



Dengue Fever

Introduction

Dengue fever (DF) is caused by an arthropod borne virus of the genus *Flavivirus*, and within the family *Flaviviridae*. Other flaviviruses include Japanese encephalitis and yellow fever. There are four distinct serotypes of dengue virus (DEN 1, DEN 2, DEN 3 and DEN 4) all of which have the potential to cause either classic dengue fever or the more serious form of the disease, dengue haemorrhagic fever (DHF). Dengue is transmitted by the bite of an infected *Aedes* sp. mosquito.

Epidemiology

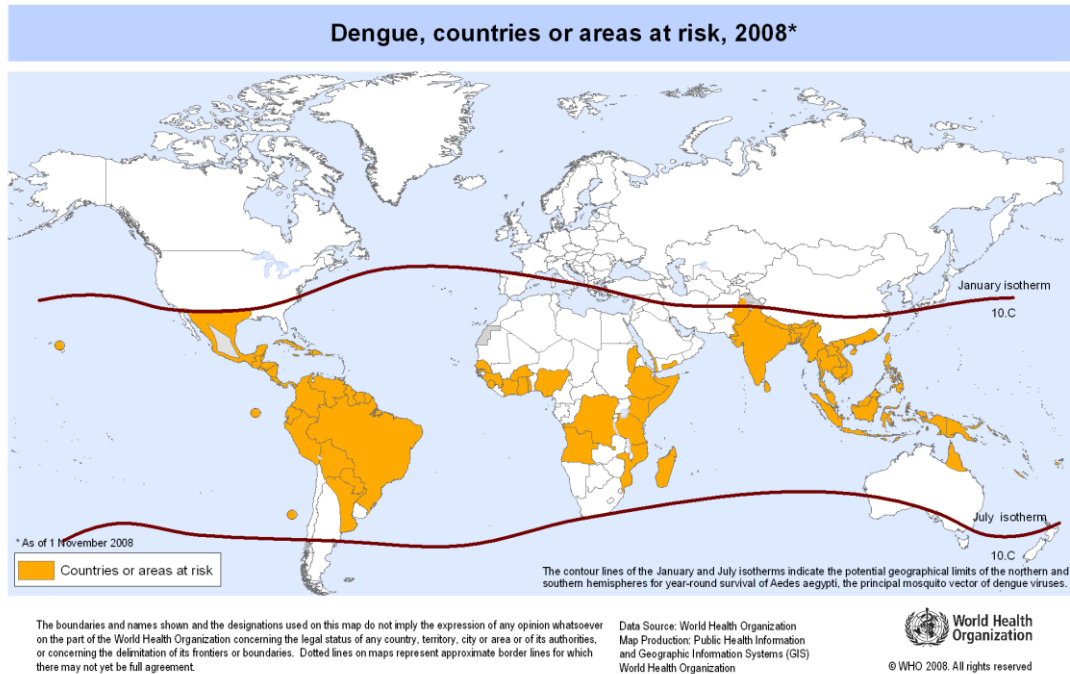
Global Epidemiology

Dengue has been reported since the 18th century. During that time major epidemics occurred at intervals of 10 to 40 years in Asia, Africa, and North America. The *Aedes* mosquito and the dengue virus were dependent on sailing vessels to transport them from one population to another, and when a new serotype was introduced, new epidemics occurred [1]. This meant that the outbreaks tended to be focused mainly in seaports. The epidemiology of dengue changed after the Second World War, due to increasing economic growth and the urbanisation of South East Asia in particular, where millions of people moved to the cities. Urban centres grew rapidly, often with inadequate water and sewage systems, thus providing an environment for the *Aedes* mosquito to breed [2]. The dengue virus spread rapidly and the disease developed into pandemic proportions [3].

An increase in commercial air travel has subsequently aided the transmission of the virus between populations so that dengue is now endemic in over 100 countries throughout tropical and sub-tropical areas of the world. The main vector *Aedes aegypti* is found worldwide between latitudes 35°N and 35°S [4]. The principle areas affected include the Caribbean, South and Central America, Mexico, Africa, the Pacific Islands, South East (SE) Asia, Indian sub-continent, Hawaii, and Australia (see Figure 1). By 2002, more than 2.5 billion people were at risk of infection (roughly 40% of the world's population). An estimated 50-100 million illnesses occur annually, 250,000-500,000 of which are dengue haemorrhagic fever, many of these in children. The estimated global mortality rate is 25,000 per annually [5].

Epidemic dengue increased in East Africa in the 1980s, and all four serotypes have now been documented throughout the African continent. The same pattern has also emerged in the Americas, notably Central and South America. In the 1980's a total of 15,000 cases of dengue haemorrhagic fever were reported, 56,000 cases in the 1990's and 15,000 in 2001 [4]. Cases are also increasingly being reported outside the tropical areas. The continued increase in urbanisation, population growth and global travel introduces the different serotypes into new populations.

Figure 1. Dengue, countries or areas at risk, 2008 [6].



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The highest burden of disease occurs in SE Asia and the Western Pacific (Figure 1), but over the last few years there has been a rising trend in South America and the Caribbean. Further information is available [7]. To standardise the reporting of dengue and improve the quality and accuracy of dengue statistics, the World Health Organization (WHO) has created DengueNet [8]. This is an online database containing dengue statistics from 1955 to 2005.

Figure 2. Average annual number of DF/DHF cases reported to WHO [9].

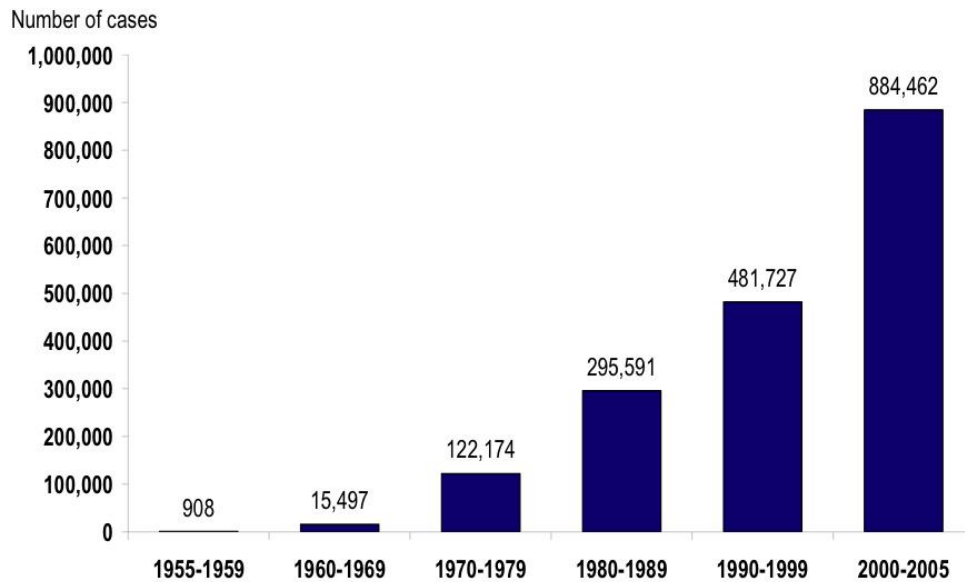


Figure 2 shows the worldwide provisional figures for dengue fever/dengue haemorrhagic fever as reported by DengueNet in 2006. There has been an increase in worldwide incidence from 1970 to 2005.

Dengue fever in UK travellers

Dengue fever does not naturally occur in the United Kingdom (UK) but is imported in small numbers. The majority of imported cases (where information is available) are associated with travel to SE Asia and the Indian sub-continent [10]. Table 1 shows the number of dengue cases that have been diagnosed by the Special Pathogens Reference Unit, Novel and Dangerous Pathogens, Health Protection Agency Centre for Emergency Preparedness and Response in 2004 and 2005.

Table 1. Number of laboratory identified dengue cases (confirmed and probable): 2004 and 2005

Source	2004	2005
England	144	163
Wales	2	1
Scotland	6	19
N. Ireland	0	0
TOTAL	152	183

N.B. A laboratory identified case = isolation and/or polymerase chain reaction positive and/or Flavivirus (Dengue) IgM antibodies detected.

Risk for travellers

The chance of contracting DF is determined by several factors including travel destination, length of exposure in endemic areas, the intensity of dengue transmission, and the season of travel. Risk is thought to be higher during periods of intense mosquito feeding activity two to three hours after dawn and during the early evening) [8].

All travellers to tropical countries where dengue is endemic are at risk of infection, although determining the actual level of risk is difficult. Several studies have demonstrated that travellers who spend a long period in endemic areas (such as expatriates or aid workers) are at increased risk; however, even short-term visitors may be exposed to dengue [11-13]. The GeoSentinel [14] global network of travel and tropical medicine clinics reported on illness in returned travellers, and determined that the regions at highest risk for dengue were SE Asia and the Caribbean [15]. The true incidence of dengue fever in travellers is probably underestimated because in many countries reporting is not obligatory and, due to its non-specific symptoms, it is probably under-diagnosed [5].

Transmission

Transmission occurs following a bite from an infected *Aedes* mosquito. It is most widely transmitted by *Ae. aegypti* and *Ae. albopictus* (Asia, Philippines and

Japan), other *Aedes* species also transmit disease in specific areas; *Ae. polynesiensis*, *Ae. scutellaris* and *Ae. pseudoscutellaris* (Pacific Islands and New Guinea), *Ae. polynesiensis* (Society Islands) and *Ae. niveus* (Philippines) [16].

The cycle of transmission typically involves humans and mosquitoes. The virus is spread from an infected human to a mosquito and then to another human, often in areas where there are dense human populations. In parts of SE Asia and Africa, the transmission cycle may also involve jungle primates that act as a reservoir for the virus.

The *Aedes* mosquito prefers to breed in water-filled receptacles, usually close to human habitation. They often rest in dark rooms (e.g. in bathrooms and under beds) and breed in small pools that collect in discarded human waste [3]. Although they are most active during daylight hours, biting from dawn to dusk, mosquitoes will feed throughout the day indoors and during overcast weather. The mosquito becomes infectious 8-10 days after feeding and remains infectious for life (2-3 months).

Signs and symptoms [4]

The disease can be classified into five presentations; non-specific febrile illness, classic dengue, dengue haemorrhagic fever, dengue haemorrhagic fever with dengue shock syndrome, and other unusual syndromes such as encephalopathy and fulminant liver damage. Clinical features vary with the age of the patient. Studies from populations where dengue is endemic suggest that between 14% and 87% of cases are asymptomatic or sub-clinical [17-19].

The incubation period is 5 to 8 days. In non-immune persons, dengue begins with a fever lasting 1 to 5 days.

Young children with dengue often have an undifferentiated febrile illness with a maculopapular rash, which typically spreads from the trunk to include the limbs and face and which occurs between days 3 and 5 of the illness. Upper respiratory tract infections are common. Most infections in children are asymptomatic or minimally symptomatic.

Classic dengue is more common amongst older children, adolescents, and adults. It has an abrupt onset with a high fever which is often accompanied by a severe headache, myalgia, arthralgia, nausea, and vomiting. Most infections are self-limiting with improvement in symptoms and rapid recovery occurring 3 to 4 days after the onset of the rash.

Dengue haemorrhagic fever (DHF) is primarily a disease of children under 15 years in hyperendemic areas. It is characterised by increased capillary permeability and haemostatic changes e.g. bleeding under the skin (purpura), from the gums and gastrointestinal tract. Mortality can be as high as 10-20% if left untreated.

DHF with shock is accompanied by respiratory and/or renal failure. Mortality, if left untreated, can be 40%. Survival rates are significantly higher if the patient is treated in hospital by experienced staff, leading to low mortality rates of 1% to 2% [20]. It is not certain what precipitates progression, although it has been suggested that previous infections with a different serotype of the virus

predisposes to DHF when a person becomes re-infected. This form of dengue is rarely seen in travellers.

Rare presentations of infection include severe haemorrhage, jaundice, parotitis, and cardiomyopathy. Neurological symptoms can include encephalitis, polyneuropathies and transverse myelitis. Guillain-Barré syndrome has also been reported.

Lifelong immunity to the infecting virus serotype occurs in those who recover, however, infection with one serotype does not confer immunity to the other three serotypes or to other flaviviruses.

Treatment

There is no specific antiviral treatment for either classic dengue or DHF. Supportive nursing care and careful management of fever, fluid balance, electrolytes, and clotting parameters are the standard treatment.

Prevention

There is no vaccine to prevent dengue fever. Prevention is by minimising mosquito bites especially during daylight hours. Particular vigilance with [bite precautions](#) should be taken around dawn and dusk.

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Reading list

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