Current Status of Dengue/Dengue Haemorrhagic Fever
in WHO South-East Asia Region

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Abstract
Dengue fever/dengue haemorrhagic fever (DF/DHF) is the most important emerging viral disease affecting nearly half of the world’s population. It is estimated that there are between 50 to 100 million cases of DF and about 500 000 cases of DHF which require hospitalization every year.

In the WHO South-East Asia Region, over the past 15 years, DF/DHF has become a leading cause of hospitalization and death among children. The annual incidence of DF cases is estimated to be between 20–30 million and of DHF between 200 000 and 400 000 cases with 10 000 deaths. During 1996–1998, an increasing trend in morbidity associated with DF/DHF has been observed in India, Indonesia, Maldives, Myanmar, Sri Lanka and Thailand. There are formal DF/DHF control programmes in most of the countries except India and Maldives. The DF/DHF control strategy relies mainly on two aspects: (1) efficient disease management in hospitals to reduce case fatality rates, and (2) vector control through the integration of chemical, biological and environmental methods of control. Source reduction programmes are largely community-based, particularly utilizing schoolchildren. This presentation also details the role of the WHO
Introduction

The global pandemic of dengue/dengue haemorrhagic fever (DF/DHF) has re-intensified greatly over the past 15 years. More than 2.5 billion people are at risk of the infection in over 100 countries worldwide\(^1\). There is an estimated incidence of tens of millions of dengue cases each year and at least 500,000 cases of DHF with a mortality of about 5% in most countries; the vast majority of these cases, at least 95%, are among children less than 15 years of age.

The South-East Asia Region of WHO comprises 10 countries, namely, Bangladesh, Bhutan, India, Indonesia, Democratic People’s Republic of Korea, Maldives, Myanmar, Nepal, Sri Lanka and Thailand, with a total population of 1.45 billion.

Ever since the recognition of DF/DHF as a disease entity in Manila in 1950, the disease has spread to many countries in South-East Asia. Notably among them was Thailand which recorded a severe outbreak in 1958, followed by Indonesia in 1968, and Myanmar in 1970. The disease has now become endemic in seven countries of the Region, except Bhutan and Nepal, and the occurrence of outbreaks has become a regular feature.

Since 1994, there has been a growing proportion of cases with haemorrhagic manifestations, particularly in Sri Lanka and India, which has contributed to an increasing trend in the case fatality rates in the Region\(^2\).
DF/DHF situation in countries of the SEA Region

Bangladesh

For the time being, DHF is not considered to be a public health problem in Bangladesh though an outbreak apparently occurred in 1964 at the same time as it occurred in Calcutta, India. DF is endemic and a serological survey has shown antibodies to DEN–3 and, to a lesser extent, to DEN–1 and DEN–2, among a high percentage of the population in Dhaka and Chittagong. *Ae. aegypti* is common in the country but is least present in Dhaka. Densities are relatively low as water is not commonly stored for household use. Nevertheless, the presence of this vector and three serotypes of dengue virus implies that the country is at some risk and must be alert to any epidemic outbreak.

India

Though DF has been known to be in existence in India for a long time, DHF was first reported in an outbreak which occurred in Calcutta in 1963. It appears that the proportion of DHF or DF cases with haemorrhagic manifestations has increased in the last 5–6 years; all the states, excepting those in the north–east, have reported outbreaks. The disease was earlier restricted to urban centres, but is now spreading out to rural areas as well. The onset of the disease occurs immediately after the monsoon season which varies in duration from state to state, between July and November. The attack rates in the outbreaks reported have ranged from 20% to 80% of the population in affected localities. All age-groups have been affected by DF, and all the four serotypes of the virus have been isolated and are in circulation in the country; more than one serotype are commonly present during many of the outbreaks in urban areas. The seropositivity of localities affected by dengue can be quite high ranging from 8% to 91%.

The vectors, *Ae. aegypti* and *Ae. albopictus*, are widespread in India and their local densities can be quite high; however, the role of *Ae. albopictus* has not yet been established. Most of the DF/DHF outbreaks have occurred in localities where the larval house index
was more than 20%. There is no regular vector surveillance and control programme in India.

Recently, India experienced a severe outbreak of DHF in Delhi during September–October 1996, which took a toll of 423 lives with 10 252 hospitalizations, giving a case fatality rate of 4.1%\(^\text{(3)}\). DHF is now a notifiable disease in Delhi since 1997.

**Indonesia**

DHF was first reported in Indonesia in 1968 when haemorrhages and mortality occurred during the dengue outbreaks in Surabaya and Jakarta. Since that time, DHF has spread rapidly and its incidence has mounted. In the first outbreak in Jakarta, 53 cases of DHF and 24 deaths were recorded. Twenty years later, by 1988, a total of 44 573 cases of DHF with 1527 deaths had been reported from 201 of the total 304 districts in the country and the incidence of DHF rose to 27.1 per 100 000 population. Considerable efforts were made to control the vectors during 1988–1996; in fact, the incidence of DHF touched a low of 6.1/100 000 in 1989. Since 1989, the incidence has fluctuated: rising again to 9.7/100 000 in 1994, and even higher in 1996. In 1994, 217 regencies/municipalities reported the occurrence of DHF with the rate per 100 000 population remaining relatively as high as 9.7. Surveillance statistics for 1996 showed an increasing trend with 44 650 reported cases and 1192 deaths. However, during 1997, the number of cases decreased to 30 730 with 681 deaths.

The Government accords a high priority to the surveillance of the disease and the control of its vector, *Ae. aegypti*. The species is very widespread throughout Indonesia and house indices are often quite high. It is felt that mass larviciding, the application of thermal fogs and ultra low volume (ULV) insecticide concentrates along with an intensive programme of health education with the active participation of the community have had a reasonable success in reducing the incidence of DHF. The larval surveys carried out in 1992 showed that the vector premise index in schools was 32.40% and that the incidence of dengue among schoolchildren 5–14 years old was 46.40% in 1993 and 40.40% in 1994.
Because of these very high rates, special efforts have been made to achieve source reduction in and around schools by enlisting the active cooperation of both teachers and students. There are about 42,689,700 students in schools in Indonesia. A school health programme has been established and a national seminar has recommended source reduction through this programme. Schoolchildren are actively participating in source reduction activities.

**Maldives**

The first reported outbreak of DF occurred in Maldives in 1979. Investigations showed that both DEN-1 and DEN-2 serotypes were circulating and that some 71% of the country’s population was seropositive. Outbreaks were again reported in 1980. In 1988, a very severe outbreak of dengue occurred in the capital, Male, which affected a large proportion of the population of children under ten years of age; nine deaths from DHF were reported. The last outbreak reported in 1998 with 1778 reported cases and no death reported.

Surveys of the mosquito population show that *Ae. aegypti* and *Ae. albopictus* are common in Male and are present in all the islands of the country; they have been found to breed in roof-top water tanks, rain water harvesting tanks, a large variety of small containers, particularly in plastic trays kept below flower pots, and in empty coconut shells and tree holes.

**Myanmar**

The first major epidemic of the disease syndrome occurred in the Capital, Yangon, in 1970. Since then, epidemics have continued to occur in a cyclic pattern and the disease has spread from Yangon to most parts of the country. Between 1970 and 1995, there were 83,381 cases of DHF with 3,243 deaths, a case fatality rate of 3.88%. Probably, the actual number of DHF cases is considerably larger as only the hospitalized cases are reported. About 90% of the DHF cases in Myanmar occur in the 5–8-year-old age-group.

During the first five years in which DHF was known to occur in the country, almost all the cases were
confined to the Yangon division. By 1975, the disease syndrome had begun to spread and, in that year, 31% of the DHF cases occurred in Mandalay and only 29% in Yangon. However, Yangon still remains the most serious focus of DHF. In 1994, 11,647 cases and 461 deaths from DHF were reported from the country as a whole.

DF and particularly DHF/DSS are increasingly becoming serious public health problems in Myanmar, especially among the 5–10 and 11–15-year-old age-groups and, as noted above, a vast majority of the cases occur in the 5–8-year-old age-group. The syndrome continues to spread geographically within the country accounting, in part, for the increased number of cases. The surveillance of DF/DHF is limited by the fact that only two laboratories can carry out the laboratory diagnosis, viz. the Department of Medical Research and the National Health Laboratory, both in Yangon.

*Ae. aegypti* and *Ae. albopictus* are found throughout Myanmar in high densities. *Ae. aegypti* is the main vector and *Ae. albopictus* has only a secondary role. Furthermore, the spread of *Ae. aegypti* within the country is increasing with the species being found in areas where it has not been previously reported. An increasing effort is being made to control the vector through community participation by reducing the larval habitats, but densities still remain very high. The country is preparing contingency plans for dengue vector control based on a better mapping of the distribution and population densities of aquatic stages. More efforts are, however, required to improve the surveillance of dengue infections and case management.

**Nepal**

There is no recorded transmission of DF/DHF in Nepal. While there have been no clinical cases of DF/DHF, the serological specimens taken near the border with India in 1980 and 1981 were seropositive for both DEN-2 and DEN-4. Although its origin is uncertain, a high percentage of the sera tested was positive which implies that surveillance for the infection must be maintained. Although *Ae. aegypti* has not been recorded in Nepal, *Ae. albopictus* is present. More surveys are needed in urban areas to verify
this situation, especially in towns bordering India.

**Sri Lanka**

Dengue was known to be endemic in Sri Lanka from the beginning of the century but its first epidemic outbreak which was serologically confirmed was in 1965. Though most of the towns throughout the country were affected during this epidemic outbreak, the western coastal belt was the most affected. Colombo recorded the highest number of cases and the first two cases of DHF also occurred at that time. There were 13 cases of DHF with five deaths in 1966; 29 cases and eight deaths in 1967, and seven cases with two deaths in 1968. Up to 1972, there were only a few scattered cases with no cases reported between 1973 and 1976; very few DHF cases were reported until 1989. Surveys, however, showed that more than one serotype were circulating. In 1989, there was a sudden outbreak of DHF with 203 clinically diagnosed cases and 20 deaths [a case fatality rate (CFR) of 9.8%]. In 1990, the number of cases rose sharply to 1350 of which 345 were serologically confirmed; DHF cases were also reported from outside Colombo. Several hundred cases have been reported annually from 1991 to 1997 with a CFR ranging from 1.2 to 4.16. The age distribution shows that 70% of the cases were related to those less than 15 years of age with the peak being seven years; more men (57%) than women (43%) were affected.

DHF is a notifiable disease in Sri Lanka. At places where DHF cases have been reported, control measures include health education, particularly in schools, and community participation in cleaning campaigns. Vector surveillance shows that though *Ae. aegypti* is more common than *Ae. albopictus*, the latter is quite common in the outskirts of Colombo.

**Thailand**

The first epidemic outbreak occurred in 1958 with 2706 cases and 296 deaths, resulting in a morbidity rate of 10.6/100 000. DHF has persisted since 1958 with the first cases outside of Bangkok being reported for the first time in 1964. Subsequently, it had spread gradually throughout the country by 1978 and now occurs in
cities, small towns and rural areas as well.

In 1987, a major epidemic occurred with the highest incidence to date of 174,285 cases and 1007 deaths. The year 1990 was another serious year when 92,002 cases and 414 deaths were reported. In 1993, there were 67,017 cases and 222 deaths and in 1997, 99,150 cases and 227 deaths.

Every year, beginning February, there is a gradual increase in the incidence of DHF cases in Thailand which peaks in July and August, with the monthly number of cases declining thereafter. All the four serotypes of dengue are circulating in Thailand though the proportion of each serotype varies from year to year.

The trend of the incidence of the disease has continued to increase in a cyclic pattern. The disease mainly affects the younger age-groups of less than 15 years with the highest proportion of cases occurring in the age-group 5–9 years, followed by the age-group 10–14 years. As can be expected, DHF is the main cause of paediatric hospitalization in the country. Despite the increased number of cases, the CFR has declined as physicians have gained experience in the treatment of young patients: the CFR decreased from more than 10% in 1958 to 0.27% in 1994 and 0.29% in 1996 (4). It was further reduced to 0.23% in 1997.

The main vector of DHF in Thailand, as elsewhere in the Region, is *Ae. aegypti*. *Ae. albopictus* is uncommon in Bangkok but its distribution and population begins to increase in the suburbs and is particularly high in rural areas. *Ae. aegypti* was initially found mainly in urban areas but in the last decade it increased steadily in rural areas as well.

An increasing amount of effort and funding is being devoted to the control of *Ae. aegypti*. Much of the effort revolves around the education of teachers and students in schools throughout Thailand as well as enlisting the cooperation of the community in the prevention of vector breeding. So far the control efforts have had only a limited impact on vector population densities. However, as more experience is gained, it is hoped that vector densities will
In summary, out of the seven endemic countries in the South-East Asia Region, only four countries, i.e. Indonesia, Myanmar, Sri Lanka and Thailand, have DHF as a reportable/notifiable disease. It shows a high endemicity in Indonesia, Thailand and Myanmar while it is moderate in India and Sri Lanka. Bangladesh and Maldives experienced outbreaks and the presence of dengue antibodies in a high percentage of the population implies high receptivity to DF/DHF outbreaks. The number of the reported cases and fatality rates of DF/DHF by country for the years 1985–1997 is given in Figure 1.

**Figure 1.** Number of Reported Cases and Case Fatality Rate of DF/DHF in the South-East Asia Region, 1985-1998
The WHO programme for the prevention and control of DF/DHF is being implemented at the global level at WHO headquarters, the regional offices and at country level. The current programme is based on a resolution of the Forty-sixth World Health Assembly in 1993 on dengue prevention and control which urged Member States to strengthen national and local programmes for the development of strategies for the prevention and control of DF/DHF and its vectors. To achieve this it is necessary to ensure that DHF and DSS are made reportable diseases in each endemic country. The surveillance capabilities of the endemic countries in respect of the disease and its vectors must be strengthened in order to obtain accurate data on the incidence and distribution of DHF. Dynamics of the disease transmission and the bionomics of the vectors will enable the vector and disease control programmes to be strengthened at local, municipal, national and regional levels. Assistance has also been provided to identify resources to broaden laboratory capacity for the diagnosis and improvement of the treatment of DHF and DSS cases.

Improvement of vector control operations and the ability to deal with emergencies caused by epidemic outbreaks can be achieved by such technical inputs and the provision of additional extrabudgetary resources.

**Technical Advisory Committee**

In 1964, the South-East Asia (SEA) and the Western Pacific (WP) regions of WHO organized the first Interregional Seminar on Mosquito-borne Haemorrhagic Fevers in Bangkok, Thailand. Since then, the Organization has been actively involved in assisting Member countries in the planning, development and implementation of control measures.

In 1974, the SEA and WP regions established a Technical Advisory Committee (TAC) on DHF. In view of the increasing occurrence of epidemics in the countries of the two regions it was felt that a guide for the diagnosis, treatment and control of dengue infection would be of value to physicians and health authorities faced with the growing risk of epidemics. The first version of this guide entitled "Technical Guide for Diagnosis, Surveillance, Prevention and Control of Dengue Haemorrhagic Fever" was published in 1975.
Dengue Newsletter/Dengue Bulletin

The SEA and WP Regional Offices have been jointly publishing annually, since 1975, a Dengue Newsletter for dissemination to Member countries of the knowledge about DF/DHF incidence and its control. The severity of the disease and the high case fatality rate has triggered off global research interest. These efforts have now culminated in the building up of sensitive diagnostic techniques for the management of cases and vector control strategies. For the dissemination of more scientific knowledge, the Dengue Newsletter was renamed as **Dengue Bulletin** to better reflect its content and scope.

**Standardization of epidemiological research**

In order to get comparable results in the countries of the SEA Region, the Research Study Group on DHF in SEAR designed a common protocol in 1979 which was made available to Member countries to serve as the basis for undertaking epidemiological research studies. Initially, Indonesia, Sri Lanka and Thailand were supported by SEARO in conducting five-year research studies on the epidemiology of DHF. Myanmar joined this group in 1984. These multicentre epidemiological studies yielded both broad information on the epidemiology of dengue and also information of practical importance on the development of a tetravalent dengue vaccine. One important accomplishment of this study was the development of laboratory competence to work with dengue viruses in the four participating national laboratories.

**Revised guidelines**

The South-East Asia Advisory Committee on Medical Research, established in 1976, identified DHF as one of the research priorities in the Region. As the CFR from DHF/DSS was very high in the first outbreaks, WHO supported research studies on pathophysiology, clinical and laboratory diagnosis, and case management during the period 1976–1983. On the basis of these studies, revised guidelines on DHF were issued by the Technical Advisory Group in 1980 and 1986, which incorporated changes in
the criteria for the diagnosis and recommended treatment.

Community-oriented DHF vector control

Following the 1983 and 1986 WHO/SEAR intercountry meetings on DHF, community-oriented DHF vector control studies have been undertaken in Indonesia, Myanmar and Thailand. As an outcome of these studies, Indonesia and Thailand developed national DF/DHF control programmes using community approaches, which have been in operation since 1990.

Monograph on dengue/DHF prevention and control

Extensive research on different aspects of vector control and the cumulative knowledge built up in the Region on the feasibility and practicability of the community-based control programme culminated in the publication in 1993\(^4\) of a monograph on DF/DHF prevention and control. It contains available information on the prevention and control of the infection. This publication was well received and has been reprinted twice. It is proposed to bring out a similar publication in the Regional Office in the near future.

Brainstorming on dengue in India

WHO and the Rockefeller Foundation supported an international conference on DHF and a national "brainstorming" session on dengue in India in 1994\(^5\). The conference recommended inclusion of DHF in the list of notifiable diseases and established control activities in India.

WHO regional strategy for prevention and control of DF/DHF

A global strategy for dengue vector control was developed as an outcome of the consultative meeting on key issues in dengue vector control towards the operationalization of the Global Strategy in June 1995 in Geneva. Following this meeting, the SEA regional consultative meeting was held in October 1995\(^6\) in New Delhi to review the guidelines for the prevention and control of DF/DHF and to develop a control strategy applicable to the countries of the Region.
Guidelines for management of DEN/DHF epidemic

Following a severe outbreak of DHF in New Delhi in September–October 1996, WHO/SEARO organized a technical meeting on the management of DF/DHF epidemic in November 1996. Guidelines for control operations and the management of epidemics were developed for use by Member countries.

Collaborative effort with WHO/WPRO

In view of the alarming trend of DF/DHF in countries of the South-East Asia and Western Pacific regions, the two regional offices organized a bi-regional meeting in Manila in June 1997 with the objective of sharing and exchanging information and preparing collaborative activities to improve control activities between the two regions.

Development of dengue vaccine

The most important progress made in the South-East Asia Region is the development of a tetravalent live attenuated dengue vaccine at Mahidol University, Thailand, with technical and financial support from WHO. The activities of this project, which started in 1980, have been reviewed in Bangkok every year by a Peer Review Group since 1983. The last 12th Peer Review Meeting on Dengue Vaccine Development was held in August 1994. The results of the clinical trials of this new vaccine in adult volunteers have shown that it is safe and its immunological response is encouraging. The Phase I and II trials of the tetravalent dengue vaccine in children are currently under way.

Current control strategies

As there is no specific treatment nor a curative drug or vaccine currently available, prevention and control of dengue transmission must be carried out through comprehensive programmes for the control of the vector. The recently-adopted global strategy for the prevention and control of the DF/DHF vector recommended five broad areas for action: (1) selective integrated mosquito control with community and intersectoral participation; (2) active surveillance based on a strong health system; (3)
emergency preparedness; (4) capacity–building, and (5) vector control research.

Capacity–building

The reduction in the CFR has been identified by Member countries and WHO as a priority area. For this purpose, WHO/SEARO has undertaken the following activities:

- Trained 46 physicians working in the established dengue training/curative wards and teaching/referral/major hospitals in the endemic countries of the Region, at the WHO Collaborating Centre in Bangkok, Thailand.

- Supported the establishment of 15 dengue training/curative wards in six endemic countries of the Region and provided basic minimum equipment.

- Developed “Guidelines for treatment of DF/DHF in small hospitals”.

- Supported the development and production, in collaboration with the WHO Collaborating Centre, of a teaching video film on the management of DHF.

- Provided technical support to Member countries in the control of dengue epidemics.

- Developed and published comprehensive regional guidelines on the prevention and control of dengue/dengue haemorrhagic fever.

As part of capacity–building for the prevention and control of dengue infection, WHO provided long–term training in epidemiology, surveillance methods, and vector control for dengue infection to three epidemiologists from India, Myanmar and Sri Lanka at the Dengue Branch of the CDC at San Juan, Puerto Rico. WHO expects that the services of the staff so trained will be optimally utilized for the implementation of respective national dengue control programmes. Also, long–term training has been provided to two laboratory technicians from the Medical Research Institute, Colombo, in the virological/serological diagnosis of dengue infection at the CDC. During 1994–1999, WHO continued to support the development of live attenuated and recombinant dengue vaccines at the WHO Collaborating Centre for Vaccine Development at the Institute of Sciences and Technology for Development, Mahidol University at Salaya, Thailand.
References


