



Dengue-like Illness, Dengue, Severe Dengue

Disease Plan

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Last updated: 11/25/2019 by Dallin Peterson

Questions about this disease plan?

Contact the Utah Department of Health Bureau of Epidemiology: 801-538-6191.

✓ CRITICAL CLINICIAN INFORMATION

Clinical Evidence									
<p>Signs/Symptoms</p> <ul style="list-style-type: none"> • Febrile phase <ul style="list-style-type: none"> ○ High fever • Critical (plasma leak) phase <ul style="list-style-type: none"> ○ Sudden onset of varying degrees of plasma leak into the pleural and abdominal cavities • Convalescence (Reabsorption) phase <ul style="list-style-type: none"> ○ Sudden arrest of plasma leak with concomitant reabsorption of extravasated plasma and fluids • Additional symptoms include: <table style="width: 100%; border: none;"> <tr> <td style="width: 33%;">○ Rash</td> <td style="width: 33%;">○ Muscle and joint pain</td> <td style="width: 33%;">○ Swollen lymph nodes</td> </tr> <tr> <td>○ Severe headache</td> <td>○ Gastrointestinal upset and loss of appetite</td> <td>○ Petechiae</td> </tr> <tr> <td>○ Eye pain</td> <td>○ Rash</td> <td>○ Nosebleeds</td> </tr> </table> 	○ Rash	○ Muscle and joint pain	○ Swollen lymph nodes	○ Severe headache	○ Gastrointestinal upset and loss of appetite	○ Petechiae	○ Eye pain	○ Rash	○ Nosebleeds
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○ Eye pain	○ Rash	○ Nosebleeds							
<p>Period of Communicability</p> <ul style="list-style-type: none"> • Not communicable human-to-human, other than blood transfusions or organ donation. 									
<p>Incubation Period</p> <ul style="list-style-type: none"> • Usually 4-7 days; ranges from 3-14 days. 									
<p>Mode of Transmission</p> <ul style="list-style-type: none"> • Bite of an infected mosquito 									
Laboratory Testing									
<p>Type of Lab Test/Timing of Specimen Collection</p> <ul style="list-style-type: none"> • Preferred specimens are acute (collected 3 to 5 days after onset of symptoms) and convalescent (collected >5 days after onset of symptoms) serum samples • RT-PCR and/or NS1 testing will be performed on the acute serum • MAC-ELISA assay will be performed on acute specimens negative for RT-PCR and on convalescent serum. • Additional tests (e.g., PRNT) may be performed on convalescent serum to distinguish between other Flaviviruses, e.g., West Nile virus • Specimens should be sent to the Utah Public Health Laboratory (UPHL) for referral to CDC. Contact UPHL 801-965-2400 for specific instructions on specimen collection, handling, and transport. 									
<p>Type of Specimens</p> <ul style="list-style-type: none"> • Serum, cerebrospinal fluid, or autopsy tissue specimens 									
Treatment Recommendations									
<p>Type of Treatment</p> <ul style="list-style-type: none"> • No specific antiviral • Analgesics containing acetaminophen • Do not use nonsteroidal anti-inflammatory drugs (e.g., ibuprofen, aspirin, etc.) due to higher risk of bleeding complications • Rest • Maintaining hydration 									
<p>Time Period to Treat</p> <ul style="list-style-type: none"> • No specific antiviral; continue supportive care until symptoms have resolved. • Should seek addition medical attention if symptoms worsen in the first 24 hours after fever breaks. 									
<p>Prophylaxis</p> <ul style="list-style-type: none"> • None 									
Contact Management									
<p>Isolation and Quarantine of Case</p> <ul style="list-style-type: none"> • None 									
Infection Control Procedures									
<ul style="list-style-type: none"> • Standard Precautions 									

✓ WHY IS DENGUE FEVER IMPORTANT TO PUBLIC HEALTH?

Dengue is a potentially life-threatening illness caused by the bite of a mosquito infected with a virus associated with dengue fever. Although dengue is not endemic in Utah, public health investigations can assist in determining the locations of exposure, and can therefore assist in determining if there is possible movement of mosquitoes potentially due to climate change.

✓ DISEASE AND EPIDEMIOLOGY

Clinical Description

Dengue is an acute, viral illness characterized by sudden onset of fever, severe headache, eye pain, muscle and joint pain, and rash. Gastrointestinal upset and loss of appetite often occur. Swollen lymph nodes, petechiae (small bleeds into the skin that resemble flea bites), nosebleeds, and bleeding gums occur frequently. Recovery is often associated with prolonged fatigue and depression.

Severe dengue, often referred to as dengue hemorrhagic fever (DHF), is a more serious form of dengue, characterized by sudden onset of fever as well as bleeding (often severe) from mucosal surfaces (e.g., nasal, gastrointestinal, vaginal, gums), liver enlargement, and in severe cases, circulatory failure. Dengue Hemorrhagic Fever can be described in three different phases as seen in figure 1: febrile, critical (plasma leak), and convalescence (reabsorption). Severe dengue also often includes abnormal blood clotting, low platelet count (thrombocytopenia), and evidence of plasma leaking through capillaries. Patients who develop gastrointestinal bleeding have a higher mortality rate than those who do not. Severe dengue can result in life-threatening hypotension (severely reduced blood pressure, shock) and generally occurs in people with a history of exposure to multiple dengue virus serotypes; the partial immune reaction contributes to the severity of the disease. If a person is re-infected with the same dengue type, the immune response eliminates the virus so quickly that the person does not become noticeably ill. If a person has a second dengue infection with a new dengue type, then the immune response is limited in activity due to Antibody-Dependent Enhancement (ADE). ADE may cause severe illness due to the enhancement of the viral infection.

Phases of infections resulting in Dengue Hemorrhagic Fever				
Phase	Febrile	Critical (plasma leak)	Convalescence (Reabsorption)	
Duration	Fever lasts 2-7 days	Plasma leak lasts 24-48 hours	Reabsorption lasts 2-4 days	
Hallmark Features	High Fever and symptoms consistent with Dengue Fever	Normal or subnormal temperatures	Resolution of plasma leakage and hemorrhage	
		Varying degrees of plasma leak into pleural and peritoneal spaces	Stabilization of vital signs	
		Varying degrees of hemorrhage	Reabsorption of accumulated fluids: including leaked plasma and administered intravascular fluids	
		Risk of developing shock and death	Improved appetite and sense of wellbeing	
Potential complications	Dehydration due to decreased fluid intake, emesis, and increased metabolic state	Unrecognized severe plasma leakage or hemorrhage leading to shock	Intravascular fluid overload due to continual aggressive volume resuscitation during convalescence phase.	
	Convulsions due to high fever	Intracranial bleed		
	Rarely, severe hemorrhage	Metabolic abnormalities (e.g. hypoglycemia, hyponatremia, hypocalcemia, metabolic acidosis)		
		Coagulopathy (abnormal INT or PTT)		
		Fulminant hepatic failure		
Prolonged shock leading to death				

Figure 1: Phases of Dengue Hemorrhagic Fever

Causative Agent

The viruses of dengue fever are flaviviruses and include serotypes 1, 2, 3, and 4. These same viruses cause severe dengue.

Differential Diagnosis

Dengue fever can easily be confused with non-dengue illnesses, particularly in non-epidemic situations. Depending on the geographical origin of the patient, other etiologies – including non-dengue flavivirus infections – should be ruled out. These include yellow fever, Chikungunya Virus, Japanese encephalitis, St. Louis encephalitis, Zika, West Nile, and other causes of fever such as malaria, leptospirosis, typhoid, Rickettsial diseases (*Rickettsia prowazeki*, *R. mooseri*, *R. conori*, *R. rickettsi*, *Orientia tsutsugamushi*, *Coxiella burneti*, etc.), measles, enteroviruses, influenza and influenza-like illnesses, and hemorrhagic fevers (Arenaviridae: Junin, etc.; Filoviridae: Marburg, Ebola; Bunyaviridae: hantaviruses, Crimean-Congo hemorrhagic fever, etc.).

Laboratory Identification

Dengue can be diagnosed by isolation of the virus, serological tests, or by molecular methods. Diagnosis of acute (ongoing) or recent dengue infection can be established by testing serum samples starting 3-4 days after symptom onset. On serum samples, for acute infection defined as ≤ 5 days after onset of symptoms dengue virus is confirmed using reverse transcription-polymerase chain reaction (RT-PCR). For convalescent infection (> 5 days after onset of symptoms), serologic tests are used.

To confirm a diagnosis of dengue, both acute and convalescent phase specimens are needed. Patients who have IgM antibodies to dengue detected in their convalescent serum specimen 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 because IgM antibodies for dengue may remain elevated for 2-3 months after the illness; the elevated IgM observed in a sample could be the result of an infection that occurred 2-3 months ago.

Dengue virus can be isolated from serum or autopsy tissue specimens, or the specific dengue virus genome is identified by from serum or plasma, cerebrospinal fluid, or autopsy tissue specimens during an acute febrile illness. Methods such as one-step, real time RT-PCR or nested RT-PCR are now widely used to detect dengue viral genes in acute-phase serum samples. This detection coincides with the viremia and the febrile phase of illness onset. Acute infections can also be laboratory confirmed by identification of dengue viral antigen (NS1) 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.

There may be cross reactivity with other flaviviruses, including West Nile virus (WNV), St. Louis encephalitis virus (SLE), Japanese encephalitis virus (JEV), Zika virus and yellow fever virus (YFV). The provider should review the patient's past medical history, recent travel history, and vaccination record (especially yellow fever vaccination) to determine the likelihood that the current acute febrile illness is due to an infection with dengue virus. The Plaque Reduction Neutralization Test (PRNT) can be used to distinguish between cross-reacting flaviviruses by measuring the titer levels of neutralizing antibodies. The Utah Public Health Laboratory (UPHL) acts as a referral agent to the CDC for PRNT confirmation of dengue viruses.

Treatment

There is no specific viral treatment available for arboviral infections, including dengue. Persons who think they have dengue should use analgesics (pain relievers) with acetaminophen and avoid those containing aspirin. They should also rest, drink plenty of fluids, and consult a physician. If they feel worse (e.g., develop vomiting and severe abdominal pain) in the first 24 hours after the fever declines, they should go immediately to the hospital for evaluation. No licensed vaccine is available for preventing dengue.

Case Fatality

Fatalities associated with dengue fever are rare. With severe dengue, case fatality rates without supportive treatment approach 50%; treated severe dengue is associated with a 3% fatality rate.

Reservoir

Dengue viruses are transmitted to humans by the bite of an infected mosquito. In the Western Hemisphere, the *Aedes aegypti* mosquito is the most important transmitter or vector of dengue viruses, although a 2001 outbreak in Hawaii was transmitted by *Aedes albopictus*. In parts of Southeast Asia and West Africa, the viruses may be maintained in a cycle involving monkeys and mosquitoes.

Transmission

Dengue is spread to humans by the bite of an infected mosquito (principally the *Aedes aegypti* mosquito). This mosquito has not been found in Utah, although the *aegypti* mosquito is currently expanding its range. Direct person-to-person spread of dengue does not occur.

Susceptibility

The elderly and children are most susceptible to dengue-related illness. Children have higher rates of dengue in endemic areas because infection confers immunity to the circulating serotype. As with most other arboviruses, infection confers immunity, but only short-term immunity to non-endemic serotypes.

Incubation Period

The incubation period for dengue is usually 4-7 days, although it may range from 3-14 days.

Period of Communicability

Arboviral infectious agents are not communicable from person-to-person, except in rare instances (blood transfusion, organ donation).

Epidemiology

Dengue has been called the most important mosquito-transmitted viral disease in terms of morbidity and mortality. Today, about 2.5 billion people, or 40% of the world's population, live in areas where there is a risk of dengue transmission. Dengue virus causes about 100 million cases of acute febrile disease annually, including more than 500,000 reported cases of severe dengue.

Currently, dengue is endemic in 112 countries. Dengue viruses are endemic in most tropical countries, including Australia and countries in Asia, Africa, the Caribbean, Central America, and South America. Hawaii, southern Texas, and the southeastern U.S., where *A. aegypti* is found, are at risk for dengue transmission and sporadic outbreaks. Puerto Rico is endemic for dengue. The world's largest known epidemic of severe dengue occurred in Cuba in 1981, with more than 116,000 persons hospitalized and as many as 11,000 cases reported in a single day. In the United States, dengue has been reported in 48 states, with nearly all cases acquiring it elsewhere through travel or immigration. This is also the case with Utah, as Utah does not have the appropriate vector to effectively transmit dengue.

✓ PUBLIC HEALTH CONTROL MEASURES

Public Health Responsibility

- Investigate all suspect cases of disease, fill out and submit appropriate disease investigation forms.
- Provide education to the general public, clinicians, and first responders regarding disease transmission and prevention.
- Identify clusters or outbreaks of disease.
- Identify sources of exposure and stop further transmission.

Prevention

Environmental measures:

People should be encouraged to reduce mosquito populations around their homes and neighborhoods by getting rid of any standing water that might support mosquito breeding. Mosquitoes will begin to breed in any puddle or standing water that lasts for more than four days. People should be advised of the following:

- Dispose of or regularly empty any metal cans, plastic containers, ceramic pots, and other containers (including trashcans) on their property that might hold water.
- Pay special attention to discarded tires. Stagnant water in tires is a common place for mosquitoes to breed.
- Drill holes in the bottom of recycling containers left outdoors so that water can drain out.
- Clean clogged roof gutters; remove leaves and debris that may prevent drainage of rainwater.
- Turn over plastic wading pools and wheelbarrows when not in use.
- Do not allow water to stagnate in birdbaths; aerate ornamental ponds or stock them with fish.
- Keep swimming pools clean and properly chlorinated; remove standing water from pool covers.
- Use landscaping to eliminate standing water.

Personal preventive measures for travelers or persons living in endemic areas:

- Repair any holes in screens, and make sure they are tightly attached to all doors and windows.
- Use mosquito netting when sleeping.
- Use repellents containing DEET (N,N-diethyl-m-toluamide), and choose a product that will provide sufficient protection for the amount of time spent outdoors. Product labels often indicate the length of time that someone can expect protection from a product. DEET is considered safe when used according to the manufacturer's directions. The efficacy of DEET levels off at a concentration of 30%, which is the highest concentration recommended for children and adults.

The following should be noted when using DEET:

- DEET products should not be used on children less than two months of age. Mosquito netting may be used to cover infant carriers or to protect other areas for children less than two months of age.
- Avoid using DEET products that combine the repellent with a sunscreen. Sunscreens may need to be re-applied often, resulting in an over-application of DEET.
- Apply DEET on exposed skin, using only as much as needed.

- Do not use DEET on the hands of young children, and avoid applying repellent to areas around the eyes and the mouth.
- Do not use DEET over cuts, wounds, or irritated skin.
- Wash treated skin with soap and water after returning indoors, and wash treated clothing.
- Avoid spraying DEET products in enclosed areas.
- Picaridin (KBR 3023) is a relatively new repellent that is now available in the U.S. Recent studies have shown it to be safe and effective. Picaridin-containing repellents should be used according to the manufacturer's recommendations.
- A number of plant-derived products are available for use as repellents, but most of these products do not provide the same level or duration of protection as products containing DEET. However, there are studies that show that oil of lemon eucalyptus [p-methane 3,8-diol(PMD)] provides as much protection as low concentrations of DEET when tested against mosquitoes found in the U.S.

Chemoprophylaxis

None.

Vaccine

No vaccine exists for dengue.

Isolation and Quarantine Requirements

Isolation: None

Hospital: Standard body substance precautions.

Quarantine: None

CASE INVESTIGATION

Reporting

Report all suspect and confirmed cases of dengue infection. In Utah, cases should be reported within three days of identification.

Table of criteria to determine whether a case should be reported to public health authorities

Criterion	Reporting	
	1	2
Clinical Evidence		
Fever as reported by the patient or healthcare provider	N	N
Laboratory Evidence		
For any patient with history of fever, the detection in serum, plasma, CSF or tissue of DENV- specific genome sequences by RT-PCR or another molecular diagnostic test; <i>OR</i>	O	
Detection in serum or plasma of DENV NS1 antigen by immunoassay; <i>OR</i>	O	
Cell culture isolation of DENV from serum, plasma, CSF or other clinical specimens; <i>OR</i>	O	
Detection of DENV antigen in tissue from a fatal case by immunofluorescence or immunohistochemistry; <i>OR</i>	O	
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 irrespective of whether there is other flavivirus transmission (e.g., WNV, SLEV) occurring or whether the person has had recent vaccination against a flavivirus (e.g., YFV, JEV); <i>OR</i>	O	
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); <i>OR</i>	O	
IgM anti-DENV seroconversion by validated¶ immunoassay in acute (i.e., collected ≤5 days of illness onset) and convalescent (e.g., collected >5 days after illness onset) serum specimens; <i>OR</i>	O	
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, and without recent vaccination against a flavivirus (e.g., YFV, JEV).	O	
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 [12]) with a ≥4-fold higher end point titer as compared to other flaviviruses tested.	O	
Epidemiological Evidence		
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, <i>OR</i>		O
During the two weeks prior to onset of fever, association in time and place with a confirmed or probable dengue case.		O

Notes:

S = This criterion alone is Sufficient to report a case.

N = All - Nil criteria in the same column are Necessary to report a case.

O = At least one of these - Oll (Optional) criteria in each category (e.g., clinical evidence and laboratory evidence) in the same column - in conjunction with all - Nil criteria in the same column - is required to report a case.

*A requisition or order for any of the - Sll laboratory tests is sufficient to meet the reporting criteria.

¶Validated diagnostic tests are defined as FDA-approved or laboratory-developed assays if supported by evaluation studies.

Case Definition

Dengue Virus Infections (2015)

Clinical Criteria

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

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

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) $>1,000$ 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

Diagnostic testing should be requested for patients in whom there is a high index of suspicion for dengue, based either on signs and symptoms, or epidemiological linkage to a confirmed or probable dengue case.

Confirmatory

- Detection of dengue virus (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 a fatal case 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 (e.g., collected <5 days of illness onset) and convalescent (e.g., 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 [12]) 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.

Criteria for 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.

Case Classification

Confirmed

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

Probable

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

Suspect

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

Table of criteria for defining a case of dengue

Criterion	Reporting of Dengue		
	Confirmed	Probable	Suspected
<i>Clinical Evidence</i>			
<i>Dengue-like illness</i>			
Fever as reported by the patient or healthcare provider	N	N	S
<i>Dengue</i>			
Fever as reported by the patient or healthcare provider	N	N	N
Nausea/vomiting	O	O	O
Rash	O	O	O
Aches and pains (e.g. headache, retro-orbital pain, joint pain, myalgia)	O	O	O
Tourniquet test positive**	O	O	O
Leukopenia (total white blood cell count <5,000/mm ³)	O	O	O
Any severe dengue warning sign***	O	O	O
<i>Severe Dengue</i>			
Dengue, as defined above	N	N	N
Severe plasma leakage leading to hypovolemic shock or fluid accumulation (e.g., pleural effusions, ascites, pericardial effusion) with respiratory distress	O	O	O
Severe bleeding from gastrointestinal tract or vagina	O	O	O
Severe organ involvement	O	O	O

Laboratory Evidence			
For any patient with signs or symptoms of suspect dengue, the detection in serum, plasma, CSF or tissue of DENV-specific genome sequences by RT-PCR or another molecular diagnostic test; OR	S		
Detection in serum or plasma of DENV NS1 antigen by immunoassay; OR	S		
Cell culture isolation of DENV from serum, plasma, CSF or other clinical specimens; OR	S		
Detection of DENV antigens in tissue from a fatal case by immunofluorescence or immunohistochemistry, OR	S		
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., YFV, JEV); OR	S		
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);		S	
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);		S	
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	S		
IgM anti-DENV seroconversion by validated immunoassay in acute (e.g., collected <5 days of illness onset) and convalescent (i.e., collected >5 days of illness onset) serum specimens; OR	S		
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 [12]) with a >4-fold higher end point titer as compared to other flaviviruses tested.	S		
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.			S
Epidemiological Evidence			
During the previous two weeks prior to onset of fever, travel to a dengue endemic country or presence in a location experiencing an ongoing dengue outbreak, OR			S
During the previous two weeks prior to onset of fever, association in time and place with a confirmed or probable dengue case.			S

Notes:

S = This criterion alone is Sufficient to classify a case.

N = All "N" criteria in the same column are Necessary to classify a case. A number following an "N" indicates that this criterion is only required for a specific disease/condition subtype (see below).

A = This criterion must be absent (i.e., NOT present) for the case to meet the classification criteria.

O = At least one of these "O" (Optional) criteria in each category (e.g., clinical evidence and laboratory evidence) in the same column - in conjunction with all - Nil criteria in the same column - is required to classify a case. (These optional criteria are alternatives, which mean that a single column will have either no O criteria or multiple O criteria; no column should have only one O.) A number following an - O indicates that this criterion is only required for a specific disease/condition subtype.*The tourniquet test is performed by inflating a blood pressure cuff on the upper arm to a point midway between the systolic and diastolic pressures for 5 minutes.

**A test is considered positive when 10 or more petechiae per 2.5 cm² (1 in²) are observed after the cuff pressure has been released for two minutes. The test may be negative or mildly positive during the phase of profound shock. It usually becomes positive, sometimes strongly positive, if the test is conducted after recovery from shock.

*** Warning signs: 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.

¶ Validated diagnostic tests are defined as FDA-approved or laboratory-developed assays if supported by evaluation studies.

Rarely, a person will present with two consecutive episodes of acute febrile illness or dengue. If they occur at least two weeks apart and are shown to be due to different infecting DENV serotypes by molecular diagnostic testing, they should be reported as two different cases. However, if diagnosed only by IgM anti-DENV in the second episode, they would be considered as separate cases only if they occur >90 days apart due to the persistence of detectable IgM anti-DENV for up to ~90 days.

Case Investigation Process

- Complete morbidity form.
- Verify case status.
- Complete disease investigation form.
- Determine whether patient had travel/exposure history consistent with acquisition of disease in Utah or elsewhere.
- If patient acquired disease in Utah, identify the source of transmission and eliminate it.

Outbreaks

An outbreak is defined as:

- A larger than normal number of cases by county.

Identification of Case Contacts

This disease is not spread person-to-person.

Case Contact Management

None.

✓ REFERENCES

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✓ VERSION CONTROL

Updated March 2015 – Included the reporting and case definition tables from CSTE. Updated terminology to dengue-like illness, dengue, and severe dengue. Updated Laboratory and Epidemiology sections.

Updated February 2017 – Added ‘Critical Clinical Information’ section and updated ‘Laboratory Identification’ and ‘Reporting’. Also, updated general formatting.

Updated October 2017 – Updated minimum data set to match EpiTrax.

Updated November 2017 – Updated Clinical Description, Laboratory Identification, Treatment, Prevention, and Outbreak.

Updated November 2019 – Added ‘Dengue Rules for Entering Laboratory Test Results’.

✓ Dengue Rules for Entering Laboratory Test Results

The following rules describe how laboratory results reported to public health should be added to new or existing events in UT-NEDSS. These rules were developed for the automated processing of electronic laboratory reports, although they apply to manual data entry, as well.

Test-Specific Rules

Test specific rules describe what test type and test result combinations are allowed to create new morbidity events in UT-NEDSS, and what test type and test result combinations are allowed to update existing events (morbidity or contact) in UT-NEDSS.

Test Type	Test Result	Create a New Event	Update an Existing Event
IgG Antibody	Positive	No	Yes
	Negative	No	Yes
	Equivocal	No	Yes
	Other	No	Yes
IgM Antibody	Positive	Yes	Yes
	Negative	No	Yes
	Equivocal	Yes	Yes
	Other	Yes	Yes
PCR/amplification	Positive	Yes	Yes
	Negative	No	Yes
	Equivocal	Yes	Yes
	Other	Yes	Yes
Total Antibody	Positive	Yes	Yes
	Negative	No	Yes
	Equivocal	Yes	Yes
	Other	Yes	Yes

Whitelist Rules

Whitelist rules describe how long an existing event can have new laboratory data appended to it. If a laboratory result falls outside the whitelist rules for an existing event, it should not be added to that event, and should be evaluated to determine if a new event (CMR) should be created.

Dengue Morbidity Whitelist Rule: If the specimen collection date of the laboratory result two years or less after the event date of the last positive laboratory result, the laboratory result should be added to the morbidity event.

Dengue Contact Whitelist Rule: Never added to contact.

Graylist Rule

We often receive laboratory results through ELR that cannot create cases, but can be useful if a case is created in the future. These laboratory results go to the graylist. The graylist rule describes how long an existing event can have an old laboratory result appended to it.

Dengue Graylist Rule: If the specimen collection date of the laboratory result is 30 days before to seven days after the event date of the morbidity event, the laboratory result should be added to the morbidity event.

Other Electronic Laboratory Processing Rules

- If an existing event has a state case status of “not a case,” ELR will never add additional test results to that case. New labs will be evaluated to determine if a new CMR should be created.

✓ UT-NEDSS Minimum/Required Fields by Tab

Demographic

- County
- State
- Date of birth
- Birth gender
- Ethnicity
- Race
- First name
- Last name
- Middle name
- Area code
- Email address
- Extension
- Phone number

Clinical

- Date diagnosed
- Date of death
- Died (Field will change to “Did patient die from the illness or complications?”)
- Disease
- Onset date
- Does the patient have fever?
- Does the patient have at least one mild symptom?
- Does the patient have aches and pains (headache, joint pain, etc.?)
- Does the patient have rash?
- Is the patient nausea/vomiting?
- Does the patient have leukopenia?
- Does the patient have a positive tourniquet test?
- Does the patient have a severe dengue warning sign?
- Does the patient have at least one severe symptom?
- Does the patient have severe plasma leakage to hypovolemic shock or fluid accumulation?
- Does the patient have severe bleeding from gastrointestinal tract or vagina?

- Does the patient have severe organ involvement?

Laboratory

- Lab test date
- Organism
- Specimen source
- Test result

Epidemiological

- Imported from?

Investigation

- Is the patient being breastfed?
- Is the patient breastfeeding?
- Has patient traveled outside of Utah, but within the U.S., in the 30 days prior to symptom onset?
- List all places and dates.
- Did the patient travel internationally in the year prior to symptom onset?
- List international travel locations and dates.
- Has the patient received a blood transfusion within 30 days prior to symptom onset?
- Date of blood transfusion
- Has the patient donated blood within the 30 days prior to symptom onset?
- Date of blood donation
- Has the patient received an organ/tissue transplant within the 30 days prior to symptom onset?
- At the time of the patient's diagnosis with dengue, was the patient immune suppressed?
- If the patient is immune suppressed, what is the immune condition?
- Date of organ/tissue transplant.
- Has the patient had any unusual arboviral exposure (e.g. breastfeeding, laboratory, etc.)?

- Describe the exposure and dates.
- Did the patient have known mosquito exposure in the 30 days prior to symptom onset?
- Date of mosquito exposure
- Has the patient had a previous exposure to the yellow fever virus, through vaccination or previous infection?
- Date of yellow fever virus vaccination or infection
- Has the patient had a previous exposure to the Japanese encephalitis virus, through vaccination or previous infection?
- Date of Japanese encephalitis virus vaccination or infection
- Has the patient had a previous exposure to the tick-borne encephalitis virus, through vaccination or previous infection?
- Date of tick-borne encephalitis virus vaccination or infection
- CDC dengue classification

Contacts

N/A

Reporting

- Date first reported to public health

Administrative

- State Case Status
- Event Name