

Dengue fever

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Dengue fever is a mosquito-borne disease caused by the dengue virus. Seen in the tropical and subtropical areas, this disease is generally asymptomatic and appears 3 days to two weeks after being exposed. Symptoms can vary with high fever, headaches, vomiting, muscle and joint pain, associated with a characteristic skin rash and itching.

Recovery may last two to seven weeks but a small proportion of cases may develop into a more severe form (Dengue Hemorrhagic fever or Dengue shock syndrome) with bleeding, low platelets levels and low blood pressure.

DENGUE SYMPTOMS

Fever with any of the following



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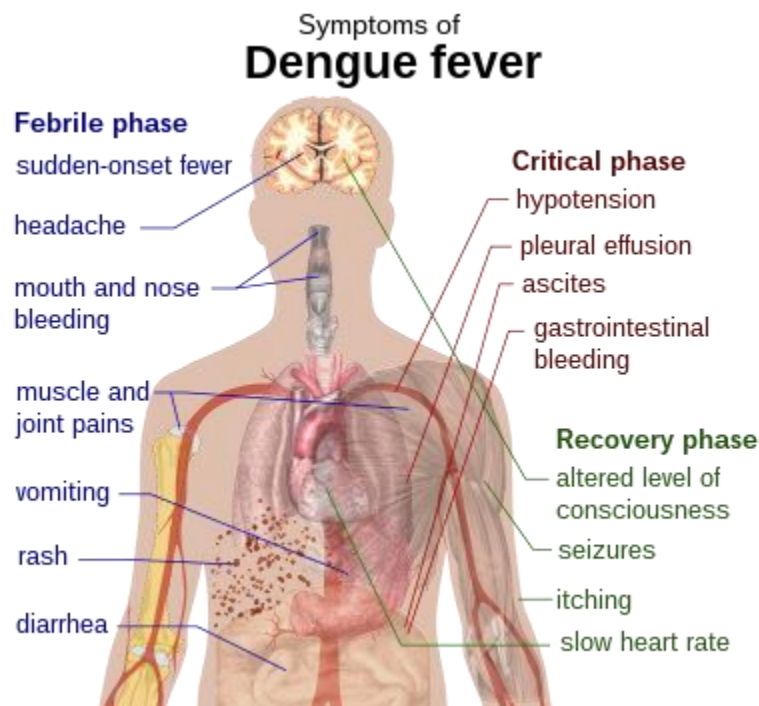
Graphic taken from the CDC

Dengue virus is believed to have four stereotypes and hopefully, infection with one type give to the patient a long-life immunity to that type but only limited immunity to the others. Repeated or subsequent infections with a different type increase the risk of severe complications. Symptoms of Dengue resemble to the symptoms of other tropical disease like Malaria, Influenza, Yellow Fever, viral hepatitis, Leptospirosis and Zika. It takes only a blood test to confirm the diagnosis in detecting the viral RNA or the antibodies to the virus. During the first few days of infection, the ELISA test (enzyme -linked immunosorbent assay) can be used to detect the NS1 antigen but four to five days later, it is possible to rely on the anti-dengue Ig

M antibodies but this does not detect the serotype. Nucleic acid amplification tests provide the most reliable method of diagnosis.

There is no specific treatment for Dengue fever. Mild cases will benefit from symptomatic treatment but any severe case may require hospitalization and supportive treatment with IV fluids (Hydration) and possibly blood for transfusion in complicated cases. *Aedes aegypti* is responsible for the transmission of the virus and it becomes natural that any prevention of the disease may rely on the elimination of the vector (mosquitoes) and as well as the prevention of bites. There are also two vaccines presently available against the disease as of March 2024: Dengvaxia recommended to prevent re-infections and Qdenga suitable for all age groups.

Dengue fever is endemic in hundreds of tropical and subtropical countries but in the southern portions of the UNITED States, it was even classified as a neglected tropical disease, a little because in 2023, 5 million infections were reported with 5000 deaths while other cases may have been under reported.



Symptoms of dengue fever

80% of patients infected with the virus of Dengue, remain asymptomatic or may present only mild symptoms while another 5% may develop severe illness but rarely life-threatening. The incubation period varies between 3 to fourteen days or may have a shorter period. Typically, a characteristic

headache behind the eyes with muscles and joint pain, nausea, vomiting, swollen lymph nodes or a rash, occasionally followed by abdominal pain and vomiting, rapid breathing, bleeding gums or epistaxis, and finally, fatigue, restlessness, extreme thirst and weakness.

For the clinicians, Dengue can be divided in three phases: a febrile phase where temperature can reach 40 degrees centigrade (104 F), with headaches for one week, a critical phase of symptoms and a phase of recovery. Most patients recover within a week although 5% will worsen and the disease will become life-threatening (severe dengue or hemorrhagic) with shock, difficulty in breathing, bloody stools etc.). A reduction in the number of platelets, chest and abdominal cavity depletion of fluids, as well as a depletion of fluid from the circulation, resulting in a decrease in the blood volume to the vital organs. A Recovery phase will follow lasting two to three days. The improvement is often striking and can be seen with severe itching and a slowing of the heart rate.

The virus of Dengue is an RNA virus like the one of yellow fever or West Nile and Zika virus.



Dengue virus is transmitted frequently by the bites of the mosquito *Aedes aegypti* to a human host but it can infect also other animals. In 2 to ten days a high level of virus particles (viremic period) is expected to allow a female mosquitoes to take back the blood from the infected host and disperse it in another. Dengue can be also transmitted via infected blood products or in organ donation or through the placenta (vertical Transmission).

The principal risk for infection with Dengue is the bite of an infected mosquito in area where the disease is endemic. One should avoid these bites by wearing clothing that fully covers the skin, using mosquito netting

while resting or using insect repellent. People suffering from chronic diseases like asthma, sickle cell, diabetes mellitus may be at risk of developing a more severe form of the disease. People who have already suffered from Dengue disease are also at risk for developing more complications because of antibody-dependent-enhancement (ADE). People with morbid obesity may also be at risk.

When a mosquito injects the virus of Dengue into a person, through a bite, the virus infects the keratinocytes, as well as the specialized immune cell located in the skin, called Langerhans cells which migrate to the lymph nodes while the infection spreads to the white blood cells. Then, the virus duplicates inside the cells and move throughout the body. The white blood cells produce specialized proteins called cytokines and interferons which are responsible for the reactive fever and the flu-like symptoms and pain.

The more severe the infection is, the more other organs like the liver and the bone marrow can be affected. Blood volume may decrease as well as the blood pressure while an increase in the permeability of the capillary become obvious and the fluid from the blood stream leaks through the wall of the small vessels. As a result of the low blood volume, the vital organs can't get their supply in blood to function. Finally, the spread of the virus to the bone marrow will also reduce the number of platelets.

Control of the mosquito to protect the population is enforced by the frequent drainage of stagnant or standing water where mosquito can breed especially, in endemic areas, where generally, a dense population lives in poor sanitation as already mentioned. The wear of long sleeves and the application of insect repellent and even the treatment of the clothes with 5% of permethrin or the use of window screens, tents and even air-conditioned can offer protection against the vector.

The primary method of controlling the mosquito is definitely by eliminating its habitats (Stagnant water) by adding insecticides (Organophosphates or Pyrethroid).

The treatment of Dengue remains symptomatic although up to now, there is no specific remedies. Acetaminophen or Ibuprofen are often used while it is not recommended to use Aspirin or Ibuprofen to avoid any bleeding complications. Bed rest and hydration with possible intravenous fluids and even blood transfusion may be needed if any life-threatening situation and any drop in the hematocrit is encountered.

Most people recover well from Dengue disease without any problem. There is a higher risk of death with severe dengue in less than 2% of the cases but it may be higher reaching up to 25% especially among individual who developed a significant drop in blood pressure. The risk of death among children less than five years old quadruples the rate seen among children over the age of 10 but at lower than 5%. The elderly may be at higher risk for a poor outcome.

A little history over significant outbreaks of dengue fever has demonstrated an endemic disease seen in at least 100 countries except in Antarctica. The Americas, Southeast Asia and the Western Pacific regions are the most seriously affected. WHO estimates that 3.9 billion people are at risk for Dengue infection. Areas where Dengue is endemic has generally one serotype of the virus in circulation. Any area where more than one serotype circulates is called ‘hyperendemic’ and brings with it the risk of more severe disease., especially if it is a case of recurrent Dengue.

Infections are generally acquired in urban environments and the species have adapted in preferring the humans as its host. In recent decade, there has been a ten-fold increase between 2010 and 2019, where 500,000 cases were registered in 2010 but now 5 million cases are recorded in 2019, which is due to a combination of urbanization and population growth as well as a warm climate. Dengue Infections peak when rainfall is optimal for the mosquito breeding. The disease infects all races, sexes and ages equally but the infection is more commonly seen in children who will acquire long-live immunity to the subtype, once infected.

The Jin Dynasty (222-420) produced the first historical record of a case similar to Dengue associated with flying insects, recorded in a Chinese medical encyclopedia and it was called “water poison”. It is believed that *Aedes aegypti* spread out Africa in the 15th to 19th centuries during the slave trade with an international expansion and was responsible for the epidemics of Dengue fever seen in Jakarta, Cairo and Philadelphia during the 18th century.

The second World war has also helped in the expansion of the disease with the urbanization in the South East Asia. Later the hemorrhagic form was reported in the Philippines (1953) and until the 1970, it was recognized as a major cause of child mortality in the South East Asia. In central and South America, another mosquito, the “*Aedes Aegypti*” re-appeared in 1980’s in hyperendemic zones after its previous eradication in the 1950’s, causing significant epidemics. Dengue continues to increase its prevalence during

the 21st century while the mosquito itself continues to expand its range by urbanization et warmer climate.

The term “Denga” comes from West Indian Spanish meaning cramp-like seizure (evil spirit). Also, the slaves who had contacted the disease had the posture and gait of a dandy, and for this reason, it was also called dandy fever. In 1780, an epidemic in Philadelphia was reported and the term Brake-bone was used by a physician to describe the muscle and joint pains. It is only in 1828 that the term Dengue fever was used to describe the disease.

On the eve of our next AMHE Annual Convention in Guatemala, this page is written to present a complete understanding of the Dengue Fever to all of our participants. Please take note of it. It is also dedicated to all of our physicians-Residents from Home participating in our AMHE Residency Rotations.

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