

Dengue Fever

WHAT IS DENGUE FEVER?

Dengue fever, a mosquito-borne tropical disease, is the most common and important arthropod-borne (arboviral) illness in humans. It is caused by four serotypes of the dengue virus, of which more than one can circulate during an epidemic.¹ Infection with one serotype confers lifelong homotypic immunity to that serotype and a brief period (~2 years) of partial heterotypic immunity to other serotypes. However, an individual can eventually be infected by all four serotypes.

SYMPTOMS AND COMPLICATIONS

Initial dengue infection may be asymptomatic (50-90%), result in a nonspecific febrile illness or produce the symptom complex of classic dengue fever, which is marked by rapid onset of high fever, headache, retro-orbital pain, diffuse body pain (both muscle and bone), weakness, vomiting, sore throat, altered taste sensation and a centrifugal maculopapular rash, among other manifestations. The severity of pain led to the term “breakbone fever” to describe dengue.² A small percentage of persons previously infected by one dengue serotype develop bleeding and endothelial leak upon infection with another dengue serotype, known as severe dengue (or dengue hemorrhagic fever), which can be deadly.³

TRANSMISSION

Dengue virus is spread by several species of female mosquitoes of the *Aedes* type, principally *A. aegypti*, which are widely distributed in subtropical and tropical areas of the world. An individual with dengue is capable of transmitting the virus for 4-5 days (maximum 12 days) to a capable vector. After an incubation period of 5-10 days, the infected mosquito can transmit virus for the rest of its life span (2 weeks to 1 month). *A. albopictus* is more cold-tolerant than *A. aegypti*, so it can survive and transmit virus in the more temperate regions of the United States and Europe.⁴



Four serotypes of the dengue virus:

- DEN-1
- DEN-2
- DEN-3
- DEN-4

Symptoms of classic dengue fever:

- High fever
- Headache
- Retro-orbital pain
- Diffuse body pain
- Weakness
- Vomiting
- Sore throat
- Altered taste
- Centrifugal maculopapular rash
- Among others

Data current as of May 18, 2020

DIAGNOSIS AND TREATMENT

A clinical diagnosis of dengue is typical, especially in endemic areas, and is based on reported symptoms and physical examination. Early disease can be difficult to differentiate from other viral infections, such as chikungunya and Zika, and some bacterial infections. A probable diagnosis is based on the findings of fever plus two of a list of other factors in individuals who live in endemic areas. Where available, laboratory tests such as cell cultures, polymerase chain reaction and serological tests/assays can aid in diagnosis.

Dengue fever is usually a self-limiting illness. There is no specific antiviral treatment currently available, and supportive care with analgesics, fluid replacement and bed rest is usually sufficient. Management of severe dengue requires careful attention to fluid management and proactive treatment of hemorrhage. Dengvaxia® is the only FDA-approved dengue vaccine on the market, and it is currently registered in a number of countries.

CURRENT SITUATION, EPIDEMIOLOGY AND WHAT'S NEXT

According to the World Health Organization (WHO), the numbers of dengue cases and deaths reported have both increased seven-fold over the past two decades, with cases increasing from 505,000 in 2000 to over 3,300,000 by 2015.⁵ Globally, 2.5-3 billion individuals live in approximately 112 countries that experience dengue transmission, and it is estimated that up to 400 million people get infected with dengue and 22,000 die from severe dengue annually worldwide.⁶ The vast majority of burden is seen in Asia/Southeast Asia, Africa and the Americas (especially Latin America).

Over the past 12 months, we have seen an increasing burden of dengue fever in areas such as Sri Lanka, Bangladesh, Malaysia and Indonesia. In addition, various countries in Latin America are also seeing a recent uptick in cases, and the U.S. and even some European countries are now experiencing increasing numbers of cases every year.

Currently, there are a number of companies developing drugs and vaccines targeting dengue fever. While it isn't clear which, if any, of these products will make it to the market, there is a large need for novel treatments and vaccines supported by government investments to combat this highly burdensome disease. But this isn't enough—there also exists a serious need to couple treatments and vaccines with increased surveillance and mitigation efforts across the many at-risk countries if we are to make great strides in the control of dengue.

7-fold

increase in dengue cases
over the past two decades

400M

infected annually
with dengue



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1 "Dengue and Severe Dengue," World Health Organization, April 15, 2019.

2 "Dengue," Darvin Smith, Medscape, May 3, 2019.

3 Ibid.

4 Ibid.

5 "Dengue and Severe Dengue," World Health Organization, March 2, 2020.

6 "Dengue," Centers for Disease Control and Prevention, February 14, 2020.

Data current as of May 18, 2020