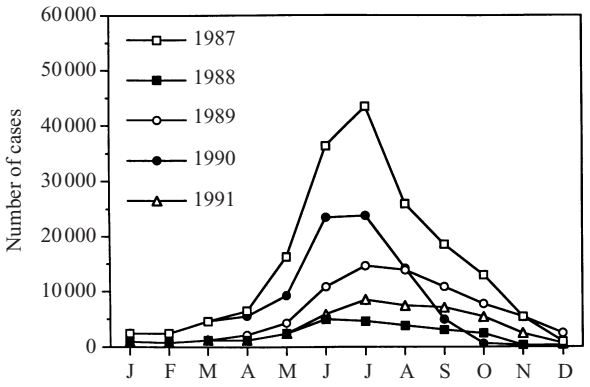

Fig. 2. Reported cases of dengue haemorrhagic fever by month, Thailand, 1987–91.

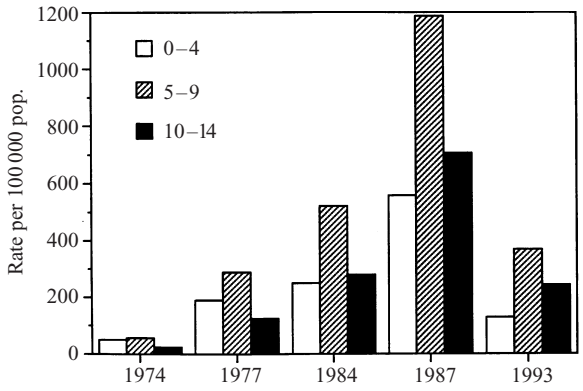

Fig. 3. Reported cases of dengue haemorrhagic fever/100000 population by age group, Thailand, for selected year 1974–93.

Age and sex distribution

Figure 3 shows incidence by age group for selected years 1974–96. Rates have constantly been highest in the 5–9 year age group with a trend of increasing mean age with time. The incidence in those over > 15 years is relatively low, 57/100000 in the large epidemic of 1987. However, rates in this age group have slowly

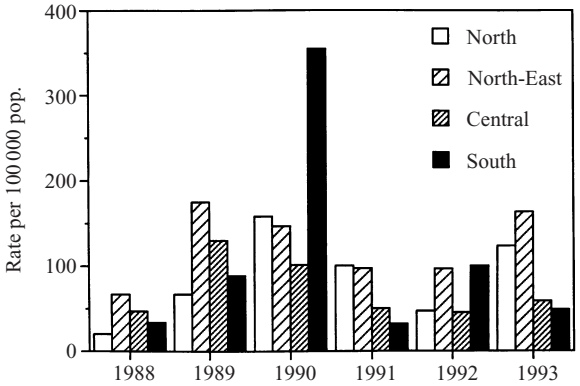

Fig. 4. Reported cases of dengue haemorrhagic fever by region, Thailand 1988–93.

increased from 1·20 in 1974 to 20·5/100000 in 1994. Rates in the 0–4 year age group were about twice of those 10–14 years old in 1974. This has reversed itself by time, and the rate of 0–4 year old children is now about half of those 10–14 years old. Age distribution follows exactly the same pattern in the metropolitan area of Bangkok as in rural areas and the South except that in the large epidemic in the south in 1990 18% of all reported cases were adults (> 15 years), instead of the usual proportion of 9%. Overall rates by sex are similar, with a slight excess in females, ratio 1000:1017.

Regional differences

Figure 4 shows the incidence by the four different regions of Thailand by year. Widespread epidemics occurred primarily in the north, central, and northeast regions, which are relatively arid, until 1990 when a major epidemic occurred in the rainy South. The south has the highest rainfall in Thailand, and in contrast to the rest of the country, the rainy season has two peaks, one in July–August, the other in late October through December. Yet the epidemic has followed the same monthly pattern in the South as the rest of Thailand, with highest rates in June–September, following the hot season. In 1989 two provinces of the south suffered severe flooding from the monsoon. This did not alter the dengue epidemic in 1989. However, rates remained high during the cold season, and the following year (1990) the South experienced a major epidemic.

Rural/urban distribution

The rate of DHF reported from rural areas has increased with time. Thus, in 1987 the rate for rural areas was 300·8/100000 total population, for mu-

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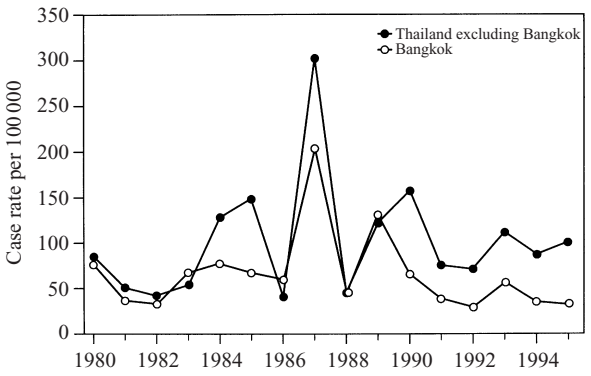

Fig. 5. Reported cases of dengue haemorrhagic fever/100000 total population for Bangkok, (○), and Thailand excluding Bangkok (●), 1980–95.

nicipal areas 405·2/100000. The corresponding rates for 1995 were 100·2 for rural and 95·4/100000 for municipal areas. The proportion of DHF reported from rural areas has thus increased: In 1989 it was 70%, in 1990 80%, in 1991 78%, in 1992 79% and in 1993 82% of all reports, a period when considerable emigration from rural to urban areas has taken place. Rates for Bangkok have decreased compared with the rest of the country (Fig. 5).

Case fatality rates

Case fatality rates, highest in children < 5 years old, has decreased with time; it was 0·99% in 1980 and declined step by step to 0·30% in 1996 (Fig. 1). In the 1960s the case fatality rate was as high as 6–8% [12]. The case fatality rate in Bangkok, where there is easy access to tertiary hospitals, averaged 0·07% and for the rest of the country it averaged 0·50 for the period 1986–95.

DISCUSSION

These data from Thailand show that DHF, which originally was thought to be a disease of major cities [2], has spread to most areas of Thailand, and is now more common in rural than urban areas. This rural spread probably accounts for the increasing national rates. *Ae. aegypti* a mosquito believed to have been imported from Africa during the 19th century, has also been tracked from large cities to smaller communities and finally into villages. Higher rates in rural areas may be due to more dependence on water storage from the rainy to the dry season. In Bangkok, as well as other municipal areas, housing has been modernized and tap water has become widely available.

The burden on the health care system is heavy, costs for hospitalization are estimated at 6–8 million $U.S. per year (unpublished data, Ministry of Public Health, Thailand). DHF is the third most common cause for hospitalization of children, exceeded only by respiratory infections and diarrhoeal diseases. Since *Ae. aegypti* has become quite common, and entomological studies show increasing infestation with this mosquito [17], it is no surprise that the incidence of DHF and DSS has increased [13]. The South of Thailand was relatively spared from DHF/DSS until 1990. However, dengue infections were documented in outbreaks of fever in 1987 [18]. Thus, the subsequent outbreak of DHF/DSS in 1990 supports the hypothesis that it is a manifestation of a second infection with a different type of dengue virus.

Only Vietnam reports more cases of DHF/DSS than Thailand, but its population is larger [6]. Malaysia reports fewer cases, and greater variation in age distribution and secular incidence [19]. The impact in other neighbouring countries is not as well documented in the accessible literature. In 1987, the year of highest incidence in Thailand; Vietnam, Malaysia and Burma also reported record incidence, whereas Taiwan and the Philippines had major epidemics the following year [6]. Whether the severe 1987 epidemic was just a chance phenomenon or due to some minor change in the predominant type 2 and 3 viruses is unknown [20].

The large epidemics seemingly consist of a composite of small independent epidemics in various areas, and the disease can sometimes be traced from village to village [21]. In cities 'brushfires' (clusters) of DHF have been noticed [22]. The proportion of DHF of all dengue infection is small, approx. 10% among school children [11, 21]. The falling case fatality rate may be partly due to more complete reporting of milder cases. However, the health care system has expanded and Thai physicians become well trained in the management of DHF/DSS in medical school.

The peak age for hospitalization of DHF was at 3 years in the 1960s [3, 12], but the highest incidence by age is now at 5–9 years with a trend towards higher age. Adults are now also being affected. The reason for this change in age distribution is incompletely understood, possibly it may be due to less frequent epidemics in the last decades so that second exposure to dengue virus is postponed.

Vector efficiency of *Ae. aegypti* increases with increasing temperature (at least to 32–35 °C) for dengue virus [23, 24]. This may explain the increasing

DHF/DSS rates during the dry hot season. Possibly global warming may contribute to wider spread of dengue infections [25]. The availability of more water and higher humidity, including higher biting rates, may augment the epidemic during rainy period [13, 25].

Control methods, such as fogging with malathion have only short term effects [24, 27–29]. Use of larvicides such as temephos has limited use because most Thais object to the smell [27]. Temephos is available through the health offices, but it is estimated that less than 10% of households make use of it; only the wealthier households can afford it. The larvae are difficult to detect for laymen, and many households are unaware of heavy infestation with larvae and thus mosquitoes. Knowledge about the mode of infection and the presence of the vector is relatively good among housewives [30]. Intensive community based health education as intervention for the control of *Ae. aegypti* with emptying and scrubbing all water containers regularly, may work, if there were a concerted effort [31, 32]. Ultimately, an effective and long lasting vaccine to be used in childhood is needed.

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