

Situation of Dengue Fever and Dengue Haemorrhagic Fever and Japanese Encephalitis in the Western Pacific Region

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INTRODUCTION

The Western Pacific Region (WPR) of the World Health Organization (WHO) is spread over a vast area extending from China, Japan and the Republic of Korea in the North to Australia and New Zealand in the South, from China, Malaysia and Singapore in the West to Cook Islands and French Polynesia in the East. Covering nearly one-third of the world's population, the WPR is perhaps the most culturally and socially diverse of the six regions of WHO. The Region embraces some of the world's least developed countries as well as its most rapidly growing economies. Geographically, most of the countries in the Region are located in tropical or subtropical zone.

There is relatively little information available on dengue fever. The presence of dengue fever (DF) or DF-like illness was known prior to World War II in countries and areas in the WPR such as South China, Indo-China Peninsula, Philippines, Fiji, New Caledonia and some other Pacific Islands. It spreads widely during the war throughout the Pacific area and appears to have occurred almost everywhere that *Ae. aegypti* or another suitable *Stegomyia* vector was present.

The first patient identified with dengue haemorrhagic fever (DHF) was recognized in Manila, Philippines in 1954. Since then, the number of patients with DF/DHF has steadily increased. In 1962, dengue virus infection has spread rapidly not only in Asia and the Pacific Islands, but also in Africa and Central and South America. In the WPR, 28 to 35 countries and areas experienced DF/DHF outbreaks during the past two decades. DF/DHF is now recognized as one of the major public health problems in most of the countries in the WPR.

Japanese Encephalitis (JE) is a serious public health problem with significant mortality and severe sequelae for children and old people in Asia. It has been under control in Japan and the Republic of Korea where better agricultural practices, vector control and immunization have been applied. Immunization with locally-produced JE vaccine has been carried out in China. Local vaccine production in Viet Nam has been supported by WHO and technology

on JE vaccine production has been transferred from Japan. Although the existence of JE in countries in the Indo-China peninsula is suspected, accurate epidemiological record is not available due to shortage of laboratory diagnostic facility and lack of experienced personnel in hospitals and laboratories.

DF/DHF EPIDEMIOLOGICAL SITUATION IN THE WESTERN PACIFIC REGION SINCE THE 1940s

China

An epidemic of febrile illness, suspected to be DF, occurred along the southeast coast of China including Shanghai City. However, outbreaks of this DF-like illness were not reported from 1950 to 1977. Since 1978, epidemics of DF/DHF have been reported and it is now endemic in South China.

Japan

DF outbreak was experienced in Japan in 1942 and the epidemics occurred until 1945 in the main southern part of Japan including Osaka, Kobe and Nagasaki. Data on the actual number of patients was unclear but it was estimated to be around 200,000 to 1-2 million and in Osaka alone, one-third to one-half of the population was ill of the disease in 1944 (Sabin, 1948). The dengue epidemic in Japan from 1942 to 1945 was one of the greatest epidemics ever recorded in a temperate zone and was unique in that the disease disappeared after 1945 and no endemic cases have been reported in the country since. By retrospective study, dengue virus type 1 (DEN-1) infection was suspected during that time in Japan (Hotta S., 1965).

Cambodia/Lao People's Democratic Republic/Viet Nam

DF was known to be widely present in the Indo-China Peninsula of WPR such as Cambodia, Lao People's Democratic Republic (Lao PDR) and Viet Nam. However, relatively little information is available due to poor health system.

In Cambodia, the presence of DHF was confirmed in 1963. However, no annual data had been received in WHO because national reporting system was initiated only in 1980. It is now endemic in Cambodia.

In Lao PDR, endemicity was first confirmed in 1984 and a major outbreak was recorded in 1985, endemicity has been reported since.

In Viet Nam, an outbreak of severe haemorrhagic disease in children occurred in Hanoi in 1958 and it was suspected as DHF outbreak. In 1960, a DHF-like illness occurred in South Viet Nam and a major DF outbreak was reported in North Viet Nam. Since 1975, major outbreaks have been reported annually from north and south Viet Nam.

Malaysia/Singapore

In Malaysia, the virus has been widespread following an outbreak in Kuala Lumpur in 1954. DHF was first reported in Penang, Malaysia in 1962 and the virus was detected as dengue virus type 2 (DEN-2). An endemic has been reported since 1973.

In Singapore, DF became endemic following the first reported outbreak of the disease in 1960 (Singapore, 1989) and is now considered endemic.

Philippines

Before World War II, DF endemic was already known in the Philippines. In 1953, new febrile and serious illness among children in Manila and Luzon islands was reported and named "Philippines Haemorrhagic Fever" (Quintos, FN. *et. al.*, 1954). Isolation of virus and serological examination were made from these haemorrhagic patients including fatal cases and were determined to be DF. Following the study in the Philippines, an illness named Thailand Haemorrhagic Fever was also confirmed as an identical disease with the Philippines Haemorrhagic Fever associated with dengue infection (Hammon, W. McD *et. al.*, 1960). It was given the name dengue haemorrhagic fever/dengue shock syndrome (DHF/DSS). After the initial recognition of DHF in Manila, cases continued to appear each year with considerable year-to-year variation in numbers.

The South Pacific countries

In the South Pacific area, DF endemic was known in the 1940s in Fiji, New Caledonia, Papua New Guinea, Samoa and Solomon Islands. However, the disease was virtually absent for 20 years after the war. Dengue viruses became active again in the Pacific region in 1964 when a dengue virus type 3 (DEN-3) outbreaks occurred in Tahiti, French Polynesia, and recurred in 1969. Early in 1971, DEN-2 epidemics occurred in Fiji, French Polynesia, Kiribati, and Papua New Guinea. Following these outbreaks, DF occurred in Nauru, New Caledonia, Samoa and Vanuatu in 1972. In Tonga, a new relatively low-intensity epidemic occurred in 1974. DF is now endemic in the South Pacific countries and areas.

PRESENT DF/DHF EPIDEMIOLOGICAL SITUATION IN THE WESTERN PACIFIC REGION

The presence of DF or DF-like illness was known prior to World War II in countries and areas in the Western Pacific Region. It spread widely during the war throughout the Pacific area, but was inactive for some time. In the 1960s, dengue virus infections have spread again rapidly in the Region. This has been attributed to rapid urbanization of countries in the Region and increase in the number of travellers associated with the progress in travel mode particularly the use of aircraft which might be an important factor in spreading the vector mosquito and the virus from one country to another. During the period 1975-1979, 19 countries/areas in the WPR reported existence of DF/DHF. It was 22 in 1980-1984, 26 in 1985-1989, and 19 countries/areas out of the 35 Member States were

reported from 1990 up to October 1993. A total of 28 out of the 35 countries and areas in the Region namely, American Samoa, Australia, Cambodia, China, Cook Islands, Fiji, French Polynesia, Guam, Kiribati, Lao PDR, Malaysia, Marshall Islands, Nauru, New Caledonia, New Zealand, Niue, Palau, Papua New Guinea, Philippines, Samoa, Solomon Islands, Tokelau, Tonga, Vanuatu, Viet Nam and Willis and Futuna Islands, experienced DF/DHF outbreaks during the past two decades. There has been no report from Brunei, Hong Kong, Macao, Mariana Islands, Micronesia and the Republic of Korea. Japan experienced a DF outbreak in the 1940s, but none was reported since 1945, as mentioned above.

China

DF/DHF had not been reported in China from 1950 to 1977. An epidemic of DF due to dengue virus type 4 (DEN-4) occurred in Foshan City, Guangdong Province in 1978. A more localized outbreak of mild DF due to DEN-1 occurred in Zhongshan Country, Foshan Prefecture, Guangdong Province in 1979, followed by a major outbreak caused by DEN-3 on Hainan Island in 1980. Annual reports have not been received regularly from the Government of China. However, a major epidemic seems to have occurred in 1983 with 85,293 cases and 3,032 deaths. In 1985-1986, DEN-2 infected DF occurred also in Hainan Island. Majority of patients in China were adolescents and adults. Multiple peripheral paralysis such as facial palsy was observed as unusual clinical manifestation in the report (Qiu FX, *et. al.*, 1993). In 1989, 37,886 cases with 807 deaths was reported. In 1990, it was reduced to 376 cases with no deaths reported. However, it increased again to 46,680 cases with unclear number of deaths.

Cambodia/Lao People's Democratic Republic/Viet Nam

In Cambodia, DF/DHF has been ranked as one of the ten leading causes of hospitalization and deaths. Statistics from the National Centre for Hygiene and Epidemiology (CNHE) in Phnom Penh show that the number of cases has steadily increased since 1980. In 1990, there was a major outbreak with 7259 and 331 deaths. Fatality cases has been very high in Cambodia ranging from 3.6% to 12.4% compared with 0.3% to 1.0% in Thailand over the same period. Prevention and control measure of DF/DHF are still inadequate in Cambodia. Total number of DHF in this country in 1992 was approximately 4800 cases with 172 deaths. This is lower than in 1990, the year of the biggest outbreak in this country, but is higher than in 1991.

In Lao PDR, a big epidemic of DF/DHF was experienced during the period 1985-1988. WPRO Data Bank recorded 365 cases with 43 deaths in 1986 and 1212 cases with 27 deaths in 1988. However in 1987 and 1989, 9699 cases with 295 deaths (T. Fukunaga, 1990) and 5263 cases with 91 deaths (A. Igarashi, 1991) was reported. Incidence report has been submitted irregularly to WHO. Unreported cases may have existed because of poor reporting system in this country.

Viet Nam reported the highest number of cases in the Region. High prevalence of DF/DHF was observed for the first time in South Viet Nam in 1960 and in North Viet Nam in 1969. The biggest outbreak occurred in 1987 with a total of 354,517 cases with 1566 deaths. However, there has been no major outbreak over the past few years.

The reporting system on communicable diseases including DF/DHF in both Lao PDR and Cambodia is poor. However, it is strongly suspected that most cases and significant epidemics on DF/DHF existed in these countries due to similar situation with neighbouring countries such as Viet Nam and Thailand.

Malaysia/Singapore

In Malaysia and Singapore, there had been outbreaks in 1965–1969 and 1970–1974, respectively. Case number had been reduced when a nationwide DF/DHF control programme was implemented. However in the 1980s, the case number has gradually increased and the present number is now higher than the last major outbreak in both countries.

Philippines

The outbreak in 1986 was the largest in the Philippines. The number of cases was 9384 with 250 deaths. Since then, the number had been decreasing gradually. However, it has increased again since 1990. The number of cases in 1990 was 4836 with 363 deaths. Incidence and mortality rates from 1958 to 1989 is indicated in Table 1. It is clear that incidence rates became higher during these 7 years. However, mortality rate was constantly at 0.2%–0.5% in this country. Mean incidence rate in all ages is 3.0%. The highest mortality rate is also indicated under 1 year old with 2.5% per 100,000 population and second rank is 1–4 years old age group with 1.0%. Mortality rate in the age group older than 5 years old is from 0% to 0.6% and the mean mortality rate in all ages is 0.4%.

South Pacific countries

After a virtual absence of DF/DHF in South Pacific for 20 years, it has become endemic since the 1970s. The biggest outbreak was observed in French Polynesia in 1979 and another one followed in 1989, which was considered as second biggest in the South Pacific. In 1964, the dominant type of dengue virus was DEN-3. However, DEN-2 was dominant in 1971–1972, DEN-1 in 1975–1978 and DEN-4 was isolated in 1979–1980. DEN-1 and DEN-3 are dominant in recent years.

Two groups are present during outbreak peaks in the South Pacific. One group has epidemic peaks in 1975–1979 and/or 1985–1989 such as French Polynesia, New Caledonia, Western Samoa and Wallis and Futuna. The other group's peak was in 1980–1984 such as Cook Islands, Nauru, Niue and Tonga. The case number had been increasing since 1990 in Cook Islands, Fiji and Tonga, but decreased in 1993.

CLINICAL FEATURES OF JAPANESE ENCEPHALITIS

Japanese encephalitis (JE), a mosquito-transmitted flavivirus (formerly of the arbovirus group B), is closely related to St. Louis encephalitis in the New World, to West Nile virus in Africa, and to Murray Valley encephalitis virus in Australia/New Guinea. Outbreaks occur during summer and affect all age groups, but with the highest mortality rate in the younger age groups, pre-teenagers, and the elderly. Pigs have been incriminated as an important vertebrate amplifying host for JE virus and several *Culicine* species seem to play a significant role as a vector mosquito during the outbreak of JE. Not all individuals bitten by infected mosquitoes develop the disease. All those who have been infected, however, develop antibodies to JE virus. The ratio of overt disease to inapparent infections varies from 1:20 to 1:1,000.

The incubation period in man, following mosquito bite, may range from 5 to 15 days. The course of the disease can be conveniently divided into three stages as follows:

- (1) Prodromal stage—The onset of the illness is usually acute and is heralded by fever. The essential features of this stage are general malaise, headache and fever often accompanied by rigors. Headache is usually severe and nausea/vomiting are common.
- (2) Acute encephalitic stage—The predominant features of this stage are continuous fever, nuchal rigidity, focal CNS signs, convulsions and altered sensorial progressing in many cases to coma.
- (3) Late stage—Convalescence is usually show. Patients may recover motor functions but cognitive abnormalities remain. The most commonly observed sequelae in patients are mental impairment, severe emotional instability, personality changes, paralysis either of the upper or lower motor neuron type. Aphasia and organic psychoses are less common.

During outbreaks, the diagnosis of the disease becomes difficult as other illnesses continue to occur. Febrile convulsions in children may accompany many illnesses. Parasitic and bacterial meningitides may be indistinguishable. Tuberculosis meningitis is commonly seen in children, but has more indolent onset. Cerebral malaria may be confused with encephalitis, particularly in regions when many persons have positive blood smears for malaria. Rabies, poliomyelitis, measles, mumps and herpes viruses may cause encephalitides. West Nile virus may cause encephalitis. Reye's syndrome and encephalitis caused by toxic substances should also be considered in the differential diagnosis.

PRESENT JE EPIDEMIOLOGICAL SITUATION IN THE WPR

The disease incidence appears to be subsiding in China, Japan and the Republic of Korea but at the same time it has been increasing and spreading over some countries in Asia such as Bangladesh, Burma, India, Nepal, Thailand and Viet Nam. The reasons for these changes are not clear but the following factors may be involved:

- (1) changes in agriculture system such as adoption of rice cultivation, use of pesticides and establishment of large modern pig farms;
- (2) changes in socio-economic status involving a shift to rice cultivation from dry land crops and promotion of pig breeding as a food source;
- (3) climates, including effects of temperature and rainfall;
- (4) effects of immunization;
- (5) possible role of additional potential amplifying hosts other than pigs; and
- (6) the wide variety of mosquito species in Southeast Asia and their different vectorial capacity.

Cambodia

There has been no report on JE in Cambodia. However, it is strongly suspected that JE is endemic in the country because neighbouring countries such as Viet Nam, Lao PDR and Thailand have reported several JE cases and the agriculture system and pig breeding in these countries, which are important factors for vector mosquito breeding, are similar with Cambodia.

China

JE is prevalent in all provinces, except in Xinjiang, Shanghai, and Xizang (Tibet). Large-scale JE vaccine production was established in the 1960s in China. Fifty million doses of inactivated JE vaccine are produced annually and another 2 million doses of live JE vaccine are produced. However, 20 000 to 40 000 patients diagnosed as "acute encephalitis syndrome" are reported each year and mortality rate is more than 10%.

Japan

Since 1967, JE has been an uncommon disease in Japan and around 10 sporadic cases are reported every year. It has become a disease of the older age groups. A gradual decrease of immunity in older persons has been taking place creating a potential for future disease outbreaks.

Republic of Korea

Prior to 1969, JE occurred annually in the Republic of Korea with more than 1,000 cases and case fatality rate of over 40%. Reported cases were from 0 to few cases since 1984. JE immunization has been used widely in the country.

Lao PDR

There are no official reports of JE cases and even acute encephalitis syndrome in Lao PDR, because JE is not included in the 16 priority communicable diseases being reported to the National Institute of Hygiene and Epidemiology. However, 13 cases clinically diagnosed as viral encephalomyelitis in Vientiane in 1989–1991 were confirmed as JE by identification of IgM antibody in CSF and sera, determined in the AFRIMS (Armed Forces Research Institute for Medical Science) in Thailand. Three of the 13 patients died (fatality rate was 23.1%). JICA/WHO programme on JE prevention and control started in 1992. A virological laboratory has been set up to determine JE and DF/DHF. A clinical training course was held in August 1993 in Vientiane.

Philippines

Only sporadic cases were reported in the medical journals. Low priority is given to JE as one of the public health problems in the country.

Viet Nam

The propagation of JE is most serious especially in North Viet Nam. Annual morbidity and mortality decreased gradually because no major epidemic occurred. However, approximately 1,000 cases and 10% of case fatality rate were reported during the recent years. The National Institute of Hygiene and Epidemiology in Hanoi started a pilot production of inactivated JE vaccine and the Government has decided to produce it on large-scale basis. WHO has supported the activity on JE vaccine production in Viet Nam and technology has been transferred from BIKEN Kanonji Institute, Research Foundation for Microbial Diseases in Osaka University, Japan, and the Institute of Tropical Medicine, Nagasaki University, the WHO Collaborating Centre for Reference and Research on Tropical Virus Diseases, Japan. Approximately 78,000 doses of JE vaccine were produced in the last ten months and field trials has been started.

DISCUSSION

DF/DHF is recognized as one of the major public health problems in most of the countries in Region such as China, Philippines, Malaysia, Singapore and the countries in the Indo-China Peninsula. In the South Pacific, several countries have experienced DF/DHF outbreaks since 1970 and are now considered endemic. There is no cure or practical use of the vaccine against the disease at present. Disease surveillance and virological diagnosis must be improved so that endemic countries in the Region will have more accurate information and proper case management. However, shortage of trained personnel, facility and equipment for clinical and virological diagnosis is a big obstacle in most of the DF/DHF endemic countries in the Region.

In May 1993, the Forty-Sixth World Health Assembly of WHO called for global ac-

tion to control DF/DHF and urges Member States to strengthen national and local programmes for prevention and control of DF/DHF.

In 1994–1995, WPRO supported study programmes of fellows from China and Viet Nam to train in Indonesia on DF virological study; and from Laos and Viet Nam to train in Thailand on case management. WHO consultants visited Viet Nam and Laos to undertake consultancy on laboratory examination. The DHF Control Committee has been organized by the Ministry of Health in Cambodia and their activities have been strongly supported by WHO and other international agencies. Printing of manuals on DF case management in local language was supported in Cambodia and Laos. Training courses on epidemiology, laboratory examination and case management were held in Viet Nam, Cambodia and Laos. The South–East Regional Office has published every year a Dengue Newsletter to exchange and share information on DF/DHF situation in both SEAR and WPR.

Vector control of DF/DHF has been under the Vector–Borne Control (VBC) Unit in WPRO. Emergency supply of mosquito nets and insecticides were provided to the South Pacific. A manual on vector control of dengue virus will be published by WPRO.

DF/DHF prevention and control should be among WPRO's top priorities and advance implementation activities should commence.

Japanese encephalitis (JE) is under control in Japan and the Republic of Korea. However, it is still serious in China and Viet Nam because of its high mortality rate in children and irreversible severe sequelae such as motor nervous paralysis and mental retardation.

Immunization with locally–produced JE vaccine (both live and inactivated) has been carried out in China. In Viet Nam, particularly in the northern part, JE is one of the serious communicable diseases. Local vaccine production in Viet Nam has been supported by WHO and technology on JE vaccine production with mouse brain culture system has been transferred from Japan, but still in the laboratory–scale. However, 78,000 doses of inactivated JE vaccines were produced from June 1992 to March 1994 and 40,000 children have been immunized with locally–produced vaccine. The quality of the vaccine met the Japanese vaccine standard by quality control examinations in Japan. The programme on local JE vaccine production in Viet Nam should be continuously supported.

The reporting system of JE and acute encephalitis syndrome, which is only a clinical diagnosis, is poor in the Indo–China countries/areas, although suspected to be endemic in these places. Shortage of laboratory diagnostic facilities and lack of experienced personnel in hospitals and laboratories are causes of poor reporting system. Activities on virological diagnosis have been encouraged and supported.