



# EMERGING THERAPY FOR DENGUE

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## ABSTRACT

*Dengue fever is acute febrile diseases, it's caused by one of four closely related virus serotypes of the genus are Flavi virus, family Flaviviridae. Each serotype is sufficiently different that there is no cross-protection and epidemics caused by multiple serotypes can occur. It's transmitted to humans by the mosquito.*

*The incidence of dengue has grown around the world in recent a period of ten years. However, several classes of agents are in under investigation as potential anti-dengue drugs, including direct host modulators, antivirals, and RNAi therapeutics. These anti-dengue drugs in development will be reviewed here.*

**KEYWORDS:** *Dengue viruses, Aedes mosquito, Treatment*

Emission and arboreal Aedes vector for enzootic transmission of the flavivirus genus including other important pathogens such as yellow fever.

Dengue viruses are the causative agent of a dengue fever. Its genome is about 11000 bases that codes for three structural proteins (Membrane protein M, capsid protein C, and envelope protein E) and seven nonstructural proteins also including the short non-coding region on both the 5' and 3' ends.

The dengue virus genome is 11644 nucleotides in length, and is composed of three structural protein genes encoding the core protein (C), envelope protein (E), a membrane-associated protein (M), and seven nonstructural protein (NS) genes.

Non-structural proteins is enveloped by glycoprotein, NS1 is of diagnostic and pathological importance. It is a 45 kDa in size and associated with viral haemagglutination and neutralization activity.

## HISTORY

In the 18th century, dengue has caused repeated epidemics worldwide [2]. H. Graham in 1903 implicated *Aedes aegypti* as the vector for the disease and the virus was isolated in 1944 by Albert Sabin et al. Dengue haemorrhagic fever gained nosologic status in 1954 and subsequently it became an endemic in many areas of tropical Asia. India belongs to category B, where dengue is an emerging disease with cyclical epidemics becoming more frequent [1, 2]. Dengue fever [1] Dengue fever (DF) and its severe forms dengue hemorrhagic fevers (DHF) and dengue shock syndromes (DSS) have become major international public health concerns. Dengue is the most prevalent arthropod-borne viral illness in humans, with the half of the world population at risk for infection and up to 50 million cases of dengue estimated each year. Dengue fever is also known as break bone fever is a mosquito borne tropical disease

it's caused by the dengue viruses. The dengue has transmitted by the several species of mosquito the genus is Aedes, The virus has five different types, and usually it gives long-life immunity to that type but only short-term immunity to the other subsequent infection with a different type increases the risk of several complications.

## A. The Dengue Serotypes

Dengue infections are caused by four closely related viruses named DEN-1, DEN-2, DEN-3, and DEN-4. These four viruses are called serotypes because each has different interactions with the antibodies in human blood serum. The four dengue viruses are similar they share approximately 65% of their genomes but even within a single serotype, there is some genetic variation. Despite these variations, infection with each of the dengue serotypes results in the same disease and range of clinical symptoms.

## B. Causes

It is caused by a virus (Dengue Virus), which has got four different types (Type I, II, III, IV). Common name of the disease is 'break-bone fever' ('Haddi Tod Bukhar') because of severe body and joint pains produced [1].

## C. Spread

The Dengue virus is present in the blood of the patient. Suffering from Dengue fever.

Whenever an aedes mosquitoes bites a patient of dengue fever, it sucks blood and, the dengue virus enters into its body. The virus undergoes further development of in the body of the mosquito for a few days. When the virus containing mosquito bites a normal human being (Healthy person), the virus is injected into the Healthy person body and he/she becomes infected and can develop the symptoms of dengue fever (1)

#### D. Life cycle

Until a few hundred years ago dengue virus it was transmitted in sylvatic cycle's in the Asia and Africa between mosquitoes of the genus Aedes and non-human primates with rare emergences into the human population [5]. The global spread of dengue virus, has followed its emergence from sylvatic and the primary life cycle now exclusively involves transmission between humans and Aedes mosquitoes. Vertical transmission from mosquito has also been observed in vector species.

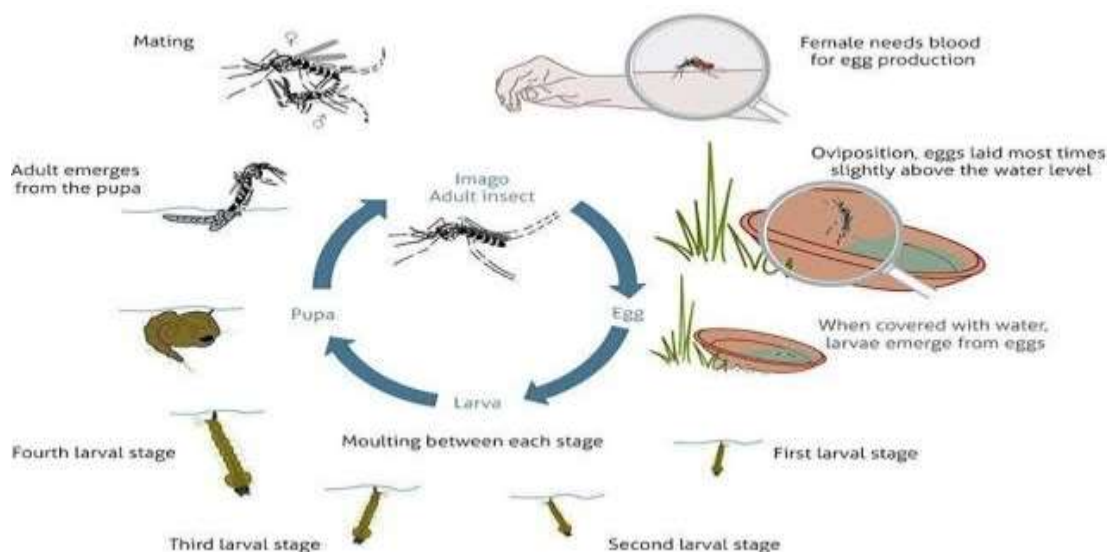


Fig.no.1

#### Dengue Hemorrhagic Fever:



Fig.no.2

EngEongOoi, Duane J. Gubler, in Tropical Infectious Diseases (Third Edition), 2011 mentions that patients with dengue fever go on to develop dengue hemorrhagic fever (DHF), a severe and sometimes fatal form of the disease. Around the time the fever begins to subside (usually 3–7 days after symptom onset), the patient may develop warning signs of severe

disease. Warning signs include severe abdominal pain, persistent vomiting, marked changing temperature (from fever to hypothermia), hemorrhagic manifestations, or change in mental status (irritability, confusion, or obtundation). The patient also may have early signs of shock, including restlessness, cold clammy skin, rapid weak pulse, and



narrowing of the pulse pressure (systolic blood pressure – diastolic blood pressure). Patients with dengue fever should be told to return to the hospital if they develop any of these signs.

DHF is currently defined by the following four World Health Organization (WHO) criteria:

- Fever or recent history of fever lasting 2–7 days.
- Any hemorrhagic manifestation. Thrombocytopenia (platelet count of  $<100,000/\text{mm}^3$ ).
- Evidence of increased vascular permeability

### WHO Guidelines 2019 Key facts

Dengue is a mosquito-borne viral infection, found in tropical and sub-tropical climates worldwide, mostly in urban and semi-urban areas.

The virus responsible for causing dengue, is called dengue virus (DENV). There are four DENV serotypes, meaning that it is possible to be infected four times.

Severe dengue is a leading cause of serious illness and death in some Asian and Latin American countries. It requires management by medical professionals.

While many DENV infections produce only mild illness, DENV can cause an acute flu-like illness. Occasionally this develops into a potentially lethal complication, called severe dengue.

There is no specific treatment for dengue/severe dengue. Early detection of disease progression associated with severe dengue, and access to proper medical care lowers fatality rates of severe dengue to below 1%.

The global incidence of dengue has grown dramatically in recent decades. About half of the world's population is now at risk. There are an estimated 100-400 million infections each year.

Dengue prevention and control depends on effective vector control measures. Sustained community involvement can improve vector control efforts substantially.

### E. Fast facts on Dengue fever

Dengue is transmitted by the mosquitoes *Aedes aegypti* and *Aedes albopictus*, which are found throughout the world.

Around 2.5 billion people, or 40 percent of the world's population, live in areas where there is a risk of dengue transmission.

These Are 8 Things To Eat During Dengue Fever For Quick Recovery

#### 1. Coconut oil

Dengue causes a lot of dehydration which leads to more problems and complications in the whole process, so do make it a point to add coconut water in your daily consumed items. Plus, it helps in flushing out the toxins from your body and makes you feel hydrated and healthy for a long time.

#### 2. Kiwi

Kiwi is one of the most recommended things to eat during

dengue since it has tons of benefits and helps a lot during the betterment process. The fruit contains an excellent amount of Vitamin E and A, along with potassium. Kiwi also helps in limiting high blood pressure and hypertension and balances the body's electrolyte levels. Most importantly, Kiwi helps in the formation

#### 3. Broccoli

Another green vegetable that parents can't get enough of is Broccoli and no matter how much you have hated it during your growing years, it has to be one of our favourite additions to our pasta and salads now. An excellent source of Vitamin K, broccoli helps in regenerating the blood platelets which is why one should absolutely include it in their dengue diet. This magic vegetable is also filled with various kinds of minerals and antioxidants.

#### 4. Spinach

We have grown listening to the fact that green vegetables are the healthiest form of energy and nutrients which is why everyone should consume it on a regular basis. Spinach is a rich source of omega-3 fatty acids and iron which boosts immunity levels of the body and helps in increasing the platelet count.

#### I. Symptoms

- Severe Headache, Pains in muscles and joints.
- Pain behind the eyeballs especially on pressing the eyes or on moving the eyeballs.
- Sudden onset of high fever with feeling of chills ("Thandi Lagna").
- Loss of appetite, feeling of nausea.
- Change in taste sensations in mouth.
- Mild pain in throat.
- Rash on the skin

#### J. Methods of bioanalysis for anti-dengue activity

##### 1. Pre-Clinical

Dengue it is a positive stranded RNA virus with an 11kb genome, encoding a polyprotein precursor cleaved to generate at least 10 proteins, including three structural proteins (core, membrane associated protein, and envelope protein), and seven nonstructural proteins (NS1, NS2a, NS2b, NS3, NS4b, NS5). DENV is transmitted by silent, urban mosquito vectors. Including *A. albopictus* and *Aedes aegypti*, *A. polynesiensis* and *A. scutellaris*, to man. Other modes of transmission include via blood products, vertical transmission and organ transplant. In man, the initial cellular target of dengue is thought to be dendritic cells, followed by lymphatic spread and then distribution to macrophages and monocytes. The full host of cells infected in vivo remain a subject of investigation, but may also include hepatocytes, myocytes, and other cell types [8].

##### 2. Clinical

Clinical methods for evaluation of anti-dengue effects are development. A major hurdle facing DENV clinical trials



is the need for establishment of accurate diagnostic testing for case identification. The current diagnostics for DENV available in the US and other high resource countries (IgM and IgG ELISA, PCR) are limited by a requirement for skilled workers, specialized and refrigeration, equipment [9]. Current point-of-care (POC) diagnostic tests for DENV. Based on lateral flow detection of secreted IgM and DENV NS1 protein in plasma/serum/blood

#### How Is Dengue Fever Diagnosed?

If you think your child might have dengue fever, call a doctor right away. You should also call a doctor if your child has recently been to a region that has dengue fever and has a fever or severe headache.

To make a diagnosis, the doctor will examine your child and evaluate the symptoms. The doctor will ask about your child's medical history and recent travels, and send a blood sample for testing.

#### How Is Dengue Fever Treated?

No specific treatment is available for dengue fever. Mild cases are managed with lots of fluids to prevent dehydration and getting plenty of rest. Pain relievers with acetaminophen can ease the headaches and pain associated with dengue fever. Pain relievers with aspirin or ibuprofen should be avoided, as they can make bleeding more.

A dengue vaccine can protect your patients:-

In May 2019, Dengvaxia® was approved external icon by the U.S. Food and Drug Administration (FDA) in the United States for use in children aged 9 to 16 years, with laboratory-confirmed previous dengue virus infection and living in an area where dengue is endemic (where dengue occurs frequently or continuously).

In June 2021, the Advisory Committee on Immunization Practices (ACIP) recommended use of Dengvaxia to prevent dengue in children aged 9 to 16 years, with laboratory-confirmed previous dengue virus infection and living in areas where dengue is endemic.

## CONCLUSION

Dengue is emerging as a global threat and is a pressing public health priority in many countries. The government and the pharmaceutical industries have been taking initiative to develop new strategies to improve the diagnosis and treatment of dengue. The challenge here lies in how effectively the strategies developed are put into use. There is also an obligatory need to globalize awareness and precautionary measures among the masses in order to control the incidence. Combined efforts of the health care industries, governing bodies and efforts at individual level would help us to tackle the prevalence of dengue.

## AUTHORS CONTRIBUTIONS

All the authors have contributed equally

## CONFLICT OF INTERESTS

Declared none