

Dengue Virus Infections

2015 Case Definition

CSTE Position Statement(s)

- 14-ID-10

Subtype(s)

- Dengue
- Dengue-like illness
- Severe dengue

Background

Dengue is a potentially fatal acute febrile illness caused by infection with any of four dengue viruses (DENV-1, -2, -3, and -4). Dengue is a major public health problem worldwide, where an estimated 400 million DENV infections and 100 million clinically apparent dengue cases occurred in 2010.

Although ~75% of individuals infected with a DENV will be asymptomatic, ~5% of individuals that develop dengue will progress to severe dengue, an illness characterized by plasma leakage leading to hypovolemic shock, hemorrhage, and potentially death. The case-fatality rate for individuals with severe dengue can be as high as 10% if untreated, or 0.1% with appropriate clinical management.

DENVs are transmitted primarily through the bite of *Aedes aegypti* and *Ae. albopictus* mosquitoes. Because these mosquitoes are endemic throughout the tropics and sub-tropics, an estimated 40% of the world's population is at risk for DENV infection. These mosquitoes are also present in the United States. *Ae. aegypti* is present throughout southern Florida, southern Louisiana, parts of New Mexico and Arizona, southern and central Texas (most prominently around urban centers such as Houston, Dallas, and Austin) [4], and have recently been detected in central California and southern Utah. *Ae. albopictus* is widely present throughout most of the southern United States and as far north as Illinois and New York.

Laboratory Criteria for Diagnosis

- Confirmatory:
 - Detection of DENV nucleic acid in serum, plasma, blood, cerebrospinal fluid (CSF), other body fluid or tissue by validated reverse transcriptase-polymerase chain reaction (PCR), or

- Detection of DENV antigens in tissue by a validated immunofluorescence or immunohistochemistry assay, or
- Detection in serum or plasma of DENV NS1 antigen by a validated immunoassay; or
- Cell culture isolation of DENV from a serum, plasma, or CSF specimen; or
- Detection of IgM anti-DENV by validated immunoassay in a serum specimen or CSF in a person living in a dengue endemic or non-endemic area of the United States without evidence of other flavivirus transmission (e.g., WNV, SLEV, or recent vaccination against a flavivirus (e.g., YFV, JEV)); or
- Detection of IgM anti-DENV in a serum specimen or CSF by validated immunoassay in a traveler returning from a dengue endemic area without ongoing transmission of another flavivirus (e.g., WNV, JEV, YFV), clinical evidence of co-infection with one of these flaviviruses, or recent vaccination against a flavivirus (e.g., YFV, JEV); or
- IgM anti-DENV seroconversion by validated immunoassay in acute (i.e., collected <5 days of illness onset) and convalescent (i.e., collected >5 days after illness onset) serum specimens; or
- IgG anti-DENV seroconversion or ≥ 4 -fold rise in titer by a validated immunoassay in serum specimens collected >2 weeks apart, and confirmed by a neutralization test (e.g., plaque reduction neutralization test) with a >4-fold higher end point titer as compared to other flaviviruses tested.
- Probable:
 - Detection of IgM anti-DENV by validated immunoassay in a serum specimen or CSF in a person living in a dengue endemic or non-endemic area of the United States with evidence of other flavivirus transmission (e.g., WNV, SLEV), or recent vaccination against a flavivirus (e.g., YFV, JEV).
 - Detection of IgM anti-DENV in a serum specimen or CSF by validated immunoassay in a traveler returning from a dengue endemic area with ongoing transmission of another flavivirus (e.g., WNV, JEV, YFV), clinical evidence of co-infection with one of these flaviviruses, or recent vaccination against a flavivirus (e.g., YFV, JEV).
- Suspected:
 - The absence of IgM anti-DENV by validated immunoassay in a serum or CSF specimen collected <5 days after illness onset and in which molecular diagnostic testing was not performed in a patient with an epidemiologic linkage.

Epidemiologic Linkage

- Travel to a dengue endemic country or presence at location with ongoing outbreak within previous two weeks of onset of an acute febrile illness or dengue, or
- Association in time and place (e.g., household member, family member, classmate, or neighbor) with a confirmed or probable dengue case.

Criteria to Distinguish a New Case from an Existing Case

DENV infection results in long-lasting immunity to symptomatic infection (dengue) with that DENV-type. However, cross-protective (heterotypic) immunity against dengue is short-lived with estimated durations of 1-3 years. In dengue endemic areas where infection pressure is high, individuals have been shown to infrequently have sequential episodes of dengue with two different infecting serotypes.

Based on these data, a person with two clinical episodes of dengue occurring at least two weeks apart and shown to be due to different infecting DENV-types confirmed by molecular diagnostic testing would be classified as two different cases.

However, for two clinical episodes of dengue in the same person diagnosed only by IgM anti-DENV on the second episode; to be considered separate cases, they would have to occur >90 days apart due to the persistence of detectable IgM anti-DENV for ~90 days.

Exposure

- During the two weeks prior to onset of fever, travel to a dengue endemic country or presence in a location experiencing an ongoing dengue outbreak, **OR**
- Association in time and place with a confirmed or probable dengue case.

Endemicity

The largest burden of dengue in the United States is in the territories of Puerto Rico and the U.S. Virgin Islands where it is endemic. As such, the majority of reported dengue cases in the U.S. come from these two territories, where existing surveillance systems are in place to capture both the incidence and to some degree the spectrum of disease. Other areas of the US where dengue is or has been endemic include American Samoa, the Northern Marianas, and Guam. In addition, hundreds of travel-associated dengue cases occur each year, primarily in the 50 United States and the District of Columbia.

Subtype(s) Case Definition [Expand all](#)

Dengue

Clinical Description

Dengue is defined by fever as reported by the patient or healthcare provider and the presence of one or more of the following signs and symptoms:

- Nausea/vomiting
- Rash
- Aches and pains (e.g., headache, retro-orbital pain, joint pain, myalgia, arthralgia)
- Tourniquet test positive
- Leukopenia (a total white blood cell count of $<5,000/\text{mm}^3$), **or**
- Any warning sign for severe dengue:
 - Abdominal pain or tenderness
 - Persistent vomiting
 - Extravascular fluid accumulation (e.g., pleural or pericardial effusion, ascites)
 - Mucosal bleeding at any site
 - Liver enlargement >2 centimeters
 - Increasing hematocrit concurrent with rapid decrease in platelet count

Dengue-like illness

Clinical Description

Dengue-like illness is defined by fever as reported by the patient or healthcare provider.

Comments

* In June 2014, the Council of State and Territorial Epidemiologists (CSTE) recommended Dengue-like illness become nationally notifiable. Dengue-like illness will be added to the list of National Notifiable Infectious Conditions when the CDC receives Office of Management and Budget (OMB) Paperwork Reduction Act (PRA) approval to receive data for this condition.

Severe dengue

Clinical Description

Severe dengue is defined as dengue with any one or more of the following scenarios:

- Severe plasma leakage evidenced by hypovolemic shock and/or extravascular fluid accumulation (e.g., pleural or pericardial effusion, ascites) with respiratory distress. A high hematocrit value for patient age and sex offers further evidence of plasma leakage.
- Severe bleeding from the gastrointestinal tract (e.g., hematemesis, melena) or vagina (menorrhagia) as defined by requirement for medical intervention including intravenous fluid resuscitation or blood transfusion.
- Severe organ involvement, including any of the following:
 - Elevated liver transaminases: aspartate aminotransferase (AST) or alanine aminotransferase (ALT) $\geq 1,000$ per liter (U/L)
 - Impaired level of consciousness and/or diagnosis of encephalitis, encephalopathy, or meningitis
 - Heart or other organ involvement including myocarditis, cholecystitis, and pancreatitis

Case Classification

Suspected

A clinically compatible case of dengue-like illness, dengue, or severe dengue with an epidemiologic linkage, as defined above.

Probable

A clinically compatible case of dengue-like illness, dengue, or severe dengue with laboratory results indicative of probable infection, as defined above.

Confirmed

A clinically compatible case of dengue-like illness, dengue, or severe dengue with confirmatory laboratory results, as defined above.

Comments

The 2009 CSTE Dengue Position Statement included the reporting of DENV-positive asymptomatic blood donors identified through pilot screening projects in dengue endemic areas. However, these screening projects have ended, no cases were reported, and the "Asymptomatic Blood or Tissue Donor" reporting category will be deleted, limiting reporting to persons with symptomatic DENV infection (i.e., dengue).