DENGUE

Dengue virus is an arbovirus transmitted through mosquitoes. It is important to make a differential diagnosis with other arboviral diseases with similar symptoms, such as chikungunya and Zika, or with other flu-like syndromes, including malaria in endemic areas.

THE DENGUE VIRUS[1,2]

- Dengue is a frequent mosquito-borne viral infection in warm, tropical, and sub-tropical climates. Dengue virus is very common in South-East Asia, but also in Central and South America, Western Pacific, and Africa, mainly in urban and semi-urban areas.
- The number of dengue cases has been increasing over the past decades due to the spread of the disease in new areas including Europe. In addition to imported cases, autochthonous transmission is now regularly reported in Europe. The risk of outbreaks also exists in these new areas.
- The dengue virus (DENV) is a single-stranded RNA virus belonging to the *Flaviviridae* family with four different serotypes.
- Life-long protection is induced against the infecting serotype, but only a short-term cross-protective immunity is built against other serotypes. Secondary infection with another serotype represents the highest risk for a severe clinical outcome.

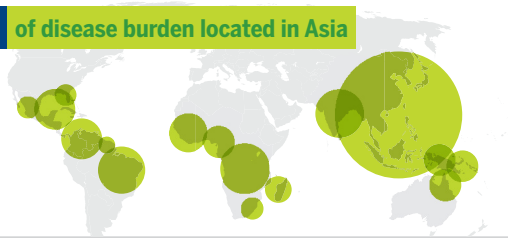
THE ANNUAL DENGUE BURDEN[1,2]

4.2 million Dengue cases reported to WHO in 2019

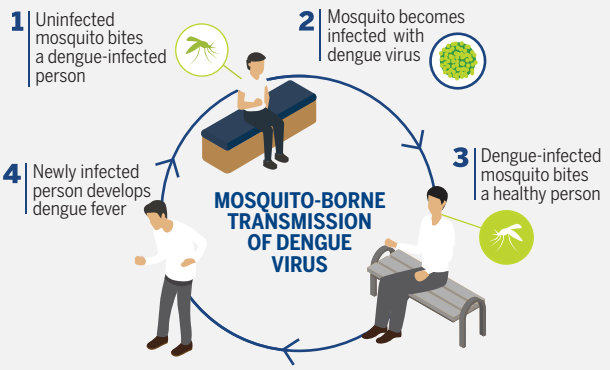
50% of world population at risk

100-400 million estimated infections each year

70% of disease burden located in Asia



HOW DENGUE IS TRANSMITTED



TRANSMISSION[1,2]

- Dengue virus is mainly transmitted to humans through the bites of infected female *Aedes* mosquitoes (mainly *Aedes aegypti* and to a lesser extent *Aedes albopictus*) which bite during daylight hours.
- There is an incubation period of 4-10 days after a bite from an infected mosquito.
- Infected humans are the main carriers and source of the dengue virus for uninfected mosquitoes.
- Other very rare routes of transmission include mother-to-child and blood transmission.

CLINICAL PRESENTATION[1,2]

- Dengue infections may be asymptomatic or cause a flu-like illness with symptoms generally lasting for 2 to 7 days.
- Dengue presents with two major clinical forms: dengue (with/without warning signs) and severe dengue.
- If left unmanaged, severe dengue can lead to death.

DENGUE CASE CLASSIFICATION (WHO)

DENGUE ± WARNING SIGNS	SEVERE DENGUE
Without warning signs	1. Severe plasma leakage
With warning signs	2. Severe hemorrhage
	3. Severe organ impairment

Probable dengue
Dengue should be suspected when a **high fever (40°C/104°F)** is accompanied by 2 or more of the following symptoms during the febrile phase:

- Nausea, vomiting
- Rash
- Aches and pain
- Positive tourniquet test
- Leukopenia
- Any warning sign

Warning Signs
3 to 7 days after illness onset, when the fever is dropping (below 38°C/100°F), the following warning signs associated with severe dengue can manifest:

- Abdominal pain or tenderness
- Persistent vomiting
- Clinical fluid accumulation
- Mucosal bleed
- Lethargy or restlessness
- Liver enlargement >2 cm
- Increasing hematocrit concurrent with rapid decrease in platelet count

DENGUE

DIAGNOSTIC APPROACH[2]

- Relevant epidemiologic exposure.
- Suggestive, though non-specific, clinical presentation.
- Non-specific laboratory findings such as thrombocytopenia and leukopenia (not exclusive).

LABORATORY CONFIRMATION[2]

Laboratory diagnostic tests include:

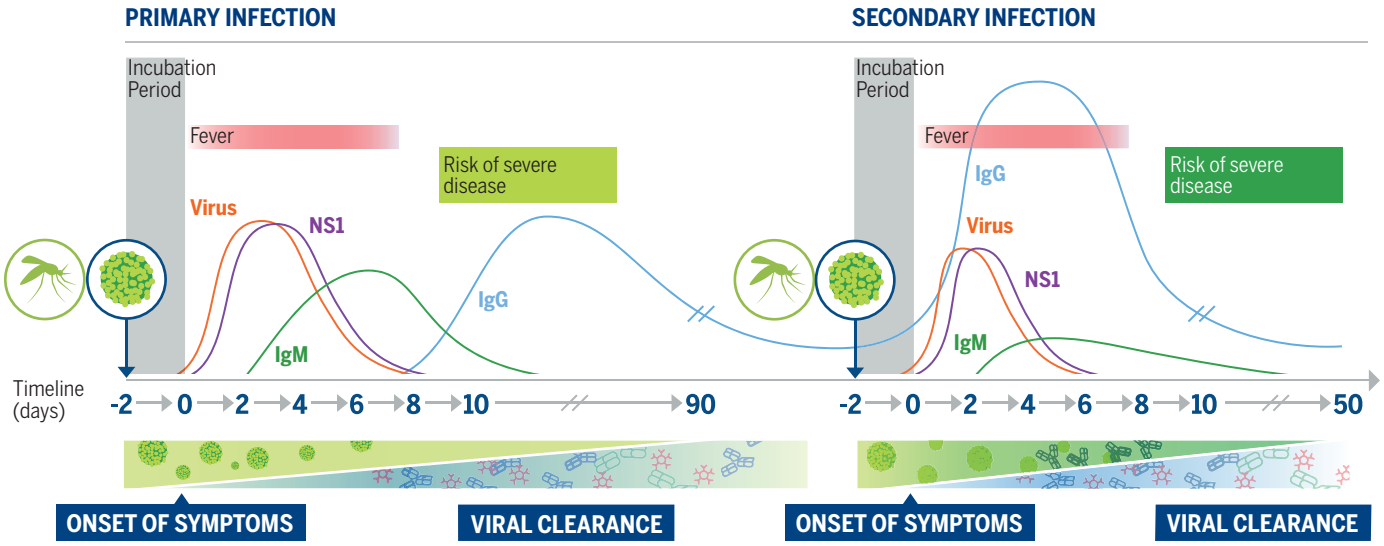
- Molecular testing for detection of viral RNA on plasma, serum, or whole blood samples (nucleic acid amplification test).
- Antigen testing for detection of the non-structural protein (NS1) of dengue virus on plasma/serum samples.
- Serology testing for detection of antibodies (IgM and IgG) on plasma/serum samples.

Timeline of laboratory diagnostic tests:

- From the onset of symptoms up to 5 to 7 days: virus isolation, nucleic acid amplification, or antigen detection tests (direct methods) can be performed.
- At the end of the acute phase (after 5 to 7 days): serology, which is an indirect method, is the choice for diagnosis.
  - Detection of IgM: after 5 days
  - Detection of IgG: after 7 days

TIMELINE OF HUMORAL IMMUNE RESPONSE AND BIOMARKER APPEARANCE DURING PRIMARY AND SECONDARY DENGUE INFECTION[3,4]

Adapted from Kerkhof K. *et al. Trends Microbiol*. 2020



TREATMENT[1,5]

- There is no specific treatment for dengue fever.
- Symptomatic treatment to reduce fever and pain may be given. The best option should be paracetamol or acetaminophen.
- Non-steroidal anti-inflammatory drugs (NSAIDS), such as ibuprofen and aspirin, should be avoided (risk of hemorrhage).
- In severe cases, hospitalization, intravenous fluid supplementation, and blood transfusions are required.
- A vaccine to prevent dengue (Dengvaxia®) is licensed and available in some countries for persons 9 to 45 years old. The WHO recommends that the vaccine only be given to persons with confirmed prior dengue virus infection.

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