Dengue Fever

Dengue is a mosquito-borne disease that is caused by a flavivirus. This Dengue virus is spread to people through the bite of an infected Aedes species (Ae. aegypti or Ae. albopictus) mosquito.

Dengue is endemic to the tropical regions of the world

Dengue fever usually results in the abrupt onset of high fever, headache, myalgias, arthralgias, and lymphadenopathy, which is then followed by a rash that appears with a 2nd temperature rise after an afebrile period.

Respiratory symptoms for Dengue fever, include cough, sore throat, and rhinorrhea.

Dengue can also cause potentially fatal hemorrhagic fever with bleeding tendency and shock. Diagnosis involves serologic testing and Polymerase chain reaction.

Treatment is symptomatic and, for dengue hemorrhagic fever, includes meticulously adjusted intravascular volume replacement.

Etiology

The causative agent for Dengue fever is known as flavivirus. Flavivirus has 4 serogroups and is transmitted by the bite of Aedes mosquitoes.

The virus circulates in the blood of infected humans for about 2 to 7 days; Aedes mosquitoes may acquire the virus when they feed on humans during this period.

Symptoms and Signs

Dengue fever can range from asymptomatic infection or mild illness to severe disease.

An estimated 1 in 4 dengue virus infections is usually symptomatic. Symptomatic dengue virus infection most commonly presents as a mild to moderate, nonspecific, acute febrile illness.

Infection with one of the four dengue viruses will induce long-lived immunity for that specific virus. Because there are four dengue viruses, people can be infected with DENV up to four times.

Approximately 1 in 20 patients with dengue virus disease progress to develop severely, life-threatening disease called severe dengue.

The second infection with DENV is a risk factor for severe dengue.

Early clinical findings are nonspecific but require a high index of suspicion because recognizing early signs of shock and promptly initiating intensive supportive therapy can reduce the risk of death among patients with severe dengue to <0.5%.

After an incubation period of 3 to 15 days, there is an abrupt onset of fever, chills, headache, retro-orbital pain with eye movement, lumbar backache, and severe prostration.

Extreme aching in the legs and joints occurs during the first hours, and because of these features, Dengue fever is also known as breakbone fever.

The temperature rises rapidly to up to 40° C, with relative bradycardia.

Bulbar and palpebral conjunctival injection and a transient flushing or pale pink macular rash (particularly of the face) may occur.

Cervical, epitrochlear, and inguinal lymph nodes are often enlarged.

Fever and other symptoms persist 48 to 96 hours, followed by rapid defervescence with profuse sweating. Patients then feel well for about 24 h, after which fever may occur again. This is known as a saddle-back pattern, it is characterized by a typically lower peak temperature than the first.

A blanching maculopapular rash spreads from the trunk to the extremities and face.

Mild cases of dengue, usually lacking lymphadenopathy, remit in < 72 hours. In more severe diseases, asthenia may last several weeks.

Immunity to the dengue fever infecting strain is long-lasting, whereas broader immunity to other strains lasts only 2 to 12 months.

Diagnosis

Dengue fever is suspected in patients in endemic areas if they develop sudden fever, headache, myalgias, and adenopathy, particularly with the characteristic rash or recurrent fever.

Evaluation should rule out alternative diagnoses, especially malaria and leptospirosis.

Diagnostic studies include serologic testing, antigen detection, Nucleic acid amplification tests (NAATs), and PCR of blood.

Serologic testing involves hemagglutination inhibiting or complements fixation tests using paired sera, but cross-reactions with other flavivirus antibodies are possible.

Antigen detection and PCR are usually done only in laboratories with special expertise.

Although rarely done and difficult, cultures can be done using mosquitoes or specialized cell lines in specialized laboratories.

Dengue virus testing is not recommended for:
- Asymptomatic patients
- Preconception screening

Patients with symptoms consistent with dengue can be tested with both molecular and serologic diagnostic tests during the first 7 days of illness. After the first 7 days of illness, test only with serologic diagnostic tests.

The initial 1-7 days after symptom onset are referred to as the acute phase of dengue. During this period, dengue virus is typically present in blood or blood-derived fluids such as serum or plasma. Dengue virus RNA can be detected with molecular tests.

The non-structural protein NS1 is a dengue virus protein that also can be detected using some commercial tests.

A negative result from a molecular or NS1 test is not conclusive. For symptomatic patients during the first 1-7 days of illness, any serum sample should be tested by a NAAT or NS1 test and an IgM antibody test. Performing both molecular and IgM antibody (or NS1 and IgM antibody) tests can detect more cases than performing just one test during this time period, and usually allows diagnosis with a single sample.

The period beyond 7 days following symptom onset is referred to as the convalescent phase of dengue.

Patients with negative NAAT or NS1 test results and negative IgM antibody tests from the first 7 days of illness should have a convalescent sample tested for IgM antibody test.

During the convalescent phase, IgM antibodies are usually present and can be reliably detected by an IgM antibody test.

IgM antibodies against dengue virus can remain detectable for 3 months or longer after infection.

Patients who have IgM antibodies against dengue virus detected in their serum specimen with an IgM antibody test and either: 1) have a negative NAAT or NS1 result in the acute phase specimen, or 2) without an acute-phase specimen, are classified as having a presumptive, recent dengue virus infection.

If a NAAT or NS1 test is positive for dengue, a current dengue diagnosis is confirmed.

If the NAAT result is negative and the IgM antibody test is positive, the laboratory diagnosis is presumptive dengue virus infection.

CBC may show leukopenia by the 2nd day of fever; by the 4th or 5th day, the WBC count maybe 2000 to 4000/?L with only 20 to 40% granulocytes.

Urinalysis may show moderate albuminuria and a few casts.

Treatment

There are no specific antiviral agents that exist for the treatment of dengue. Treatment is symptomatic.

Supportive care is advised: Patients should be advised to stay well hydrated and to avoid aspirin (acetylsalicylic acid) because aspirin-containing drugs and other nonsteroidal anti-inflammatory drugs (such as ibuprofen) possess anticoagulant properties.

Aspirin increases the risk of Reye's syndrome in children and should be avoided for that reason.

Fever should be controlled with acetaminophen and tepid sponge baths.

Febrile patients should avoid mosquito bites to reduce the risk of further transmission.

For those who develop severe dengue, close observation and frequent monitoring in an intensive care unit may be required.

Prophylactic platelet transfusions in dengue patients are not beneficial and may contribute to fluid overload.

Administration of corticosteroids has no demonstrated benefit and is potentially harmful to patients; corticosteroids should not be used except in the case of autoimmune-related complications (e.g., hemophagocytic lymphohistiocytosis, immune thrombocytopenia purpura).

Prevention

People in endemic areas should try to prevent mosquito bites.

To prevent further transmission by mosquitoes, patients with dengue should be kept under mosquito netting until the 2nd bout of fever has resolved.

A vaccine to prevent dengue (Dengvaxia®) is licensed and available in some countries for people aged 9 to 45 years. The World Health Organization recommends that the vaccine only be given to persons with confirmed previous dengue virus infection. Three doses of vaccine are required. Each shot is spaced 6 months apart.