Major Epidemics of Dengue in Taiwan in 1981-2000:
Related to Intensive Virus Activities in Asia

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Abstract
Major epidemics of dengue fever/dengue haemorrhagic fever/dengue shock syndrome (DF/DHF/DSS) in Taiwan in the last 20 years were strongly associated with imported cases. The data analysis showed that three major epidemics including the first outbreak of DF in Hsiao-Liu-Chiu in 1981 since 1950s, the largest epidemic of DF in Pingtung and Kaohsiung in 1987-1988, and the most important epidemic of DHF in Tainan in 1998, had statistically significant association with the increasing numbers of dengue cases in several Asian countries before or during the epidemic (p=0.028, p=0.043, p=0.08, respectively). Imported dengue cases in Taiwan were primarily travellers who had come from Thailand, Indonesia, the Philippines, Myanmar and Malaysia. The earlier indigenous dengue cases in Taiwan always used to appear later than the peaks of monthly-distributed dengue cases in those countries. On the other hand, active surveillance, epidemiological investigation, mosquito control activities and effective public health administration at various levels indeed reduced the number of confirmed indigenous dengue cases in 1996 and 1997. Taiwan’s experience in surveillance further proves the feasibility of avoiding a large-scale epidemic of DHF/DSS as well as hyper-endemicity of dengue viruses. International collaboration in surveillance, epidemic information exchange, and statistical analysis can play an important role in the prevention and control of DF/DSS in the future.

Key words: Dengue, Viral haemorrhagic fever, surveillance, imported case, Epidemiology Taiwan
Introduction

Dengue fever (DF), dengue haemorrhagic fever (DHF) and dengue shock syndrome (DSS) are the most important re-emergent arbovirus diseases of humans(1). The epidemiological activities have intensified in the past 20 years because of rapid population growth, uncontrolled and unplanned urbanization with inadequate systems of water and solid waste management, increased frequency of air travel and usage of artificial containers, which provide excellent breeding sites for the mosquitoes(2). Most importantly, epidemics of the severe form of DHF/DSS occur where increased transmission of multiple serotypes of dengue viruses becomes hyper-endemic and has resulted in more fatal cases(3). In recent years, the expanding geographical spread of dengue viruses and their mosquito vectors has facilitated a dramatic increase in the frequency of epidemics of DF/DHF/DSS in the Western Pacific, South-East Asia and South American regions(4). Dengue will continue to be a growing public health problem in most tropical and subtropical regions of the world in the 21st century, unless more effective measures are taken to control the main vectors, Aedes aegypti and Aedes albopictus(5). Therefore, the World Health Assembly urged Member States to strengthen their national and local programmes for the control of DF/DHF. WHO has published guidelines on different aspects of dengue(6,7). International efforts in formulating collaborative prevention and control strategies among dengue endemic countries become more and more important and necessary in the future.

Dengue surveillance, the most cost-effective prevention and control approach, is generally neglected as it is difficult to maintain with continuous enthusiasm by public health professionals at both local and national levels(8). Surveillance is particularly useful in identifying index cases early, followed by prompt mosquito control activities. In countries without intensive dengue control activities and where imported dengue cases can spread rapidly because of the presence of Aedes aegypti and Aedes albopictus, surveillance of febrile patients returning from these areas provides valuable epidemiological information for future planning, implementation and evaluation. In fact, active surveillance and monitoring of indigenous transmission of dengue is a crucial step to avoid a large-scale epidemic. Unfortunately, difficulties in dengue surveillance are multi-factorial, including: (i) a high proportion of mild and asymptomatically-infected individuals in areas where dengue is endemic or sporadic; (ii) a complex disease whose symptoms/signs are not distinguishable from other common febrile illnesses; (iii) unrecognized disease by physicians in many places where DF and/or DHF cases rarely occur; (iv) few or inappropriate specimens collected promptly for laboratory confirmation and haematological tests; and (v) insensitive clinical surveillance because most Chinese patients prefer to be self-treated with non-prescriptive drugs rather than visit doctors.

Historical epidemics of dengue in Taiwan had been documented in 1902, 1915 and 1922 in Penghu Islet, in 1924 and 1927 in southern Taiwan, 1931 in Tainan, and 1942-43 in island-wide Taiwan(9), partially because the dengue cases came from epidemic/endemic countries in South-East Asia, and the high prevalence of water storage tanks among households during wartime. The virus was silent for almost 37 years until 1981, when the DEN-2 epidemic
of DF recurred on the islet of Hsiao-Liu-Chiu, which belongs to the Pingtung County administratively and located off southern Taiwan (10). Fortunately, it did not result in an epidemic in main Taiwan Island. The DEN-1 epidemic of DF then exploded in 1987-1988 in southern Taiwan, particularly Kaohsuing and Pingtung. The first DHF epidemic due to DEN-3 appeared in 1994. Four years later, the largest epidemic of DHF caused by DEN-3 occurred in Tainan. Up to now, Taiwan is a very unique dengue epidemic country where the total number of reported DHF/DSS cases have remained below 30 for 57 years since 1943, even though many tourists travel between Taiwan and other Asian countries where the numbers of DHF/DSS were very high. The specific aim of this study was to analyse the trend of major dengue epidemics in Taiwan and whether it was related to the status of dengue in other Asian countries, imported cases, and success and failure in the surveillance system.

Materials and methods

Study area

Taiwan, located 160 km from the south-east coast of mainland China, is about 392 km long and 143 km wide. The population was over 21 million during 1999-2000, with a very high population density. Nearly all Taiwanese are graduated from elementary school and the GNP for the year 2000 was more than US$ 14,000.

Sources of data

Surveillance of dengue in Taiwan

The most unique feature of dengue surveillance in Taiwan is the active epidemiological investigation of each suspected case reported to the Department of Health. This active surveillance system was established in 1988 by the Division of Epidemiology, National Institute of Preventive Medicine. Once physicians at local clinics or hospitals reported suspected dengue cases with persistent fever and one of dengue-like symptoms, the neighbouring 50 households were interviewed to determine the possible source of infection. More than 100 of their blood specimens were mandatory to be collected regardless of their febrile history by local public health personnel after informed consent for dengue-specific IgM test. All DHF cases were evaluated by experienced physicians who had been trained at the Children’s Hospital in Thailand. According to the revised guideline by WHO (6), all confirmed dengue cases were defined by positive virus isolation, reverse-transcriptase polymerase chain reaction (RT-PCR), dengue-specific IgM, 4-fold sero titre rise or fall by ELISA IgG, or haemagglutination inhibition (HI) antibody. Data of active and passive surveillance were pooled to analyse the trend of the epidemic, the role of imported cases, monthly distribution of indigenous cases, and the effectiveness of surveillance and control.

In addition, the epidemiology unit of infectious disease laboratory at the Institute of Epidemiology, National Taiwan University (NTU), also established ‘active sentinel-physician surveillance’ by collaborating with several enthusiastic physicians with a public health bent of mind and having experience in reporting dengue cases, in Tainan, Kaohsiung and Pingtung. In early July of each year, special visits to sentinel physicians and medical technologists of the sentinel clinics/hospitals were made for increasing awareness. Suspected blood samples were
delivered to NTU by express mail within eight hours on the same day for RT-PCR test. Once the positive dengue cases were identified by RT-PCR, blood samples from the family members were encouraged to be collected. The national surveillance data were obtained from the National Institute of Preventive Medicine (renamed as the Center for Disease Control after reorganization since July 1998).

**Other sources of data**

Cases of dengue in respect of other Asian countries were obtained from the WHO website[12]. In addition, Dr Sai-Kit Lam provided several annual reports on dengue from Malaysia. Data on dengue in Thailand were also obtained from published papers and government reports in Thailand, Indonesia, the Philippines and Myanmar.

**Statistical analysis**

All data were entered into the database and analysed by SAS (Statistical Analytical System, Wisconsin, 6.12 version). Due to the small sample size, the Wilcoxon signed ranks test was performed to compare the trend in the increasing number of dengue cases between two consecutive years in those Asian countries that the Taiwanese people liked to visit. The p-values were calculated to test for statistical significance.

**Results**

A. **Recent major epidemics of dengue in Taiwan**

**Trends of dengue epidemics in Taiwan**

In the last 20 years, the epidemic patterns of dengue in Taiwan remained cycled with small-scale outbreaks occurring almost every three years and large-scale epidemics occurring nearly every ten years (Figure 1). The number of reported dengue cases was much higher in 1981, 1987-1988, 1991, 1994-1995 and 1998 than in other years[11]. Whenever mosquito control activities were not effective enough, the epidemic continued into the following years as was the case with the DEN-1 epidemic in 1987-1988. On the other hand, problems in control were also detectable when the total number of the confirmed indigenous dengue cases was higher than that of the confirmed imported cases in 1991, 1994, 1995, 1998 and 2000. However, when active surveillance was started early enough and multiple channels of reporting were implemented, the total number of confirmed indigenous dengue cases became less than the confirmed imported dengue cases in the years 1996-1997. In other words, the effectiveness of surveillance and control of dengue was easily reflected in whether the number of confirmed indigenous cases increased during that period of time.

**Statistical association between Taiwan’s major epidemics and dengue activities in Asian countries**

To investigate the possible relationship between major dengue epidemics in Taiwan and the status of dengue in other Asian countries at around those times, we reviewed the number of dengue cases reported to WHO from Asia during 1955-1998. A detailed analysis of those cases made it evident that increased numbers of dengue cases were statistically significant in
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six countries from 1979 to 1980 (p=0.028), in five countries from 1986 to 1987 (p=0.043), and in nine countries from 1997 to 1998 (p=0.08) (Figure 2).

Prior to the first epidemic of DF caused by DEN-2 in Hsiao-Liu-Chiu in 1981, after the long silence of dengue activity since World War II, the Philippines, Thailand, Viet Nam, Indonesia and the Lao People's Democratic Republic had reported increased numbers of dengue cases (p=0.028) (Figure 2). In particular, a series of clusters of the imported cases of this epidemic were fishermen who came from the Philippines, which was also consistent with the striking increase in the number of reported dengue cases from 392 in 1979 to 968 in 1980 in that country.

A similar trend was noticed before the DEN-1 epidemic in Pingtung and Kaohsiung during 1986-1987 when the dengue status in Asia was also statistically high in five countries, including Indonesia, Thailand, Malaysia, Myanmar and Viet Nam, when the most number of imported dengue cases were reported in Taiwan (p=0.043) (Figure 2). This was the time when many Taiwanese businessmen and visitors went to Thailand after rapid increase of the GNP in 1987, which was on parallel with the fact that dengue cases had a striking 6.25-fold increase in Thailand from 27,837 in 1986 to 174,285 in 1987. In addition, Viet Nam also faced a severe dengue problem in 1987 with 354,517 reported cases, a figure much higher than the 46,266 cases reported in 1986.

In 1998, the pandemic of dengue spread in many countries. The majority of the confirmed imported dengue cases in Taiwan in 1998 primarily came from five countries: Thailand, Indonesia, Malaysia, the Philippines and Myanmar where the number of dengue cases had a statistically significant increase from 1997 to 1998 (p=0.043) (Figure 2). Of these countries, Indonesia reported the highest increase from 30,730 cases in 1997 to 71,087 in 1998, with many DEN-3 viruses isolated in 1998.

With the opening of the south-east Asia business policy advocated by the Government of Taiwan since 1996, more commercial exchanges between Taiwan and Indonesia took place. Interestingly, DEN-3 was also isolated from the imported cases of two brother businessmen, who returned from Indonesia through an active surveillance system established at the National Taiwan University. Subsequently, the predominant serotype of dengue virus isolated in most of the confirmed indigenous dengue cases, including DF and DHF/DSS, was also DEN-3 during this largest epidemic of DHF in Tainan since the 1950s.

Similarities and differences in dengue epidemic patterns in five major Asian countries related to Taiwan dengue epidemics

A comparison of the dengue epidemic patterns in these five countries from where Taiwan’s imported cases primarily originated, revealed that Thailand also had a 3-year cycle of small-scale epidemics in the years 1987, 1990, 1993 and 1997 (Figure 2). The years of 1987 and 1998 when Thailand
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reported the highest number of dengue cases also witnessed the largest epidemic of DF (1987) and of DHF (1998) on the main Taiwan island. However, the peaks of Thailand’s dengue cases in those important years were much higher and earlier than the peaks in Taiwan. On the other hand, the time intervals of dengue epidemics in Indonesia were much longer, with the highest number of cases reported in 1998. The cycling of dengue epidemics in the Philippines and Myanmar was not clear. All these five countries had almost the highest number of dengue cases in 1998 as compared to other years during the last 20 years of the 20th century.

B. Contribution of imported cases and monthly distribution of dengue cases in major epidemics in Taiwan

(1) 1981. The dengue fever epidemic was attributed to four successive groups of a total of 71 fishermen, who crossed the country’s fishing border, were arrested and detained in the Philippines for some time, and acquired dengue the infection there.

(2) 1987-88. The DF epidemic in 1987 resulted in 1387 reported and 488 laboratory-confirmed DF cases, with most of them distributed in Kaohsiung city, Kaohsiung county and Pingtung county. The Government officials at the Bureau of Communicable Disease Control received the first reported case of one female patient with persistent fever, rash, itching and red swelling of the feet and hands on 19 November 1987 from a physician at the Mackay Memorial Hospital in Taipei (Figure 3). The epidemic became known only after two months during which it spread affecting a total of 152 cases in Pingtung, and even more (225 cases) in Kaohsiung, because most of the physicians there were not aware of dengue since there had been no activity for almost 44 years.

(3) 1998. The imported dengue cases in 1998 appeared even during winter months (January-February) and then continued to increase during summer months (July-September). The indigenous dengue cases began to rise in August but peaked in November. Finally, the epidemic resulted in 1430 reported and 348 confirmed dengue cases, which included 334 cases of DF and 14 cases of DHF (Figure 4).

C. Monthly distribution of dengue cases in some Asian countries

Malaysia and Viet Nam, where many Taiwanese prefer to visit, witnessed rising trends of dengue cases about 2-3 months earlier than in Taiwan in 1998 (Figure 5). A similar pattern was also noticed in the distribution of dengue cases in Thailand, with DHF cases peaking in June-August of that year (data not shown). On the other hand, indigenous dengue cases in Taiwan began to rise towards the end of summer and after the peak months of DF/DHF in those Asian countries which have a close relationship with Taiwan.
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Figure 1. Number of reported, confirmed imported and indigenous dengue cases in Taiwan in 1981 and 1987-2000

Figure 2. Number of dengue cases reported in five countries, including the Philippines, Thailand, Viet Nam, Indonesia, Lao People’s Democratic Republic, 1979-1998
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Figure 3. Number of dengue cases and incidence rates in October 1987 - December 1988 in Taiwan

- Confirmed Cases
- Incidence

Month, 1987-1988

No. of Confirmed Dengue Cases in Taiwan

Incidence Rate (per 100,000)

Confirmed Cases

Incidence

Figure 4. Monthly distribution of dengue cases in 1998 in Taiwan

- Reported Cases
- Indigenous Cases
- Imported Cases

Month in 1998

No. of Dengue Cases in Taiwan

**Discussion**

According to WHO reports of dengue cases and deaths during 1995-1998, many countries and areas such as Malaysia, Cambodia, Viet Nam, Thailand, the Philippines, Indonesia, Myanmar in the south-east Asia; Guam, Cook Islands, Fiji, New Caledonia, Kiribati in the western Pacific, and Brazil, Venezuela and Colombia in Latin America had experienced unusually higher levels of dengue/dengue haemorrhagic fever activity in 1998 than in previous years\(^{12}\). Therefore, a future pandemic of dengue is possible. Countries, which are located in areas neighbouring those where the transmission of dengue virus is intensive, should use surveillance as the most effective prevention and control strategy for dengue.

Dengue epidemics always happen when the chain of transmission cannot be interrupted because of under-diagnosis, incomplete or delayed reporting, and lack of specimens for laboratory diagnosis. Laboratory surveillance of dengue confirms DF and DHF cases, but it is also most helpful in monitoring serotypes and strains circulating in the population. For example, the introduction of a new serotype, which has not been conferred enough high-herd immunity, may serve as an important indicator of future epidemics of DHF/DSS. Therefore, strengthening surveillance of imported cases at local level, coupled with international collaboration on exchange of epidemiological information, will upgrade and improve the efficiency of dengue control.
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