



## A global health problem: “Dengue fever”

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### Abstract

Dengue is currently regarded globally as the most important mosquito-borne viral disease. The mosquito-borne viral disease dengue has become one of the worst nightmares of the country. Also called 'break bone fever' or 'dandy fever', it is caused by a family of viruses and is transmitted via *Aedes* mosquitoes. Dengue begins suddenly, with more benign symptoms at first but which may get severe with time. The symptoms of the disease show in three to seven, and sometimes fifteen, days. Recovery from dengue does not take over a week unless the condition gets severe. Mostly asymptomatic, if the condition gets critical, dengue can be life-threatening. The fever of dengue can attack anyone but those with weaker immunity are more prone to the disease getting severe when they are attacked. As it is caused by any of the four serotypes of the *Aedes Aegypti*, also called the yellow fever mosquito, dengue can happen multiple times to the same person. However, the person acquires immunity to the particular viral serotype which has already attacked him. A more severe form of dengue is dengue hemorrhagic fever.

The Centers for Disease Control and Prevention (CDC) estimate that 400 million people are infected each year. Dengue fever is rare in the United States (U.S.), but around 100 cases are reported each year, mostly among people traveling from outside the country. Outbreaks have occurred in Texas, Florida, and Hawaii. Around 2.5 billion people, or 40 percent of the world's population, live in areas where there is a risk of dengue transmission. Dengue is endemic in at least 100 countries in Asia, the Pacific, the Americas, Africa, and the Caribbean. In India, according to the Directorate of National Vector Borne Disease Control Programme (NVBDCP), till December 2017 the total dengue cases in the country were 157220 with 250 deaths.

Symptoms usually begin 4 to 7 days after the mosquito bite and typically last 3 to 10 days. Symptoms range from mild to severe. Severe symptoms include dengue shock syndrome (DSS) and dengue hemorrhagic fever (DHF). These require hospitalization. The best method of prevention is to avoid mosquito bites. Treatment is possible if diagnosis occurs before the patient develops DSS or DHF.

The threat of Dengue is increasing day by day due to the increase in the number of breeding mosquitoes. It is very important to manage Dengue Fever very carefully otherwise it may lead to severe complications.

**Keywords:** aedes aegypti mosquitoes, dengue hemorrhagic fever (DHF), dengue shock syndrome (DSS), fever, morbidity, mortality etc.

### Introduction

The origins of the Spanish word dengue are not certain, but it is possibly derived from *dinga* in the Swahili phrase *Ka-dinga pepo*, which describes the disease as being caused by an evil spirit <sup>[1]</sup>. Slaves in the West Indies having contracted dengue were said to have the posture and gait of a dandy, and the disease was known as "dandy fever" <sup>[2]</sup>.

Dengue fever virus is considered the most important arbovirus in terms of morbidity, mortality and economic cost with an estimated 100 million cases of dengue fever occurring throughout the world annually. Dengue is transmitted by mosquito and occurs in epidemic and endemic proportions throughout tropical and subtropical regions of the world. Infection with dengue virus causes a wide number of clinical symptoms which range in severity. These include fever, a maculopapular rash and headache. Primary infection with dengue usually results in a febrile, self-limiting disease, however, secondary infection may result in severe complications such as dengue shock syndrome (DSS) or

dengue haemorrhagic fever (DHF). Patients diagnosed with dengue in endemic areas such as South East Asia generally have secondary infection, whereas patients in non-endemic areas are usually diagnosed with primary infection. Characteristic antibody responses to the disease enable serological diagnosis and differentiation between primary and secondary dengue <sup>[3]</sup>.

International Anti-Dengue Day is observed every year on 15 June. The idea was first agreed upon in 2010 with the first event held in Jakarta, Indonesia in 2011. Further events were held in 2012 in Yangon, Myanmar and in 2013 in Vietnam.<sup>[4]</sup> Goals are to increase public awareness about dengue, mobilize resources for its prevention and control and, to demonstrate the Asian region's commitment in tackling the disease <sup>[5]</sup>.

### Aims and Object

- Explain the growing significance of dengue and dengue hemorrhagic fever in public health.
- Focus on effective prevention and risk reduction strategies,

and promote school, Family, and the community in to prevention programs.

- Focus the management and control of the dengue vector: *Aedes Aegypti* and other species of *Aedes*.
- Focus the prevention and control programs among communities and local health care workers.

### Material and Method

This study is carried out by literature search and critical review of the obtained facts. The various medical research databases like PubMed, Google scholar and another national research databases. The terms entered for search are “Dengue Fever (DF), also known as Dengue Haemorrhagic Fever (DHF) and Dengue Shock Syndrome (DSS)”. Manual search was made by going through the reference list of retrieved articles to identify relevant additional study.

### Epidemiology of dengue

Dengue was classified by The World Health Organisation (WHO) in 2012, as the most important mosquito-borne viral disease in the world. Dengue is also the world’s most rapidly spreading and geographically widespread mosquito-borne disease. WHO has reported that there has been a marked rise of annual dengue cases since 1950’s. Dengue epidemics are observed to be larger, more frequent and associated with more severe disease than they were in the past.

Up to 3.6 billion people are estimated to now live in tropical and subtropical areas where the dengue viruses have the potential to be transmitted. Globally it is estimated that approximately 50 million to 200 million dengue infections, 500,000 cases of severe dengue, and over 20,000 dengue related deaths occur annually.

The geographical distribution of dengue is linked to the areas where the mosquito species *Aedes Aegypti* and *Aedes Albopictus* can be found. Uncontrolled urbanisation, expanding urban population, poverty, ineffective public health infrastructure, indiscriminate disposal of waste, faster modes of transportation, globalisation of trade and increased international travel have all been implicated as factors leading to the spread of dengue around the world <sup>[6]</sup>.

### Causes (vector/virus)

Dengue is caused by the bite of one of the many types of mosquitoes in the genus *Aedes Aegypti*. The spread of the dengue virus cannot happen directly from one person to another. It is not contagious and cannot spread through direct human contact. It needs an *Aedes* mosquito for the virus to be transferred.

DF is mosquito-borne and the primary vector is *Aedes Aegypti*. The female *Aedes* mosquitoes acquire the virus while feeding on an infected person. After a period of 8-12 days, the mosquito becomes infective and can transmit the virus to another human through its bites throughout its life. There may be transovarial transmission from the infected female mosquitoes to their offspring’s.

Dengue viruses are members of the genus *Flavivirus* and family *Flaviviridae*. They are single-stranded RNA virus with an icosahedral nucleocapsid surrounded by an envelope. There are four distinct serotypes: DEN-1, DEN-2, DEN-3, and DEN-4. Infection by one dengue serotype can give rise to life-long

immunity to the serotype but only partial protection to other serotypes. Sequential infection by different serotypes of dengue virus has been generally accepted as the predisposing factor of dengue haemorrhagic fever (DHF) and dengue shock syndrome (DSS). DHF is more likely to occur when dengue virus affects a person with immunity to a heterologous serotype. The frequency of each serotype causing DHF/DSS is in descending order of: type 2, 3, 4, and 1. All four dengue virus serotypes (DEN-1 to DEN-4) are presently circulating in different geographical areas <sup>[7]</sup>.

### Sign and Symptoms

#### Mild dengue fever

Symptoms can appear up to 7 days after being bitten by the mosquito that carries the virus.

They include:

- Aching muscles and joints
- Body rash that can disappear and then reappear
- High fever
- Intense headache
- Pain behind the eyes
- Vomiting and feeling nauseous
- Symptoms usually disappear after a week, and mild dengue rarely involves serious or fatal complications.

#### Dengue hemorrhagic fever

At first, symptoms of DHF may be mild, but they gradually worsen within a few days. As well as mild dengue symptoms, there may be signs of internal bleeding.

- Bleeding from the mouth, gums, or nose
- Clammy skin
- Damage to lymph and blood vessels
- Internal bleeding, which can lead to black vomit and faces, or stools
- A lower number of platelets in the blood
- Sensitive stomach
- Small blood spots under the skin
- Weak pulse
- Without prompt treatment, DHF can be fatal.

#### Dengue shock syndrome

DSS is a severe form of dengue. It can be fatal.

- Intense stomach pain
- Disorientation
- Sudden hypotension, or a fast drop in blood pressure
- Heavy bleeding
- Regular vomiting
- Blood vessels leaking fluid
- Without treatment, this can result in death.

The above symptoms appear in the first phase of dengue, which ideally last for up to four days. The second phase will begin with a drop in body temperature and sweating. But before this, you may experience that your body temperature has come down to normal and you would feel relatively better, but this will not last for more than a day and would lead you to the second phase of dengue symptoms. The third phase may see a rapid rise in temperature again, with rashes developing all over your body but your face. If the situation worsens, there can be a drop in the level of blood platelets, blood

plasma leakage or the blood pressure can drop down to a critically low point which may lead a circulatory collapse (shock).

### Warning Signs

- Worsening abdominal pain
- On-going vomiting
- Liver enlargement
- Mucosal bleeding
- High haematocrit with low platelets
- Lethargy or restlessness
- Serosal effusions

### Transmission of the dengue virus

Dengue viruses infect humans and some species of lower primates and humans are the main amplifying host of the virus. Dengue virus circulating in the blood of viraemic humans is ingested by female mosquitoes during feeding. The virus then infects the mosquito mid-gut and subsequently spreads systemically over a period of 8 to 12 days. After this extrinsic incubation period, the virus can be transmitted to other humans during subsequent probing or feeding. There are several factors which can determine virus transmission, including environmental and climate factors, host-pathogen interactions and population immunological factors<sup>[8]</sup>.

Dengue can also be transmitted via infected blood products and through organ donation<sup>[9]</sup>. In countries such as Singapore, where dengue is endemic, the risk is estimated to be between 1.6 and 6 per 10,000 transfusions<sup>[10]</sup>. Vertical transmission (from mother to child) during pregnancy or at birth has been reported<sup>[11]</sup>. Other person-to-person modes of transmission have also been reported, but are very unusual. The genetic variation in dengue viruses is region specific, suggestive that establishment into new territories is relatively infrequent, despite dengue emerging in new regions in recent decades<sup>[12]</sup>.

### Clinical Features

The virus may cause disease in humans after an incubation period of maximum 14 days. Dengue viruses cause three main clinical syndromes: DF, DHF and DSS. DF is an acute febrile viral disease characterised with fever, headache, myalgia, arthralgia, retro-orbital pain and maculopapular rash. The pain can be so severe that it is sometimes called “break-bone fever”. Most often, DF presents as a mild illness and rarely causes death, with case-fatality rate less than 1%. For DHF, the initial presentation is similar to DF but the patient may have bleeding and/or circulatory collapse after 2-7 days of high fever. This is due to a combination of thrombocytopenia (which is usually more severe than in DF) and plasma leakage from ‘porous’ capillaries leading to effusions such as pleural effusion, ascites and pericardial effusion.

For DSS, the patient with DHF may develop hypovolemic shock. In general, the period of shock is short and usually lasts only 1-2 days before the patient dies. However, the response to treatment with fluid replacement and oxygen administration is prompt. Case fatality rates of DHF/DSS vary in different countries. Expert treatment in a modern ICU reduces the mortality to less than 1%<sup>[13]</sup>.

### Laboratory Diagnosis

The diagnosis of dengue fever may be confirmed by microbiological laboratory testing<sup>[14]</sup>. This can be done by virus isolation in cell cultures, nucleic acid detection by PCR, viral antigen detection (such as for NS1) or specific antibodies (serology)<sup>[15]</sup>. Tests for dengue virus-specific antibodies, types IgG and IgM, can be useful in confirming a diagnosis in the later stages of the infection. Both IgG and IgM are produced after 5–7 days. The highest levels (titres) of IgM are detected following a primary infection, but IgM is also produced in reinfection. IgM becomes undetectable 30–90 days after a primary infection, but earlier following re-infections. IgG, by contrast, remains detectable for over 60 years and, in the absence of symptoms, is a useful indicator of past infection<sup>[16]</sup>.

Diagnosis of DF is usually confirmed by demonstrating a fourfold or greater rise in antibody titre to one or more dengue virus antigens between acute and convalescent serum samples. It can also be confirmed by the detection of dengue virus genome in, serum, cerebrospinal fluid or autopsy tissues by polymerase chain reaction (PCR). However, this is limited by the timing of specimen collection as virus can be detected in clinical samples during the viraemic phase usually within five days of disease onset. PCR has the advantage of enabling differentiation between the four dengue serotypes and allows further molecular epidemiological studies by sequencing. While the isolation of virus from clinical samples is the most specific diagnostic method, the time needed to obtain results (one to two weeks) is long. Besides, culture technique and facility may not be available in routine diagnostic laboratory. Thus, virus isolation is not routinely performed<sup>[17]</sup>.

Platelets help the blood clot and stop bleeding. Very low levels – the normal range is between 150,000 and 450,000 platelets per microliter of blood – lead to internal bleeding and shock, which results in death from multi-organ failure. You need to rush to a hospital if you have Platelets count under 30,000.

### Treatment

No specific antiviral medication is currently available to treat dengue. The treatment of dengue fever is symptomatic and supportive in nature. Bed rest, to take plenty of fluid and mild analgesic-antipyretic therapy are often helpful in relieving lethargy, malaise, and fever associated with the disease<sup>[18]</sup>. Blood platelets transfusion is done in serious cases of dengue fever.

### Prevention and Control

As the dengue virus is mostly active during daylight hours, particularly early morning and late afternoon, special precautions should be taken during these times of the day. Tropical and sub-tropical areas are more prone to the disease, hence travelling from and to these regions should be avoided. The following precautions can be adhered to in order to prevent the incidence of dengue:

- Ensure improved water storage
- Ensure proper waste disposal
- Strictly avoid water stagnancy

- Use mosquito repellents containing 10 per cent DEET but ensure that you read the warning label on them carefully
- Avoid dark colored clothing as mosquitoes are attracted to darker shades
- Wear light colored, full-sleeved clothes
- Opt for natural mosquito repellents like marigold and lemon grass

### Vaccination

Also, in 2016, World Health Organization has approved a vaccination for dengue, Sanofi Pasteur's Dengvaxia (CYD-TDV). It can be administered to people in the age group of 9 - 45 years in three doses in areas where the incidence of dengue is endemic <sup>[19]</sup>.

### Vector Control

*Aedes Aegypti* is the commonest vector of DV in India, followed by *A. Albopictus*. Larval indices indicate that *A. Aegypti* is well established in peri-urban areas and is beginning to displace *A. Albopictus*. Water-holding containers, viz. plastic, metal drums and cement tanks facilitate breeding of *A. Aegypti* <sup>[20]</sup>. Expansion in the risk area of diseases borne by it in the context of urbanization, transport development and changing habitats is a major concern <sup>[21]</sup>.

Vector control is known to be a good method for prevention of vector borne diseases. There are several reports from India which have demonstrated resistance of mosquito vector with anti-larval substances like DDT and dieldrin but susceptibility to malathion is reported <sup>[22]</sup>. Temephos is relatively more effective in controlling *A. Aegypti*, followed by fenthion, malathion and DDT <sup>[23]</sup>. Peridomestic thermal fogging reduced the resting and biting for the 3 days after treatment, whereas indoor fogging suppressed adult populations for 5 days <sup>[24]</sup>.

Plant based repellent against mosquito borne diseases have also been described. Flavonoid compounds derived from *Poncirus trifoliata* compounds have various activities against different life stages of *A. Aegypti*. Larvicidal and ovicidal activities of benzene, hexane, ethyl acetate, methanol and chloroform leaf extract of *Eclipta Alba* have shown potential for controlling *A. Aegypti* mosquito <sup>[25]</sup>. Hydrophobic nanosilica at 112.5 ppm is effective against mosquito species <sup>[26]</sup>.

### Public awareness on dengue virus infection

Dengue is one of the major public health problems which can be controlled with active participation of the community. Need is to organize health education programmes about dengue disease to increase community knowledge and sensitize the community to participate in integrated vector control programmes <sup>[27]</sup>.

### Conclusion

It can be concluded that dengue fever is a dangerous and life threatening disease and it's a growing threat to global health problem in tropical and sub-tropical regions of the world causing large scale mortality every year. Since the disease has no any specific treatment hence effective prevention is the only way to avoid the chances of infection. Prevention should be by minimizing mosquito bites especially during the

daylight hours. Furthermore, particular alertness with bite precautions should be taken around dawn and dusk.

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