

Dengue and Dengue Haemorrhagic Fever in the Americas: An Overview of the Problem

Background

Dengue-like illness has been reported in the Americas for over 200 years. Most dengue outbreaks occurred at intervals of one or more decades, until the 1960's, but thereafter the intervals have become shorter.

The first laboratory documented epidemic of classic dengue fever in the Americas was associated with dengue-3 serotype, and affected the Caribbean Basin and Venezuela in 1963-64. Prior to that only dengue-2 virus had been isolated in the Region, in Trinidad in 1953-54, in a non-epidemic situation. In 1968-69, another epidemic affected several Caribbean islands, during which both dengue serotypes 2 and 3 were isolated.

During the early and mid 1970's, Colombia was affected by extensive outbreaks associated with serotypes 2 and 3; during this period these serotypes became endemic in the Caribbean. In 1977 dengue serotype 1 was introduced into the Americas and after its initial detection in Jamaica, subsequently spread to most Caribbean islands causing explosive outbreaks. Similar outbreaks were observed in northern South America (Colombia, Venezuela, Guyana, Suriname and French Guiana), Central America (Belize, Honduras, El Salvador, Guatemala) and Mexico. Indigenous transmission of dengue-1 was also documented in the state of Texas, United States of America, during the second half of 1980. About 702,000 cases of dengue were reported by the affected countries during the period 1977-80 in which dengue-1 was practically the only serotype circulating in the Americas. It is likely, however, that during this period, millions of persons were infected with the virus, since in Cuba alone about 42% of its 10 million inhabitants were infected with dengue-1.

Magnitude of the Dengue Problem in the 1980's

During the 1980's, there was a considerable increase in the magnitude of the dengue problem in the Americas which was characterized by a marked geographic spread of dengue activity in the Region. In 1982, an epidemic caused by serotypes 1 and 4 occurred in northern Brazil. In 1986, a major outbreak due to dengue-1 affected Rio de Janeiro and subsequently the virus propagated to several other Brazilian states. Four other countries, with no previous history of dengue or absence of the disease for several decades suffered extensive epidemics due to dengue-1: Bolivia (1987), Paraguay (1988), Ecuador (1988) and Peru (1990). During the Peruvian outbreak, dengue-4 was also isolated. Serologic studies suggested that several million persons were affected during these outbreaks although only about 240,000 dengue cases were reported by the five countries during the period 1986-90. On the other hand, there was a marked increase in the occurrence of dengue haemorrhagic fever/dengue shock syndrome (DHF/DSS).

DHF/DSS in the Americas

To date the outbreak of DHF/DSS that affected Cuba in 1981 was the most important event in the history of dengue in the Americas. During this epidemic associated with dengue-2 virus, a total of 344,203 cases of dengue were reported which included 10,312 classified as severely ill (WHO grades II-IV) and 158 deaths (of which 101 were children). A total of 116,143 persons were hospitalized, the majority of them during a three-month period. The Cuban government quickly implemented an effective *Aedes aegypti* control program which resulted in the elimination of dengue, and almost eradicated the vector. The second American outbreak of DHF/DSS took place in Venezuela. The outbreak started in October 1989, peaked in January 1990, then showed a marked decline and apparently ended in April; however, cases of DHF continued to be notified in Venezuela throughout 1990. A total of 5,990 DHF cases (2,665 in 1989 and 3,325 in 1990) including 70 deaths* (18 in 1989 and 52 in 1990) were reported. Approximately two-thirds of these cases and fatalities were among children under 14 years of age. Isolations of serotypes 1, 2 and 4 were obtained during the outbreak.

Prior to the Cuban outbreak, only sporadic suspected cases of DHF were reported in the Americas. These reports originated from Curaçao and Venezuela in the 1960's, and from Honduras, Jamaica and Puerto Rico in the 1970's. Only a few cases were laboratory confirmed. However, from 1981 through 1991 with the exception of 1983, confirmed cases of DHF which meet the WHO case definition have been reported annually. Countries reporting DHF or cases of severe haemorrhagic disease included Suriname, Mexico, Dominican Republic, Aruba, Nicaragua, Colombia, Puerto Rico, St. Lucia, the U.S. Virgin Islands, Brazil, El Salvador, and Honduras, in addition to Cuba and Venezuela. Most countries have reported fewer than 10 cases, but others such as Brazil, El Salvador, Colombia, and Puerto Rico, have each had over 40 cases. Puerto Rico has reported laboratory confirmed cases of DHF/DSS every year from 1985 through 1990 and the disease is considered to be endemic on the island. Brazil reported a few sporadic cases associated with dengue-1 infection during 1986-87. Following the introduction of dengue-2 in 1990, an outbreak of DHF was reported in Rio de Janeiro in the latter part of 1990 with 274 cases and 3 deaths, and an additional 161 cases were reported in 1991 (provisional figure through November 1991). In 1991 dengue-2 virus spread to two other Brazilian states, one of which was previously infected with dengue-1, but to date no haemorrhagic disease has been reported from these states. El Salvador reported 153

*The Ministry of Health and Social Welfare of Venezuela had notified 73 deaths for the period October 1989 to April 1990. (*Epidemiological Bulletin*, Vol. 11, No. 2, 1990.)

cases (7 fatal) of DHF in 1987-88, and 1 in 1991, but only a few were laboratory confirmed. Colombia reported 40 confirmed DHF cases in 1990 and an additional 95 cases in 1991 (provisional figure through 21 December 1991). The fact that Venezuela reported 1,980 cases of DHF (26 deaths) in 1991 suggests that DHF is becoming endemic in that country. It should be noted that several cases did not meet WHO's DHF case definition (e.g. Curaçao, 1968; Jamaica, 1977; Aruba, 1985; Brazil in 1986) or the clinical information was insufficient or absent to determine if they fulfilled such definition (e.g. Venezuela, 1968, Honduras, 1978, Nicaragua, 1985, El Salvador 1987-1988).

Thus it appears that DHF/DSS is gradually becoming endemic in several countries of the Americas, consequently mimicking the situation observed in Asia. The marked increase of DHF/DSS incidence observed in several Asian countries during the past 10 years compared to the preceding years illustrates the potential threat that American countries face in the future.

Reports of Dengue Cases

Information on the number of reported cases of dengue by country in the Americas for the period 1980-90, and circulating dengue serotypes are reported periodically to PAHO. With the exception of 1981, when there were about 388,000 cases, numbers for the other years range from about 39,000 (1984) to about 134,000 (1987). The marked underreporting of dengue cases is illustrated in Ecuador, where only 25 cases were reported in 1988, while a serological survey in Guayaquil estimated that 422,000 of its inhabitants were infected. In 1986-87 a similar situation was observed in Brazil which reported 136,764 cases; however serological surveys estimated that over one million infections occurred in Rio de Janeiro during this biennium. With the exception of 1981, when Cuba reported 344,203 cases, most dengue fever case reports during 1980-84 came from Mexico. In 1985 Aruba and Nicaragua reported more cases than any other country; in 1986-87 and in 1990 most came from Brazil, whereas Colombia in 1988 and Paraguay in 1989 reported the highest number of cases.

Dengue Virus

Dengue virus belongs to the family *Flaviviridae*. Four serotypes can be distinguished by serologic methods, designated dengue-1, dengue-2, dengue-3 and dengue-4. The infection in man by one serotype produces only temporary and partial protection against other serotypes. All serotypes have been isolated from autochthonous cases in the Americas; during the period 1978-1991 however, only dengue serotypes 1, 2 and 4 have been circulating; dengue-3 was last isolated in Colombia and Puerto Rico in 1977. Although dengue-2 was associated with the major outbreak of dengue and DHF/DSS in Cuba in 1981, dengue-1 and dengue-4 were the predominant circulating serotypes during the 1980's. In addition to the outbreaks in five South American countries discussed above, dengue-1 also caused important outbreaks in Aruba, Mexico and Nicaragua. The introduction of dengue-4 in the

Americas in 1981 was followed by epidemics of dengue fever in the Caribbean, Central America, Mexico and northern South America during 1981-83, and subsequently caused major epidemics associated with cases of DHF in Mexico (1984), Puerto Rico (1986) and El Salvador (1987). Dengue-4 virus is now endemic in the Region. Simultaneous circulation of serotypes 1, 2 and 4 over a period of several years has been observed in several countries, creating a hyperendemic situation that puts these countries at high risk for epidemic DHF.

Molecular studies on the nucleotide sequences of dengue virus genomes allow classification of the agent into genotypes. One genotypic group of dengue-1 virus and two of dengue-2 virus are known to be circulating in the Americas. Another dengue-1 genotype was isolated only in Mexico in 1980. The clinical significance of the infection due to these genotypes in man is presently unknown, but they are useful for the understanding of the epidemiology of dengue viruses.

Dengue Virus Transmission

In the Americas, dengue virus persists in nature through a man - *Aedes aegypti* - man transmission cycle. Following an infective blood meal, the mosquito can transmit the agent after a period of 8-12 days of extrinsic incubation. Transmission may also occur when feeding is interrupted and the mosquito immediately feeds on a nearby susceptible host. *Aedes albopictus*, now present in the Americas, is a maintenance vector of dengue in Asia, but so far it has not been associated with dengue transmission in the Americas. The epidemiologic significance of transovarial transmission of dengue virus in *Ae. aegypti* and other vectors in the Americas is presently unknown.

Cost and Economic Impact

Few studies have been conducted to estimate the economic impact of dengue and DHF/DSS in the Americas. A study done in Puerto Rico during the 1977 dengue epidemic estimated that the costs in medical services and loss of work was between US\$6 and US\$16 million; according to recent studies the cost of epidemics of the disease in Puerto Rico since 1977 is estimated to be between US\$150 and US\$200 million.

The cost of the DHF/DSS Cuban epidemic was estimated at about US\$103 million including control measures and medical care. Of this total US\$41 million was for medical care, US\$5 million for salaries paid to adult patients, US\$14 million for lost production and US\$43 million for the direct initial cost of the *Ae. aegypti* control program. It should be mentioned that the cost of this epidemic would be considerably higher today due to inflation.

It is conceivable that the disease has caused significant impact on tourism, particularly during epidemics. However, no estimates are available on the costs due to such impact.

(Source: Communicable Diseases Program, PAHO, based on country reports.)