Chapter 1

Introduction

Dengue Haemorrhagic Fever (DHF) is the most serious form of the dengue fever, caused by the Dengue virus categorised in the family of Flaviviridae. It is a serious health problem in tropical regions. In the decade from 1978-87, there were 633,068 cases of DHF in Myanmar, Indonesia and Thailand. It killed 1047 persons in Myanmar, 4324 in Indonesia, and 3613 in Thailand (Jatanasen & Thongcharoen, 1993). The case-fatality rate was thus 1.4%. Even when not fatal, DHF is a serious illness that can incapacitate its victims for lengthy periods. In its least severe form, the disease is characterized by fever, headache, joint and muscular pain in various parts of the body, skin rash, and leucopenia (Jatanasen & Thongcharoen, 1993).

The first reported outbreak of DHF occurred in the Philippines in 1953 (Quintos et al, 1954). DHF has been one of the major public health problems in Thailand since it was first identified in 1958 in Bangkok and nearby provinces. DHF transmission in highly populated provinces in Southern Thailand, including Nakhon Si Thammarat and Songkhla, is of concern.

The *Aedes aegypti* mosquito is the most important vector of dengue virus transmission in the South East Asian region. The vector ecology and bionics of DHF were described in detail by Pant & Self (1993). The virus multiplies rapidly in mosquito larvae. The mosquito deposits its larvae in water containers used by humans for drinking, bathing, agriculture, and fire prevention. The virus is transmitted to humans who get bitten by an infected mosquito. A vaccine has not yet been developed.

There have been reports that climatic factors including rainfall, temperature, and humidity may be important determinants of DHF incidence including studies conducted by Foo et al (1985), Gubler (1988), Gould et al (1970) and Kuno (1997). However, other studies (for example, Jatanasen et al, 1961, Ghosh et al 1974, and Eamchan et al, 1989)(Kuno, 1997) have reported contradictory evidence for the effects of climatic factors on dengue incidence. The relationship between the climatic factors and DHF incidence is thus still inconclusive.

In 1998 in Thailand, there were 98,123 cases of DHF, 341 deaths, with incidence rate of 161.3 per 100,000 and mortality rate 0.35%. The DHF incidence rate of Region 11 in Southern Thailand was highest at 272.4, whereas Regions 7 and 6 in the Northeast has the incidence rate of 247.8 and 219.2 respectively and Region 8 in the North having the lower rate 102.3. (Office of The Permanent Secretary for Public Health). From these reported cases it is thus seen that DHF is a problem in Southern Thailand. Therefor, we should investigate the factors influencing DHF incidence of Southern Thailand.

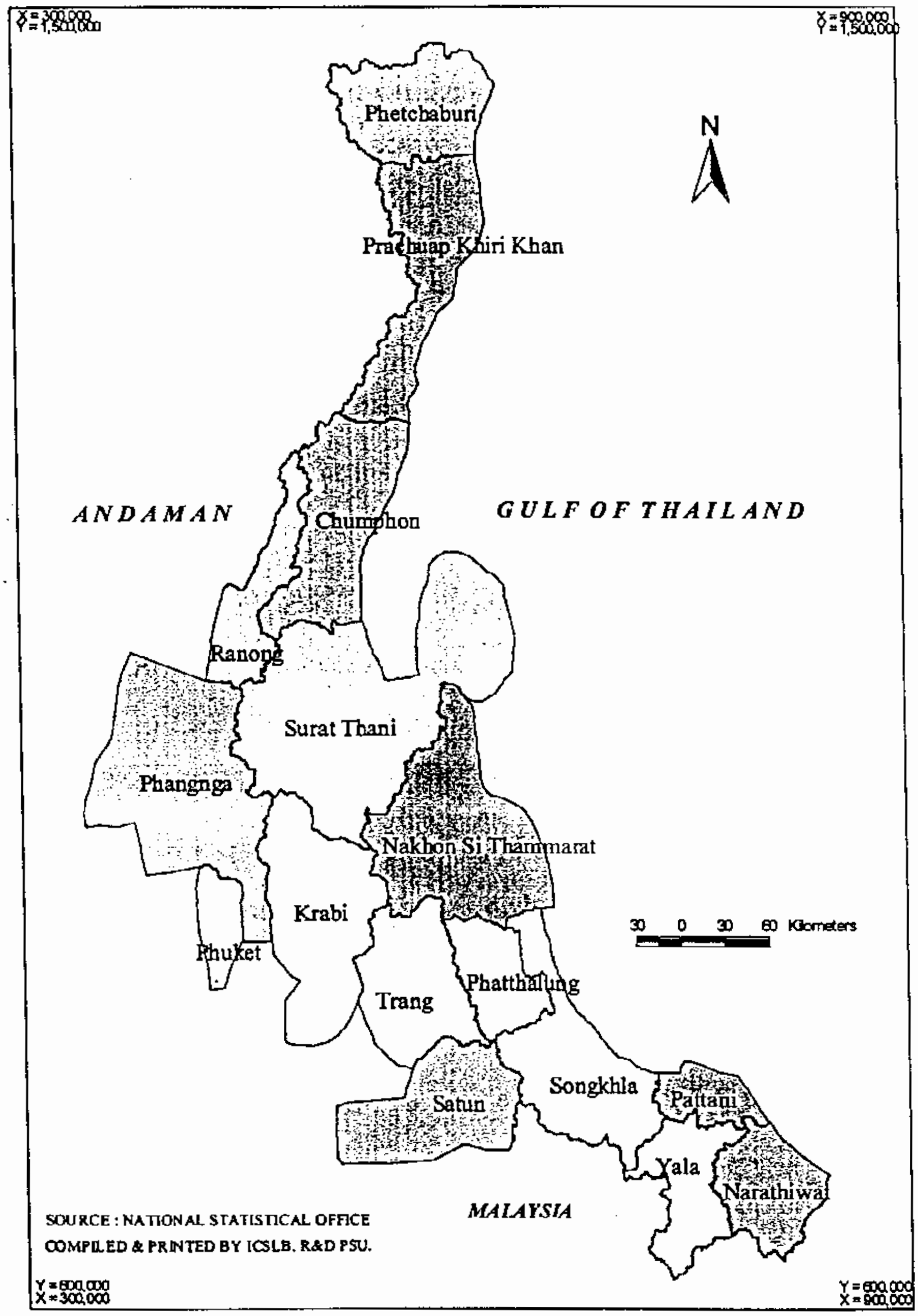
In this study, we investigate the climatic factors influencing the incidence of DHF in Southern Thailand. The central mountains divide Southern Thailand into an east coast, facing the Gulf of Thailand, and thus the northeast monsoon, and a west coast receiving the south west monsoon. The climatic data comprise monthly total rainfall and number of rain days, monthly maximum and minimum recorded temperatures, and average relative humidity.

Objectives

The main goal is to determine the climatic factors that directly influence the occurrence of DHF. Our study embraces the monthly incidences of DHF in four selected provinces in Southern Thailand, located on the Malay Peninsula. Since the climate, particularly the rainfall pattern, is different on the two sides of the Peninsula, two provinces are selected on the west coast and another two on the east coast.

The secondary objective is to develop a model for forecasting rainfall and DHF incidence using time series analysis. This method is also used to model the association between the climatic determinants and DHF incidence, after adjusting for the seasonal variation.

Figure 1.1 Map of Southern Thailand



The research hypotheses can be described as follows:

1. Climatic factors are directly related to the incidence of DHF in Southern Thailand,
2. The differing climatic factors of the west and east coasts influence the incidence of DHF in Southern Thailand.

Scope

The climatic factors related to the incidence of DHF, such as temperature, humidity, rainfall and number of rain days per month in Southern Thailand are investigated. The provinces selected for the study comprise Krabi, Nakhon Si Thammarat, Trang and Songkhla. The climatic factors were collected over a twenty-year period (1978 - 1997).

Definitions of terms

Maximum temperature means the highest temperature recorded in each month. The unit of temperature is degrees Celsius.

Minimum temperature means the lowest temperature in each month.

Humidity means are average percentile of humidity in each month.

Rainfall means quantity of rain in each month. The unit of rainfall is millimeters.

Number of rain days means the number of days in each month in which some rainfall was recorded.

Incidence of DHF means the number of DHF cases per 1,000 population in each month. This means total DHF cases divided by the average population, multiplied by 1,000.

Variables in the study

The independent variables are as follows:

1. Average maximum and minimum temperature in each month,

2. Average humidity in each month,

3. Total rainfall in each month and

4. Number of rain day in each month.

The dependent variable is the incidence of DHF in each month in Krabi, Nakhon Si Thammarat, Trang and Songkhla.

Review of Literature

The review of the literature is divided into two sections as follows:

1. Dengue Haemorrhagic Fever; and
2. Relationship between Climatic Factors and Dengue Incidence

1. Dengue Haemorrhagic Fever

1.1 Clinical presentation and case definition

Dengue hemorrhagic fever is a dengue-like disease in which the course of illness changes sharply on or about the time of defervescence. Family members describe a child with several days of high fever, sudden weakness or apathy. Physicians note that the patient has tachycardia, diaphoresis, cool extremities, a pale face and blood pressure within the normal range (Halstead, 1997). Laboratory studies reveal hypovolemia due to increased vascular permeability documented either as an elevated level of hematocrit or the collection of fluid in serous spaces seen on radiography or ultra-sonography. In cases with severe vascular permeability there may be hypoalbuminemia. All patients have evidence of altered hemostasis, but may not have serious hemorrhages. The classical and alternate pathways that activate the complement system, liver enzymes (such as aspartate aminotransferase, AST, and alanine aminotransferase, ALT) are elevated, the prothrombin time prolonged, and there is increased consumption of fibrinogen. Hematological studies regularly show thrombocytopenia (Halstead, 1997). There are increased numbers of blast-like abnormal lymphocytes in the peripheral blood. The bone marrow shows total maturation arrest before defervescence. Patients with dengue shock syndrome have the above symptoms and signs plus a pulse pressure, which is less than 20 mm Hg, or hypotension for age.

A minimal case definition of DHF is derived from the above clinical findings. DHF is a dengue illness with recent fever, thrombocytopenia ($\leq$ 100,000 mm^{-3}) and elevated hematocrit ($\geq$ 20 percent above recovery value) or other objectives of increased vascular permeability while DSS includes the above symptoms plus a narrow pulse pressure ($\leq$20 mmHg) or hypotension for age.

1.2 Epidemiologic features

1.2.1 Infection parity

DHF is associated with secondary-type dengue infections in individuals aged one or more years and with primary dengue infections in infants born to dengue-immune mothers (Halstead *et al.*,1970).

1.2.2 Viral strain

DHF has been found to be associated with secondary infections with dengue viruses of Asian origin (Deubel *et al.*, 1993).

1.2.3 Enhancing antibodies

Dengue viral infection-enhancing antibody activity in undiluted serum has been shown to strongly correlate with DHF/DSS in individuals who experience a subsequent secondary dengue infection (Kliks *et al.*, 1989).

1.2.4 Protective antibodies

It has been found that low levels of cross-reactive neutralizing antibody protect against DHF/DSS (Kliks *et al.*, 1989).

1.2.5 Age

Classical DHF is almost always confined to children. From an admittedly small sample, the modal age of greatest susceptibility to shock is 8 to 10 years (Kouri *et al.*, 1989).

1.2.6 Sex

Shock cases and death occur more frequently in female than male children (Halstead *et al.*, 1970).

1.2.7 Race

Black people are less susceptible to shock syndrome than are white and Asian people (Guzman *et al.*, 1990).

1.2.8 Nutritional status

Moderate to severe protein-calorie malnutrition has been found to reduce risk to DHF in dengue-infected children (Thisyakorn and Nimmannitya, 1993).

1.2.9 Preceding host conditions

Peptic ulcer and menstrual periods may be risk factors for severe bleeding during some dengue infections (Tsai *et al.*, 1991).

1.3 Causation

Dengue is a widespread human infection. It has signs and symptoms shared by many other infections (e.g. parasitic, bacterial and viral). Isolation of a dengue virus from a patient, even from autopsy materials, establishes infection, but it does not prove causation of any particular syndrome (Halstead, 1997). In medical science, causation may be a process of elimination. Reports of dengue epidemiologic studies frequently fail to describe the complete clinical and laboratory data which would help to rule out other causal infections. It is not widely appreciated that routine laboratory and clinical data are often inaccurate. A great deal of confusion in the dengue epidemiologic literature has been contributed by authors who give the same value to data from retrospective clinical studies as to protocol-designed, research-prospective studies. Patient charts, particularly from non-academic centers, rarely contain enough high quality clinical and laboratory data to contribute meaningfully to an understanding of dengue pathogenesis. Their greatest value may simply be to record relative degrees of disease severity.

2. Relationship between Climatic Factors and Dengue Incidence

2.1 Rainfall

In Southeast Asia and other parts of the world, a relationship between rainfall and dengue incidence has been well established in many locations (Foo *et al.*, 1985). Peak transmission occurs in the particular months of the year that have high rainfall and high temperature, even though principal larval habitats for *Aedes aegypti* in those locations are water storage containers (Kuno, 1997). In some locations dengue outbreaks may occur and cease before the arrival of the rainy season (Kuno, 1997), or occur in relatively dry areas. Also, even in location with a rainy season, such as Singapore, sometime a positive correlation between rainfall and vector population density could not be obtained (Kuno,1997). In addition, in parts of the tropics where there are two annual rainy seasons, a positive correlation has been observed in only one season (Aitken *et al.*, 1980).

The impact of rainfall on the adult vector density is not the same for all vector species. *Aedes aegypti*, which prefers indoor habitats, is less affected by rainfall than *Ae. albopictus* or other vectors that have outdoor larval habitats. Thus, in a computer simulation, a positive correlation between *Aedes aegypti* larval density and dengue incidence was not observed (Fock *et al.*, 1993).

2.2 Temperature

Ambient temperature is of importance in dengue transmission because of its influence on vector distribution, blood activity of the vector, the extrinsic incubation period (EIP) and adult longevity. *Aedes aegypti* has been shown to transmit dengue when the temperature is above 20°C but not when it is 16°C (Kuno, 1997). Temperature is clearly a major factor controlling the seasonality of dengue outbreaks in subtropical or temperate regions. On the other hand, ambient temperature alone does not explain vector distribution and dengue occurrence. It has been reported that *Ae.aegypti* could survive indoors in locations at altitudes as high as 1700 m above sea level in Mexico and 2000 m above sea level in Columbia (Kuno, 1997).

Furthermore, meteorologic conditions may not remain the same in any locality. Global warming, if it is comfirmed, may further facilitate the expanded distribution of dengue mosquito vectors in temperature regions, such as northern parts of North America or Europe (Kuno, 1997). This concern has become a far more serious matter with the expanding distribution of *Ae. albopictus* (Kuno, 1997). This species, which has spread to parts of North America, Mexico, Central America, the Caribbean, South America, the Pacific, Africa and Europe, not only has become an indoor breeder in parts of tropical Asia, but also has demonstrated a similar potential in a temperate region (Kuno, 1997).