

Dengue

(Also Known as Dengue Fever,
Dengue Hemorrhagic Fever, and Breakbone Fever)

DISEASE REPORTABLE WITHIN 24 HOURS OF DIAGNOSIS

Per N.J.A.C. 8:57, healthcare providers and administrators shall report by mail or by electronic reporting within 24 hours of diagnosis, confirmed cases of dengue to the health officer of the jurisdiction where the ill or infected person lives, or if unknown, wherein the diagnosis is made. A directory of local health departments in New Jersey is available at <http://localhealth.nj.gov>.

If the health officer is unavailable, the healthcare provider or administrator shall make the report to the Department by telephone to 609-826-5964, between 8:00 A.M. and 5:00 P.M. on non-holiday weekdays or to 609-392-2020 during all other days and hours.



1 THE DISEASE AND ITS EPIDEMIOLOGY

A. Etiologic Agent

Dengue viruses are flaviviruses and include serotypes DENV-1, 2, 3, and 4. All four serotypes can cause dengue and have been associated with severe dengue. Long-term, serotype-specific protective immunity is produced by infection with each serotype, but there is no long-term cross-protective immunity following infection. Short-term cross-immunity against other DENV types lasts for about two months. Sequential infections have been associated with a greater risk for dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS). Antibody dependent enhancement (ADE) occurs when preexisting antibodies from a primary (first) dengue virus (DENV) infection bind to an infecting DENV particle during a subsequent infection with a different dengue serotype. The antibodies from the primary infection cannot neutralize the virus and enhance viral entry into host cells, resulting in a high viral load which is thought to lead to more severe disease.

B. Clinical Description

Dengue can be a painful, debilitating disease but is rarely fatal. Symptoms appear 3-14 days after the bite of an infected mosquito and include sudden onset of fever (usually lasting 2-7 days), intense headache, severe retro orbital pain (behind eyes), muscle and joint pain (nickname "breakbone fever"). Anorexia, vomiting, facial flushing, macular or maculopapular rash, and mild bleeding manifestations (e.g., petechiae, nose or gum bleed, or easy bruising) may occur. Laboratory findings commonly include leukopenia, thrombocytopenia, hyponatremia, and elevated liver enzymes. About 75% of dengue infections are asymptomatic.

As the fever begins to wane, severe dengue may develop in 2-4% of patients. Warning signs include severe abdominal pain or persistent vomiting; mucosal bleeding; vomiting blood; black, tarry stools; drowsiness or irritability; pale, cold or clammy skin; and difficulty breathing. Patients may have a rapid decline in platelet count with a rise in hematocrit and have signs of internal bleeding. Patients with severe plasma leakage have pleural effusions or ascites, hypoproteinemia, and hemoconcentration. Severe dengue can also present as hepatitis, myocarditis, pancreatitis, and encephalitis. If untreated, DHF can lead to shock and possibly 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.

C. Reservoirs

Where endemic, dengue virus is maintained in a human / *Aedes aegypti* mosquito cycle. Dengue outbreaks have been attributed to *A. aegypti*, and to a lesser extent, *Aedes albopictus*. There is a sylvatic monkey/mosquito cycle, which may spill over into human populations in southeastern Asia and western Africa.

D. Mode of Transmission

The dengue virus (DENV) is primarily transmitted from person to person through the bite of an infected *Aedes aegypti* or *Aedes albopictus* mosquito. Humans are the main host and the primary source of virus for female mosquitoes.

Some people never have significant symptoms but can still infect mosquitoes. After entering the mosquito in the blood meal, the virus will require an additional 8-12 days of incubation before it can then be transmitted to another human. The mosquito remains infected for the remainder of its life, which might be days or a few weeks.

In rare cases, dengue can be transmitted in organ transplants and blood transfusions from infected donors. There is also evidence of transmission from an infected pregnant woman to her fetus.

E. Incubation Period

Usually 4-7 days, although it may range from 3-14 days

F. Period of Communicability or Infectious Period

In order for transmission to occur, a mosquito must feed on a person during a 5- day period when large amounts of virus are in the blood; this period usually begins a little before the person becomes symptomatic.

G. Epidemiology

Dengue is the most rapidly spreading mosquito-borne viral disease in the world. In the last 50 years, incidence has increased 30-fold with increasing geographic expansion to new countries and, in the present decade, from urban to rural settings. Dengue is endemic in essentially all tropical and subtropical tourist destinations, worldwide (<http://www.healthmap.org/dengue/en/>). About 40% of the world's population lives in areas where there is risk of dengue transmission. In most areas disease incidence is highest in children, although increasing numbers of adult cases are being reported from both rural and urban areas. Most dengue endemic areas experience epidemic cycles at 2-5 year intervals.

Persons from dengue-nonendemic countries who travel to dengue-endemic countries are at risk for infection. In the United States, dengue is the leading cause of febrile illness among travelers returning from the Caribbean, South America, and South Central/Southeast Asia. Factors that

increase a traveler's risk of infection include duration of time in country, travel during "dengue season," and not using personal protection from mosquito bites.

Nearly all dengue cases reported in the US continental states were acquired elsewhere by travelers or immigrants. Imported cases rarely result in secondary transmission. The last reported continental dengue outbreak was in south Texas in 2005. A small dengue outbreak occurred in Hawaii in 2001.

Mosquitoes that transmit dengue are present in the United States. *A. aegypti* is present throughout southern Florida, southern Louisiana, parts of New Mexico and Arizona, southern and central Texas, 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, including in New Jersey.

2 CASE DEFINITION

The NJDOH Infectious & Zoonotic Disease Program follows the most current dengue case definition as published on the CDC National Notifiable Disease Surveillance System (NNDSS) website.

Dengue Case Definition: <https://www.cdc.gov/nndss/conditions/dengue/>

Case definitions enable public health to classify and count cases consistently across reporting jurisdictions, and should not be used by healthcare providers to determine how to meet an individual patient's health needs.

The 2015 case definition includes three subgroups, which differ by clinical presentation:

- Dengue
- Dengue-like Illness
- Severe Dengue

CLINICAL PRESENTATION:

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)
- 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 the healthcare provider.

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/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

EPIDEMIOLOGICAL 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.

LABORATORY CRITERIA FOR DIAGNOSIS:

Confirmatory:

- Detection of DENV nucleic acid in serum, plasma, blood, cerebrospinal fluid (CSF), other body fluid or tissue by RT-PCR, or
- Detection of DENV antigens in tissue, or
- Detection in serum or plasma of DENV NS1 antigen; or
- Cell culture isolation of DENV from a serum, plasma, or CSF specimen; or
- Detection of IgM anti-DENV in a serum specimen or CSF in a person living in the US without evidence of other flavivirus transmission (e.g., WNV, SLEV, Zika) or recent vaccination against a flavivirus (e.g., YFV, JEV); or
- Detection of IgM anti-DENV in a serum specimen or CSF in a traveler returning from a dengue endemic area without ongoing transmission of another flavivirus (e.g., WNV, JEV, YFV, Zika), clinical evidence of co-infection with a flavivirus, or recent vaccination against a flavivirus (e.g., YFV, JEV); or
- IgM anti-DENV seroconversion 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 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 in a serum specimen or CSF in a person living in the US with evidence of other flavivirus transmission (e.g., WNV, SLEV, Zika), or recent vaccination against a flavivirus (e.g., YFV, JEV).
- Detection of IgM anti-DENV in a serum specimen or CSF in a traveler returning from a dengue endemic area with ongoing transmission of another flavivirus (e.g., WNV, JEV, YFV, Zika), clinical evidence of co-infection a flavivirus, or recent vaccination against a flavivirus (e.g., YFV, JEV).

CASE CLASSIFICATION

Confirmed

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

Probable

A clinically compatible case of dengue-like illness, dengue, or severe dengue with probable laboratory results

Possible

A clinically compatible case of dengue-like illness, dengue, or severe dengue with an epidemiologic linkage. Note: cases who meet clinical and epidemiological criteria whose only positive laboratory result is an IgG would be considered “possible.”

Not a Case

Does not meet requirements for other case classifications

CRITERIA TO DISTINGUISH A NEW CASE FROM AN EXISTING CASE

A person with 2 clinical episodes of dengue occurring at least 2 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 diagnosed only by IgM 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.

Note: commercial laboratories do not perform DENV subtyping, so in most cases the subtype will be unknown.

3 LABORATORY TESTING

Dengue can be diagnosed by isolation of the virus, by serological tests, or by molecular methods. Diagnosis of acute (on-going) or recent dengue infection can be established by testing serum samples during the first 5 days of symptoms and/or early convalescent phase (more than 5 days of symptoms). Dengue testing is widely available at commercial laboratories. The Public Health and Environmental Laboratories (PHEL) has the capacity to test for dengue. Local Health Departments should call 609-826-5964 for public health testing inquiries.

Acute infection is confirmed when the virus is isolated from serum or autopsy tissue specimens, or the specific dengue virus genome is identified by reverse transcription-polymerase chain reaction (RT-PCR) from serum or plasma, cerebrospinal fluid, or autopsy tissue specimens during an acute febrile illness. Acute infections can also be laboratory confirmed by identification of dengue viral antigen or RNA in autopsy tissue specimens by immunofluorescence or immunohistochemical

analysis, or by seroconversion from negative to positive IgM antibody to dengue or demonstration of a fourfold or greater increase in IgG antibody titers in paired (acute and convalescent) serum specimens.

Patients who have IgM antibodies to dengue detected in serum via an IgM antibody capture enzyme-linked immunosorbent assay (MAC-ELISA) and had either 1) A negative RT–PCR result in the acute phase specimen or 2) Did not submit an acute phase specimen, are classified as having a recent probable dengue infection. This is due to the fact that IgM antibodies for dengue may remain elevated for 2 to 3 months after the illness. The elevated IgM could be the result of an infection that occurred 2 to 3 months ago. In addition, there is cross reactivity with other flaviviruses including Zika, West Nile virus (WNV), St. Louis encephalitis virus (SLE), Japanese encephalitis virus (JEV) and yellow fever virus (YFV).

4 PURPOSE OF SURVEILLANCE AND REPORTING

- To identify imported cases and better understand the epidemiology of imported dengue cases in the US
- To ensure that cases are appropriately contained and prevent the introduction of virus into native mosquito populations
- To identify locally acquired cases, if they occur, so that appropriate active surveillance and mosquito control interventions can be taken
- To provide travelers with appropriate preventive health information

5 CASE INVESTIGATION

A. Investigation

It is important to investigate dengue cases in a timely manner to identify the source of exposure (travel vs blood transfusion vs suspected local mosquito transmission) and to provide patient education. A case report form is not required, as long as information is captured in CDRSS. LHDs should complete the investigation and close cases in CDRSS within 3 months of case creation. Cases that remain open for ≥ 3 months and have no investigation or update notes will be closed by NJDOH.

B. Key CDRSS Fields Specific for Dengue

CDRSS Screen	Required Information
Patient Info	Based on clinical presentation, select the appropriate subgroup: dengue, dengue-like illness, or severe dengue
Signs/Symptoms	Check appropriate boxes for signs and symptoms and indicate their onset/resolution dates. Complete clinical symptoms are important for ensuring appropriate case classification. Enter additional symptoms and laboratory findings in comments box.
Risk Factors	<ul style="list-style-type: none"> • Travel history or relocation to the US – enter country in attribute field and departure/arrival dates • Document if patient received a blood transfusion or organ transplant in 30 days prior to symptom onset – enter dates
Case Comments	<ul style="list-style-type: none"> • Document if the patient had a previous diagnosis of dengue and enter approximate date • Document if the patient was previously vaccinated against another flavivirus (e.g., YFV, JEV) and enter approximate date

6 CONTROLLING FURTHER SPREAD

A. Isolation and Quarantine Requirements

There are no isolation or quarantine requirements. However, to prevent transmission of dengue virus into the local mosquito population, persons with dengue should be advised to protect themselves from mosquito bites for 1 week after symptom onset. The local health department should instruct patients regarding this precaution.

B. Protection of Contacts

N/A

C. Managing Special Situations

Locally Acquired Case

A locally acquired case of dengue would be an unusual occurrence, as the *A. aegypti* mosquito is not well established in New Jersey. If a local health officer determines during the course of an investigation that a patient does not have a recent travel history to a dengue-endemic country, s/he should notify NJDOH/CDS at 609-826-5964. Environmental and vector-control efforts, in collaboration with state and county mosquito control agencies, to locate the focus of infection, and active surveillance for additional cases may be necessary.

D. Preventive Measures

There is no vaccine available in the US to prevent dengue and there are no specific medications to treat a dengue infection. This makes prevention the most important step, and prevention means avoiding mosquito bites if you live in or travel to an endemic area. Key prevention messages are available at <http://www.nj.gov/health/cd/topics/vectorborne.shtml>.

International Travel

Because epidemics of dengue can be extensive and may affect a high percentage of the population, travelers should avoid areas with ongoing epidemics. However, for those who do travel to endemic areas, it is recommended that –

- Travelers protect themselves from mosquitoes by using insect repellents, wearing protective clothing, and using mosquito nets when rooms are not screened. Unlike other vectors, the *A. aegypti* mosquitoes bite during daytime hours, and these mosquitoes like to bite inside as well as around homes.
- Recent travelers to endemic countries with acute onset of fever and other compatible symptoms should seek medical attention immediately.
- Travelers to countries with mosquito-borne diseases should take extra precautions to avoid mosquito bites for 3 weeks after return, to prevent transmission to mosquitoes in NJ, which might go on to bite others in the household or nearby area, and possibly spreading the disease.

Additional information regarding international travel and dengue can be found at [the CDC's Traveler's Health Office \(https://wwwnc.cdc.gov/travel\)](https://wwwnc.cdc.gov/travel)

Additional Information

NJDOH: <http://www.nj.gov/health/cd/topics/dengue.shtml>

CDC: www.cdc.gov/Dengue/

References

Centers for Disease Control and Prevention. National Notifiable Diseases Surveillance System (NNDSS): 2015 Case Definition. <https://www.cdc.gov/nndss/conditions/dengue/case-definition/2015/>

Centers for Disease Control and Prevention. Dengue: <https://www.cdc.gov/Dengue/>

Centers for Disease Control and Prevention. Dengue Clinical Case Management Course (DCCM): <https://www.cdc.gov/dengue/training/cme.html>

Chin J, ed. *Control of Communicable Diseases Manual*. 20th ed. Washington, DC: American Public Health Association; 2014.

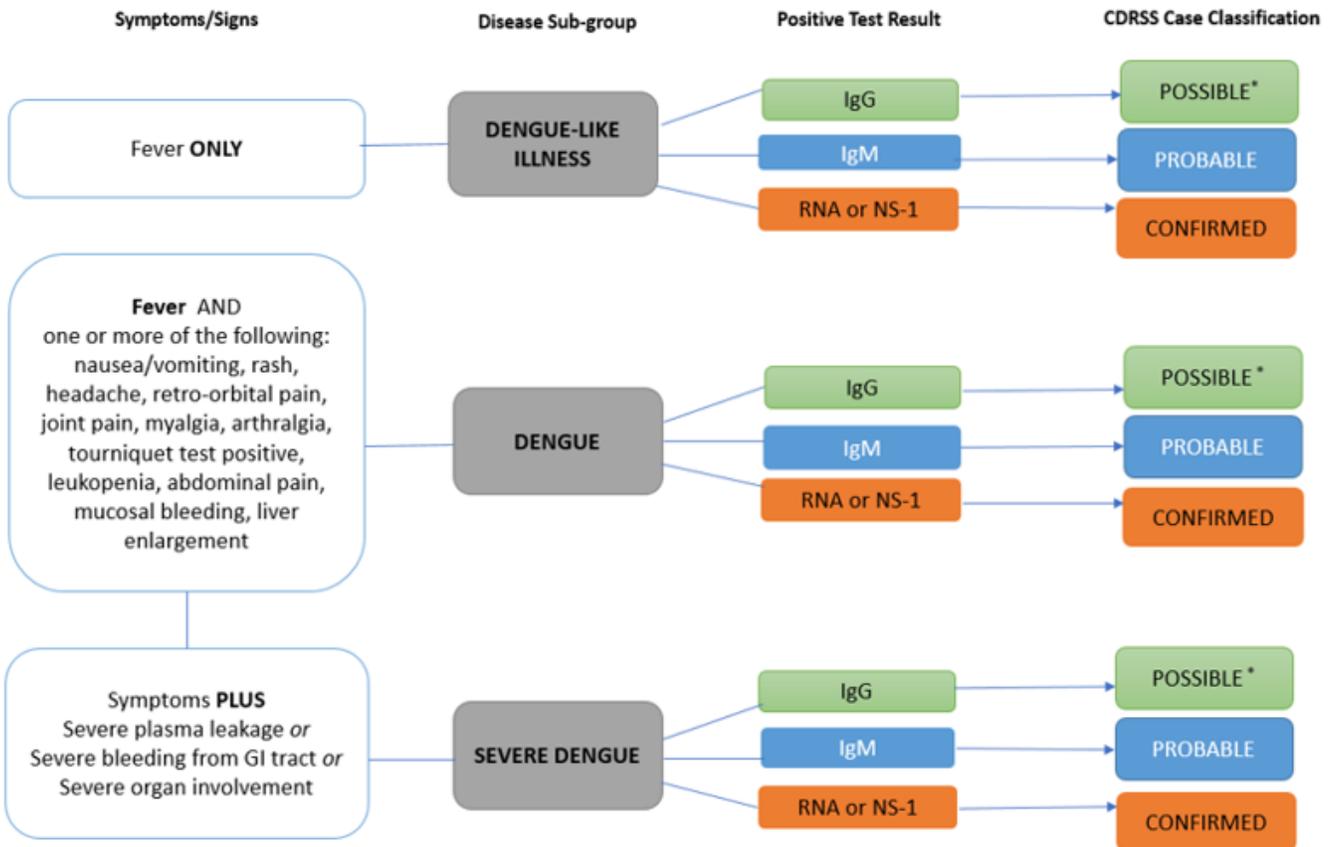
Florida Department of Health, *Diseases and Conditions, Dengue*: <http://www.floridahealth.gov/diseases-and-conditions/dengue/index.html>.

World Health Organization, *Dengue – Guidelines for Diagnosis, Treatment, Prevention, and Control*, 2009. http://apps.who.int/iris/bitstream/10665/44188/1/9789241547871_eng.pdf

Communicable Disease Service Manual

NJDOH DENGUE INVESTIGATION WORKSHEET		CDRSS #: _____
DEMOGRAPHICS		
Race <input type="checkbox"/> White <input type="checkbox"/> Black <input type="checkbox"/> American Indian or Alaskan Native <input type="checkbox"/> Asian <input type="checkbox"/> Pacific Islander <input type="checkbox"/> Unknown		Ethnicity <input type="checkbox"/> Hispanic <input type="checkbox"/> Non-Hispanic
Occupation: _____	Pregnancy status <input type="checkbox"/> Pregnant <input type="checkbox"/> Not pregnant <input type="checkbox"/> N/A <input type="checkbox"/> Unknown	
CLINICAL INFORMATION		
Date first seen by a medical professional: ____ / ____ / ____	Onset Date (mm/dd/yy) ____ / ____ / ____	Diagnosis: _____
General signs and symptoms:		Warning signs for severe dengue:
<input type="checkbox"/> Fever Temp: _____ F	<input type="checkbox"/> Rash. Describe: _____	<input type="checkbox"/> Abdominal pain/tenderness
<input type="checkbox"/> Headache	<input type="checkbox"/> Anorexia	<input type="checkbox"/> Persistent vomiting
<input type="checkbox"/> Pain behind eyes	<input type="checkbox"/> Nausea or vomiting	<input type="checkbox"/> Extravascular fluid accumulation (pleural or pericardial effusion, ascites)
<input type="checkbox"/> Joint pain (arthralgia)	<input type="checkbox"/> Other, specify: _____	
<input type="checkbox"/> Muscle pains (myalgia)	Site(s): _____	<input type="checkbox"/> Increasing hematocrit concurrent with rapid decrease in platelet count
Severe dengue symptoms:		
<input type="checkbox"/> Severe plasma leakage defined by: <input type="checkbox"/> a) Hypovolemic shock	<input type="checkbox"/> Severe GI tract bleeding <input type="checkbox"/> Severe vaginal bleeding	<input type="checkbox"/> Hepatitis <input type="checkbox"/> Encephalitis, meningitis, or encephalopathy, specify: _____
<input type="checkbox"/> b) Extravascular fluid accumulation with respiratory distress	<input type="checkbox"/> Treatment with IV fluids or blood transfusion	<input type="checkbox"/> Myocarditis or other cardiac syndrome
Was patient hospitalized because of this illness? <input type="checkbox"/> Yes, specify location and date(s) Hospital name: _____ Admission: ____ / ____ / ____ Discharge: ____ / ____ / ____ <input type="checkbox"/> No <input type="checkbox"/> Unknown		Did the patient die because of this illness? <input type="checkbox"/> Yes, Date _____ <input type="checkbox"/> No <input type="checkbox"/> Unknown
Was patient previously diagnosed with Dengue? <input type="checkbox"/> Yes Date: _____ <input type="checkbox"/> No <input type="checkbox"/> Unk	Was patient vaccinated against Yellow Fever? <input type="checkbox"/> Yes Date: _____ <input type="checkbox"/> No <input type="checkbox"/> Unk	Was patient vaccinated against Japanese Encephalitis? <input type="checkbox"/> Yes Date: _____ <input type="checkbox"/> No <input type="checkbox"/> Unk
LABORATORY TESTING		
Platelet count _____ (L / McL)	Hematocrit (%) _____ Elevated liver enzymes (U/L)	Tourniquet test <input type="checkbox"/> Positive <input type="checkbox"/> Negative <input type="checkbox"/> Not performed
WBC count _____ (L / McL)	ALTs _____ ASTs _____	
RISK FACTORS		
Was there travel to or relocation from a dengue endemic areas in the 3 weeks prior to onset? <input type="checkbox"/> Yes Dates: ____ / ____ / ____ - ____ / ____ / ____ Location: _____ <input type="checkbox"/> No <input type="checkbox"/> Unknown	Did the patient recently donate blood or organs? <input type="checkbox"/> Yes Date: ____ / ____ / ____ Location of donation: _____ <input type="checkbox"/> No <input type="checkbox"/> Unknown	
Did the patient receive a blood transfusion in the past 30 days? (If yes, specify)	Did the patient receive an organ transplant in the past 30 days? (If yes, specify)	

Dengue Virus Case Classification



* Possible cases have travel exposure to dengue endemic country within two weeks of illness onset or associated with a confirmed or probable dengue case