

## Dengue

Dengue is caused by the dengue virus, which is an RNA virus and member of the flavivirus family. As such, it is positive-sense single stranded and linear. This virus is transmitted by the Aedes mosquito typically in tropical regions. In classic dengue fever, clinical features include fever, arthralgias, myalgias, a maculopapular rash, retro-orbital pain, and thrombocytopenia. In the severe form, dengue hemorrhagic fever, patients may present with petechiae due to increased capillary permeability and leakage, or even full blown hemorrhagic shock. Diagnostic tests include complete blood cell count and antibody testing. Management include supportive care and vaccination for certain populations.



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### Characteristics

#### RNA Virus

##### RNA-rhino

Dengue virus is an RNA virus, meaning its genetic code consists of ribonucleic acid as opposed to deoxyribonucleic acid.

#### Flavivirus

##### Flavi-Flav-Virus

Dengue virus is part of the Flavivirus family. Other Flaviviruses include hepatitis C virus, Yellow fever virus, West Nile virus, Zika virus, and the virus that causes St. Louis encephalitis.

#### SS Positive Linear

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Dengue virus has RNA in a linear arrangement as opposed to a circular formation. Single stranded positive sense linear viruses have their genome directly utilized as mRNA. Host ribosomes translate the RNA genome directly into a single protein that is modified by the host and viral proteins to form the various proteins necessary for replication.

#### Transmitted by Aedes Mosquito

##### Hades Mosquito

Dengue virus is transmitted by the bite of mosquitos, particularly the Aedes aegypti species, commonly found in tropical and subtropical regions of the world. Yellow fever virus, Zika virus, and Chikungunya virus are also transmitted by this mosquito, possibly resulting in coinfection.

#### Tropical Regions

##### Tropical Hawaiian Surfer

Dengue is widespread in tropical and subtropical regions of the world. It is typically found in central and South America, south and south-east Asia, Africa, and Oceania.

### Classic Dengue Fever

## Fever

### Fever-Beaver

Dengue fever classically begins with a high fever (40°C/104°F) and malaise that lasts approximately 1 week. Other nonspecific symptoms, such as nausea and vomiting, may also be present.

## Arthralgias and Myalgias

### King Arthur-algae and Mayo-algae

In addition to fever, patients may present with bone, joint (arthralgia), and muscle (myalgia) aches and pain.

## Maculopapular Rash

### Mac-glow-papule-people

A macular or maculopapular rash is a common clinical finding that can initially resemble measles. This rash is usually asymptomatic. In some cases, individual lesions coalesce to form a generalized erythema, with rounded islands of sparing; sometimes referred to as “white islands in a sea of red”.

## Retro-orbital Pain

### Retro-eye Pain-bolt

A severe headache, particularly pain behind the eyes, is characteristic of dengue fever.

## Thrombocytopenia

### Trombone-side-toe-peanut

Thrombocytopenia is defined as abnormally low levels of platelets. It is a common clinical manifestation in patients with dengue fever and is characteristic of the more severe infections, dengue hemorrhagic fever and shock syndrome. Though the pathogenesis is poorly understood, it is suggested that Dengue virus infects circulating platelets as well as their progenitor megakaryocytes in bone marrow. Development of thrombocytopenia in dengue patients is primarily due to both decreased production of platelets in the bone marrow and increased destruction of platelets in peripheral blood. Thrombocytopenia is one of the major causes of bleeding in severe cases of infection.

## Dengue Hemorrhagic Fever

## Petechiae

### Tiki-mask

Petechiae are small red spots under the skin that do not blanch, and occur due to capillary leakage. In Dengue virus infection, they may herald progression to a more severe form of Dengue virus infection. Petechiae are rarely seen in dengue fever, but are a common manifestation of dengue hemorrhagic fever and dengue shock syndrome. If a patient is suspected to be infected with Dengue virus and develops petechiae, the tourniquet test may be considered. This test is a marker of capillary fragility, and is considered positive when  $>20$  petechiae/ $2.5\text{ cm}^2$  are observed. Other minor hemorrhagic manifestations may include purpura, epistaxis, gingival bleeding, or ecchymosis.

## Increased Capillary Permeability and Leakage

### Up-arrow Caterpillar Leaking

Endothelial dysfunction leading to increased vascular permeability is a hallmark of severe dengue, leading to leakage of fluid into pleural and peritoneal cavities and shock. The mechanism of increased vascular permeability is not completely understood; however, there is evidence suggesting that reactive oxygen species, enzymes, and pro-inflammatory molecules (for example, TNF- $\alpha$ , IL-6, IL-8 and IFN- $\gamma$ ) break down the endothelial glycocalyx layer, allowing plasma to leak out of the blood vessel.

## Hemorrhagic Shock

### Hemorrhage-hammer Shocked

Patients with dengue can rapidly progress into Dengue Shock Syndrome (DSS), a form of hypovolemic shock due to hemorrhage. DSS is a dangerous complication of dengue infection and is associated with high mortality. The onset of DSS is usually abrupt. Increased vascular permeability, together with myocardial dysfunction and hypovolemia, contribute to the development of shock, with resultant multiorgan failure. The four criteria of the WHO classification of DSS include fever, bleeding (including a positive tourniquet test), thrombocytopenia ( $<100\text{ 000}$  platelets/mm $^2$ ), and

hemoconcentration (a rise in the hematocrit  $\geq 20\%$  or signs of plasma leakage such as ascites, pleural effusion, proteinemia).

## Diagnosis

### Complete Blood Cell Count

#### Blood Cell Count-dracula

A complete blood count (CBC) may be done to assess low platelet count typical of Dengue virus infection. A CBC may also detect changes in hemoglobin (Hb) and hematocrit (Hct). In earlier stages of the disease, an increase in Hb and Hct may indicate plasma leakage; while decreases in Hct and Hb, along with a decreased red blood cell count, could indicate blood loss associated with severe disease. Leukopenia may also be seen with Dengue virus infection. Be aware that the CBC in an individual with dengue may vary, due to varying disease progressions and manifestations.

### Antibody Testing

#### Ant-tie-body with Test-Tubes

For patients with suspected dengue virus infection, who are symptomatic for 7 days or less, nucleic acid amplification tests (NAATs) are the preferred method of laboratory diagnosis. For patients presenting  $>1$  week after symptom onset, IgM antibody detection is most useful. However, know that the IgM antibody testing may be complicated by cross-reactivity with other flaviviruses (such as Zika, West Nile, Yellow Fever, and Japanese encephalitis viruses). A patient found to have IgM antibodies strongly suggests a recent dengue virus infection, and is considered confirmatory for dengue if the travel history has minimal risk for other cross-reactive flaviviruses. Note that IgG is not a useful diagnostic tool, as it remains detectable for life after a Dengue virus infection.

## Management

### Supportive Care

#### Supportive IV Bags

Dengue begins abruptly after a typical incubation period of 5–7 days, and most cases are self-limited. Approximately 1 in 20 patients with Dengue virus disease progress to develop severe, life-threatening disease. Patients should stay well hydrated and avoid NSAIDs, because of their anticoagulant properties. Fever should be controlled with acetaminophen and tepid baths. Febrile patients should avoid mosquito bites to reduce risk of further transmission. For those who develop severe dengue, close observation and frequent monitoring in an intensive care unit may be required.

### Vaccination

#### Vaccination-syringe

An attenuated live vaccine has been approved for use in children between 9–16 years of age, who live in endemic areas, and who have a confirmed prior dengue virus infection.