

Dengue Fever and Severe Dengue Fever

Merlin reporting code = 06100 Dengue Fever (Imported)
 = 06100 Dengue Fever (Locally Acquired) **!**
 = 06101 Dengue Fever, Severe

Case report form (CRF): [Florida Confidential Vector-borne Disease Infection CRF](#)
MERLIN EXTENDED DATA REQUIRED

Clinical description

Dengue fever

- Fever as reported by the patient or health care provider.
- One or more of the following signs and symptoms may be present (not required):
 - Nausea/vomiting
 - Rash
 - Headache
 - Retro-orbital pain or ocular pain
 - Myalgia
 - Arthralgia (joint pain)
 - Thrombocytopenia (platelet numbers of $<200,000/\text{mm}^3$)
 - Leukopenia (a total white blood cell count of $<5,000/\text{mm}^3$)
 - Abdominal pain or tenderness
 - Persistent vomiting
 - Mucosal bleeding at any site (e.g., gums, urinary tract)
 - Liver enlargement >2 centimeters

Severe dengue (including dengue hemorrhagic fever [DHF] and dengue shock syndrome [DSS])

- Fever as reported by the patient or health care provider **AND**
- One or more of the following:
 - Hypovolemic shock with respiratory distress
 - Pleural effusion (fluid around the lungs)
 - Pericardial effusion (fluid around the heart)
 - Ascites (abdominal fluid)
 - Elevated hematocrit value for patient age and sex (often with rapid decrease in platelet count)
 - 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
 - Elevated aspartate aminotransferase (AST) or alanine aminotransferase (ALT) $\geq 1,000$ units 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

Laboratory criteria for case classification

Confirmatory:

- Isolation of dengue virus from or demonstration of dengue-specific arboviral antigen or genomic sequences in tissue, blood, cerebrospinal fluid (CSF), or other body fluid by culture, polymerase chain reaction (PCR), or immunohistochemistry (IHC);

OR

- Demonstration of a four-fold rise in plaque reduction neutralization test (PRNT) end point titer (as expressed by the reciprocal of the last serum dilution showing a 90% reduction in plaque counts)

compared to the virus infected control) between dengue viruses and other flaviviruses tested in a convalescent serum sample;

OR

- Both of the following:
 - Virus-specific IgM antibodies (e.g., EIA/ELISA, MIA, or IFA) in CSF **and**
 - Negative result for other IgM antibodies in CSF for arboviruses endemic to the region where exposure occurred;

OR

- Both of the following:
 - Seroconversion from negative for dengue-specific serum IgM or IgG antibody in an acute phase (≤ 5 days after symptom onset) specimen to positive for dengue-specific serum IgM or IgG antibodies in a convalescent-phase specimen collected ≥ 5 days after symptom onset (e.g., enzyme-linked immunosorbent assay [EIA/ELISA], microsphere immunoassay [MIA], or immunofluorescence assay [IFA]) **and**
 - Negative or indeterminate for Zika IgM antibodies (e.g., EIA/ELISA, MIA, or IFA).

Presumptive:

- Virus-specific IgM antibodies (e.g., EIA/ELISA, MIA, or IFA) in serum or CSF,
AND
- No other testing for arboviruses endemic to the region where exposure occurred,
AND
- More than 90 days from most recent previous dengue infection.

Epidemiological criteria for case classification

A person who is epidemiologically linked with a confirmed or probable dengue fever case.

Case classification

Confirmed:

A clinically compatible illness in a person with confirmatory laboratory evidence.

Probable:

A clinically compatible illness in a person with presumptive laboratory evidence.

Suspect:

A clinically compatible illness in a person with epidemiological criteria.

Comments

Cases meeting the criteria for severe dengue fever (including DHF and DSS) should be reported as severe dengue fever (Merlin reporting code=06101), not as dengue fever (Merlin reporting code=06100). Zika EIA/ELISA or PCR is recommended to rule out Zika virus infection. If a case also tests positive for Zika IgM antibodies, please see the flavivirus disease and infection case definition.

Dengue re-infection

There are four dengue viruses, or serotypes. Dengue virus (DENV) infection results in long-lasting immunity to symptomatic infection with that particular DENV-serotype. However, it is possible to be re-infected with any of the remaining dengue viruses. CDC estimates approximately 20% of dengue cases that have been previously exposed to another dengue virus may have transient or no significant elevation in dengue IgM titers, making identification of such cases extremely difficult without PCR testing on the acute sample. An individual with a dengue re-infection may show elevated IgG titers but no IgM titers. During an epidemiological investigation, it is important to ask if there has been any

lifetime travel to a dengue endemic country; first dengue infection may have occurred years prior and with few or no symptoms.

Differentiating between DENV and West Nile virus (WNV) infections in patients with positive flavivirus labs:

- WNV IgM titers are negative or low positive in dengue fever patients (or vice versa); however the WNV IgG can be quite elevated in dengue patients since IgG strongly cross-reacts between flaviviruses.
- Neuroinvasive disease is relatively uncommon with dengue infections and more likely to be WNV infection than dengue. Confusion differentiating WNV and dengue infections is most likely in patients without symptoms of neuroinvasive disease (fever patients).
- Travel to a dengue endemic country in the 2 weeks prior to febrile illness onset or travel of a household member to a dengue endemic country in the 4 weeks prior to patient illness should increase suspicion of dengue.
- Joint pain is often much more severe in cases of dengue fever compared to WNV fever.
- Thrombocytopenia and leukopenia are more common and severe in cases of dengue fever compared to WNV fever.

Guide to Interpretation and Classification of Common Dengue Laboratory Tests

Laboratory test	Days post-onset of sample collection	Interpretation of positive result	Explanation
Real-time PCR	≤ 5 days	Confirmatory (*Note)	Patient viremic while febrile; days 0-7
IgM (paired specimens, acute and convalescent)	≤ 5 days for acute specimen, > 5 days for convalescent. (ideally 2 weeks apart)	Confirmatory	Negative IgM in an acute specimen followed by a positive IgM in a convalescent specimen
IgG (paired specimens, acute and convalescent)	≤ 5 days for acute specimen, > 5 days for convalescent. (ideally 2 weeks apart)	Confirmatory	Negative IgG in an acute specimen followed by a positive IgG in a convalescent specimen OR 4 fold increase in titer between acute and convalescent specimen and confirmed by PRNT
IgM (single serum specimen)	> 5 days	Probable	IgM can remain positive for ≥ 3 months in cases of acute dengue infection

*Note: Only PCR for dengue or IgM ELISA-based antibody test can be used for diagnosis of dengue in single serum specimens

NB: Previous flavivirus infections and the high prevalence of dengue IgG antibody in some populations (e.g., those resident in, or long-term visitors of dengue endemic countries) complicate interpretation of dengue serological test results. Therefore, a single serum sample tested using a dengue-specific IgG or combined IgM/IgG (“all antibody”) test is generally not helpful for diagnosis of confirmed or probable cases of dengue. For this reason suspect cases are defined clinically and epidemiologically, without IgG or combined IgG/IgM serological testing.

 **Acute and convalescent sera from people with infections believed to be Florida-acquired must be sent to the Bureau of Public Health Laboratories (BPHL). Acute sera from people with infections believed to be acquired outside Florida should also be sent to BPHL.**

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