

# DENGUE FEVER TECHNICAL FACTSHEET

## KEY FACTS

- Dengue fever is an acute febrile disease caused by any of the four existing dengue virus serotypes (DENV1,2,3,4).
- Dengue is found worldwide in tropical and sub-tropical regions, mostly in urban and semi-urban areas. It is endemic in about 100 countries, including in tropical areas of Africa.
- Dengue virus is primarily transmitted to humans through the bites of infected *Aedes* species mosquitoes (*Ae. aegypti* and *Ae. albopictus*).
- Most dengue infections are asymptomatic (~75%). Symptomatic patients usually present with a mild febrile illness and the most common signs and symptoms include nausea, vomiting, rash, aches and pains, and minor bleeding. Occasionally, dengue can progress to severe disease, with shock, severe bleeding and organ involvement (heart, liver, brain), and can be fatal.
- Patients with dengue should be monitored for the presence of warning signs (refer to clinical features for warning signs).
- Diagnostic testing to confirm cases involves using real-time or conventional polymerase chain reaction (PCR) and dengue nonstructural protein 1 (NS1) antigen by immunoassay. Serology could also be used if testing is performed >5days from symptom onset.
- Infection with one serotype confers lifelong immunity against that specific serotype, but not the others.
- Dengvaxia is the only vaccine prequalified by the World Health Organization (WHO) against dengue fever. It is recommended for seropositive individuals ages 9 to 45 years.

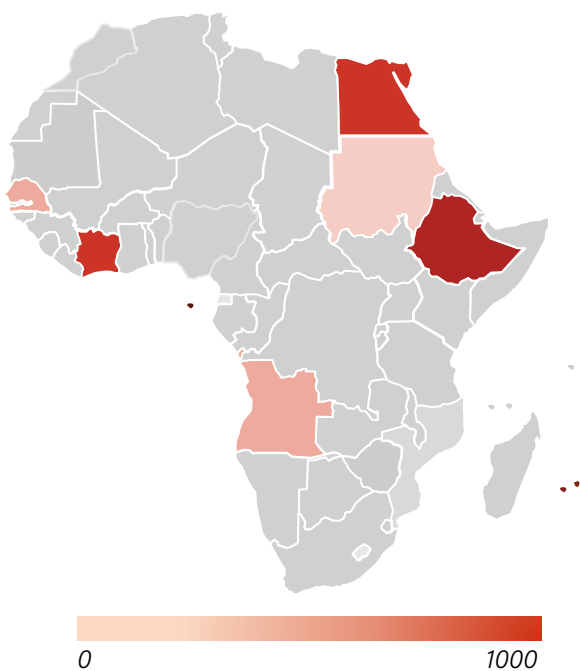


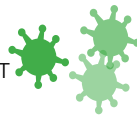
Figure 1. Map of confirmed dengue fever cases reported from African Union Member States, 1 January to 27 August 2023.

### What is dengue virus?

Dengue virus is an arbovirus (arthropod-borne virus) in the Flaviviridae family, transmitted primarily by *Aedes* mosquitoes; the same vector responsible for the transmission of chikungunya, yellow fever, and Zika viruses. There are four distinct, but closely related, serotypes of the virus (DENV-1, DENV-2, DENV-3, and DENV-4). In Africa, the first reported dengue fever outbreak occurred in the 19<sup>th</sup> century in Tanzania, however the virus was first isolated in Nigeria in 1960.

### Distribution in Africa

As of August 2023, dengue fever has been reported from nine (9) African Union (AU) Member States (MS): Angola, Chad, Côte d'Ivoire, Egypt, Ethiopia, Mauritius, Sao Tome and Principe, Senegal, and Sudan (Figure 1). Prior to 2023, confirmed outbreaks of dengue fever had been reported in at least 20 countries on the continent. However, the primary dengue vectors (*Aedes aegypti* and *Aedes albopictus*) are present in 50 AU Member States which makes dengue virus introduction and transmission possible in these countries.



## Transmission

Dengue viruses are mainly spread to people through the bites of infected *Aedes aegypti* or *Aedes albopictus* mosquitoes. Humans are known to be the main host and amplifiers of the virus maintaining the human-mosquito epidemic cycles of the disease in urban areas. Infected pregnant mothers can transmit the virus to their fetus during pregnancy or around the time of birth. In rare events, dengue fever can be transmitted through blood transfusion, needle stick injuries and organ transplant.

## Clinical Features

Symptoms of the disease can include fever, headache, muscle ache, chills, pain at the back of the eye, nausea, vomiting and rash. Some warning signs of the disease (requiring immediate medical attention) include; abdominal pain, bleeding from nose or gums, restlessness, fatigue. In its severe form, cases may present with severe plasma leakage (fluid accumulation with respiratory distress, and dengue shock syndrome), severe hemorrhage (vomiting of blood and severe bleeding) and severe organ (liver, heart and brain) impairment. The disease is usually self-limiting, and the average case fatality rate of dengue is less than 1%, but in its severe form can be up to 15% if untreated.

## Surveillance and Contact Tracing

Surveillance is critical for the early detection of infectious disease outbreaks, including dengue fever as it provides a basis for an effective response. Dengue surveillance strategies should include early detection of cases, environmental surveillance (to identify potential mosquitoes breeding sites) and harmonizing entomological and epidemiological efforts within existing health systems. Below are several different types of surveillance systems that can be used for dengue fever.

### 1. Event-based Surveillance

Event-based surveillance (EBS) using a One Health (OH) approach can support the prompt detection and reporting of dengue fever. The various modalities are explained in detail within the [Africa CDC EBS Framework](#). For dengue fever, it is important to strengthen the community and facility-based EBS to facilitate detection within the community. Media monitoring and hotlines can also play a vital role in early detection within the country and across borders. Human and environmental signal definitions should be developed and incorporated into an existing EBS system to help identify dengue fever events.

### 2. Case-based Surveillance

This involves the timely collection, analysis and interpretation of linked-clinical, laboratory and epidemiological data using standard case definitions (see callout box for WHO case definitions) of the disease. The surveillance system for dengue should be a part of the national health information system, and thresholds for alerting and response should be well defined and adapted to the context of occurrence. This could enable structures like health facilities, to quickly identify new cases of dengue fever and also outbreaks even in endemic countries. Sentinel sites should be established especially in endemic countries and age- stratified seroprevalence and burden of disease studies should be initiated to improve understanding of the distribution and epidemiology of the disease in targeted geographical areas.

#### Examples of Signal Definitions

##### Human Signals

- Rapid increase of persons with unexplained fever based on the clinician's judgement or available data
- Two or more persons presenting with similar signs and symptoms from the same community, school or workplace within a week

##### Environmental Signals

- Increase in mosquitoes and or mosquito breeding sites in the community



### The WHO Recommended Case Definitions<sup>1,2</sup>

**Dengue fever suspected case:** Any person who lives or with history of travel to a dengue endemic area, with acute febrile illness of 2-7 days duration and presenting with two or more of the following: headache, retroorbital pain, myalgia, arthralgia, rash, haemorrhagic manifestations, leukopenia.

**Dengue fever Confirmed case:** A suspected case with laboratory confirmation (positive Immunoglobulin M (IgM) antibody, fourfold or greater increase in Immunoglobulin G (IgG) antibody titres in paired (acute and convalescent) serum specimens, positive PCR, NSI or isolation of the dengue virus using cell culture.

**Dengue hemorrhagic fever:** A probable or confirmed case of dengue with bleeding tendencies as evidenced by one or more of the following: positive tourniquet test; petechiae, ecchymoses or purpura; bleeding: mucosa, gastrointestinal tract, injection sites or other; haematemesis or melaena; and thrombocytopenia (100 000 cells or less per mm<sup>3</sup>) and evidence of plasma leakage due to increased vascular permeability, manifested by one or more of the following: 20% rise in average haematocrit for age and sex, 20% drop in haematocrit following volume replacement therapy compared to baseline, signs of plasma leakage (pleural effusion, ascites, hypo-proteinaemia).

**Dengue shock syndrome:** All the above criteria, plus evidence of circulatory failure manifested by rapid and weak pulse, and narrow pulse pressure ( $\leq 20$  mm Hg) or hypotension for age, cold, clammy skin and altered mental status.

### 3. Entomological Surveillance

Entomological surveillance when strategically and appropriately implemented can provide insights about the changes in geographical distribution of vectors and the performance of interventions (including vector susceptibility to insecticides) to guide decision making and outbreak response efforts. In non-endemic areas or areas where the vector is not present, entomological surveillance may help detect new vector introductions promptly before they become widespread.

### 4. Contact tracing

Tracing contacts of probable and confirmed cases could help detect other active cases within the exposure area. It could also help in identifying households and mosquito breeding sites to facilitate the implementation of vector control measures.

## Laboratory Diagnosis

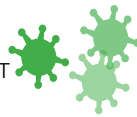
### Specimen collection

When confirmatory testing is available, a serum sample should be collected during the acute phase of the disease and a second sample collected from the sixth day after the onset of symptoms. Acute-phase samples should be used mainly for molecular testing to detect viral ribonucleic acid (RNA). Convalescent-phase samples (collected  $\geq 6$  days after onset of symptoms) should be used mainly for the detection of IgM anti-dengue antibodies by IgM antibody capture enzyme-linked immunosorbent assay (MAC-ELISA).

### Packaging and shipment of Dengue specimen

Serum or plasma samples should be refrigerated at 4°C or preserved on ice for no longer than 24 hours and transported in cold packs maintained at 4°C within 24 hours. Serum or plasma samples should be transported to the laboratory as soon as possible (ideally within the first four hours after collection). If sample storage or transport would exceed 24 hours, freeze serum or plasma at -20°C or lower.

1 [Dengue guidelines for diagnosis, treatment, prevention and control](#)  
2 <https://shorturl.at/dqtwD>



## Virus isolation

Specimens for virus isolation (serum, plasma and peripheral blood mononuclear cells) should be collected during the acute phase (usually before day 5 after the onset of fever). Virus may be isolated from tissues collected after death for autopsy. Specimens awaiting transport to the laboratory should be kept in a refrigerator or packed in wet ice. For storage up to 24 hours, specimens should be kept at between +4 °C and +8 °C. For longer storage, specimens should be frozen at -70 °C in a deep-freezer or stored in a liquid nitrogen container. Storage at -20 °C irrespective of the duration is not recommended.

## Laboratory Testing

There are a number of diagnostic options for dengue disease in humans and the choice of test varies depending on the number of days post disease onset, and laboratory capacity.

### 1. Nucleic acid detection

Nucleic acid amplification tests (NAATs) are the preferred method of laboratory diagnosis for dengue virus. Laboratory confirmation using NAAT can be made (using serum obtained  $\leq 7$  days after fever onset) by detecting viral genomic sequences using reverse transcription polymerase chain reaction (rRT-PCR) or dengue nonstructural protein 1 (NS1) antigen by immunoassay.

**Real-time RT-PCR:** The real-time RT-PCR assay is the most accurate method for detection during the acute phase, although viral RNA may only be detectable in serum or plasma for 5–7 days after symptom onset. The RT-PCR multiplex assays are recommended for their ability to detect all four dengue virus serotypes in a single reaction

### 2. Detection of antigens

ELISA and dot blot assays could be used to make an early diagnosis of dengue virus infection. This technique could also detect the virus in cases with primary and secondary dengue infections within the first nine days of illness onset.

### 3. Serological tests

#### MAC-ELISA

The IgM antibody-capture enzyme-linked immunosorbent assay (MAC-ELISA) can be used for detection of IgM if samples (blood, serum and saliva) are taken within the appropriate time frame (i.e. five days or more after the onset of fever). MAC-ELISA has good sensitivity and specificity but only when performed on samples collected within the aforementioned timeline.

#### IgG ELISA

The IgG ELISA is used for the detection of recent or past dengue infections. This method can be used to detect IgG antibodies in serum, plasma and filter-paper stored blood samples. It could also support the identification of primary and secondary infections in cases.

### 4. Hemagglutination-inhibition test

The haemagglutination-inhibition (HI) test is based on the ability of dengue antigens to agglutinate red blood cells (RBC) of ganders or trypsinized human (O) RBC. WHO recommends the HI test as a technique for distinguishing between primary and secondary infection.



## Prevention and Control

### Protection Against Mosquito Bites

- **Protective clothing:** Wear clothes that cover as much of the body as possible.
- **Sleeping protection:** Use pre-treated mosquito nets, especially if resting during daylight hours.
- **Home safety:** Install window screens to prevent mosquito entry.
- **Repellents:** Utilize mosquito repellents containing diethyltoluamide, Picaridin, or ethyl butylacetylaminopropionate.

### Caution for Babies and Infants

- Do not use insect repellent on babies younger than 2 months old.
  - *Dress up babies in clothing that covers arms and legs.*
  - *Cover strollers and baby carriers with mosquito netting.*
- Do not use products containing oil of lemon eucalyptus (OLE) or para-menthane-diol (PMD) on children younger than 3 years old.

### Vector Control

- **Targeted spraying:** Use indoor residual spraying, particularly in dengue-affected areas, with insecticides like bifenthrin and deltamethrin.
- **Water container treatment:** Treat water-filled containers with growth inhibitors or pesticides to prevent mosquito breeding.
- **Vector mapping:** Identify and map potential mosquito breeding sites to coordinate effective outdoor spraying during outbreaks.

### Treatment and Care

There are no specific treatments for dengue fever currently. However, most patients can be sent home with supportive care with acetaminophen, fluid replacement, and bed rest. Therefore, there is need in training of health care workers and clinicians in the detection, diagnosis and treatment of dengue cases. Acetaminophen (paracetamol) may be used to treat fever and relieve symptoms. Avoid non-steroidal anti-inflammatory drugs, such as ibuprofen and aspirin. Monitor for warning signs and consult a healthcare professional immediately if any arise.

### Vaccination

According to the WHO, one dengue vaccine has been prequalified, Dengvaxia® (CYD-TDV), developed by Sanofi Pasteur<sup>3</sup>. This vaccine is recommended to be administered to persons with previous exposure (seropositive individuals) between the ages of 9 and 45 years as a three-dose series given six months apart. Serological testing for past dengue infection (e.g. dengue IgG ELISA) should be used to identify persons who have had previous dengue infections. Qdenga is another vaccine which has been approved by the European Medicines Agency to be administered to all persons over the age of five years.



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