

# Dengue Fever (Dengue Hemorrhagic Fever) (Dengue Shock Syndrome)

## ✓ DISEASE AND EPIDEMIOLOGY

### Clinical Description:

Dengue Fever (DF) 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 also occur frequently. Recovery is often associated with prolonged fatigue and depression. Dengue Hemorrhagic Fever (DHF) is a more serious form of DF, 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. DHF is associated with 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. Dengue shock syndrome (DSS) includes all of the criteria for DHF described above, as well as life-threatening hypotension (severely reduced blood pressure, shock). DHF generally occurs in people with a history of exposure to multiple dengue virus serotypes, and the partial immune reaction contributes to the severity of the disease.

### Causative Agent:

The viruses of Dengue fever are flaviviruses and include serotypes 1, 2, 3, and 4. These same viruses cause Dengue Hemorrhagic Fever.

- **USLPH:** USLPH will act as a referral agent to the CDC for confirmation of arboviruses outside of WNV and SLE.

### Differential Diagnosis:

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

### Laboratory identification:

Laboratory diagnosis is based upon demonstration of specific IgM in serum or CSF, or antibody rises between early (acute) and late (convalescent) specimens of serum. IgM

antibodies are the first to appear. These antibodies are detectable in 50% of patients by days 3-5 after onset of illness, increasing to 80% by day 5 and 99% by day 10. IgM levels peak about two weeks after the onset of symptoms and then decline generally to undetectable levels over 2–3 months. Anti-dengue serum IgG is generally detectable at low titers at the end of the first week of illness, increasing slowly thereafter, with serum IgG still detectable after several months, and probably even for life. Cross-reactions may occur within related virus groups also, the virus occasionally can be isolated from blood or CSF.

### **Treatment:**

There is no specific treatment available for arboviral infections. 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.

### **Case fatality:**

Fatalities associated with DF are rare. With DHF, case fatality rates without treatment approach 50%. Treated DHF/DSS is associated with a 3% mortality rate.

### **Reservoir:**

The 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 arboviral infections does not occur.

### **Susceptibility:**

The elderly and children are more susceptible. Children have higher rates of dengue in endemic areas, because infection confers immunity to that serotype. As with most other arboviruses, infection confers immunity, but only short-term immunity to other 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 infections or agents of transmission 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. Dengue virus causes about 100 million cases of acute febrile disease annually, including more than 500,000 reported cases of dengue hemorrhagic fever (DHF)/ dengue shock syndrome (DSS). Currently, dengue is endemic in 112 countries. DF and DHF 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 DHF/DSS occurred in Cuba in 1981, with more than 116,000 persons hospitalized and as many as 11,000 cases reported in a single day.

## **PUBLIC HEALTH CONTROL MEASURES**

### **Public health responsibility:**

- Investigate all suspect cases of disease and 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 this 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 trash cans) 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 that are 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/Education*

People should be advised to take the following precautions if they live in or visit an area with mosquitoes:

- Use repellents containing DEET (N,N-diethyl-m-toluamide) during the time of greatest mosquito activity, 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. 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. The following precautions should be observed when using DEET products:
  - Avoid using DEET products that combine the repellent with a sunscreen. Sunscreens may need to be reapplied too 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.
- Picardin (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. Picardin-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.
- Fix any holes in screens, and make sure they are tightly attached to all doors and windows.
- Use mosquito netting when sleeping.

**Chemoprophylaxis:**

None.

**Vaccine:**

No vaccine exists for Dengue Fever.

## Isolation and quarantine requirements:

**Isolation:** None

**Hospital:** Standard body substance precautions.

**Quarantine:** None .

## ✓ CASE INVESTIGATION

### Reporting:

Report all suspect and confirmed cases of dengue.

### Case Definition:

## Dengue Fever (Dengue Hemorrhagic Fever) (Dengue Shock Syndrome) (2010)

### Laboratory Criteria

- Confirmatory
  - Isolation of dengue virus from or demonstration of specific arboviral antigen or genomic sequences in tissue, blood, cerebrospinal fluid (CSF), or other body fluid by polymerase chain reaction (PCR) test, immunofluorescence or immunohistochemistry, OR
  - Seroconversion from negative for dengue virus-specific serum Immunoglobulin M (IgM) antibody in an acute phase ( $\leq 5$  days after symptom onset) specimen to positive for dengue-specific serum IgM antibodies in a convalescent-phase specimen collected  $\geq 5$  days after symptom onset, OR
  - Demonstration of a  $\geq 4$ -fold rise in reciprocal Immunoglobulin G (IgG) antibody titer or Hemagglutination inhibition titer to dengue virus antigens in paired acute and convalescent serum samples, OR
  - Demonstration of a  $\geq 4$ -fold rise in PRNT (plaque reduction neutralization test) 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
  - Virus-specific immunoglobulin M (IgM) antibodies demonstrated in CSF.
- Presumptive/Probable
  - Dengue-specific IgM antibodies present in serum with a P/N ratio  $\geq 2$ .

### Exposure

- Travel to a dengue endemic country or presence at location with ongoing outbreak within previous two weeks of dengue-like illness, OR
- Association in time and place with a confirmed or probable dengue case.

### **Case classification**

*Suspected:* A clinically compatible case of DF, DHF or DSS that is epidemiologically linked to a confirmed case

*Probable:* A clinically compatible case of DF, DHF, or DSS with laboratory results indicative of presumptive infection

*Confirmed:* A clinically compatible case of DF, DHF, or DSS with confirmatory laboratory results

## **Dengue Fever (2010)**

### **Clinical Description**

Dengue fever (DF) is most commonly an acute febrile illness defined by the presence of fever and two or more of the following, retro-orbital or ocular pain, headache, rash, myalgia, arthralgia, leukopenia, or hemorrhagic manifestations (e.g., positive tourniquet test, petechiae; purpura/ecchymosis; epistaxis; gum bleeding; blood in vomitus, urine, or stool; or vaginal bleeding) but not meeting the case definition of dengue hemorrhagic fever. Anorexia, nausea, abdominal pain, and persistent vomiting may also occur but are not case-defining criteria for DF.

## **Dengue Hemorrhagic Fever (DHF) (2010)**

### **Clinical Description**

Dengue hemorrhagic fever (DHF) is characterized by all of the following

- Fever lasting from 2-7 days
- Evidence of hemorrhagic manifestation or a positive tourniquet test
- Thrombocytopenia ( $\leq 100,000$  cells per  $\text{mm}^3$ )
- Evidence of plasma leakage shown by hemoconcentration (an increase in hematocrit  $\geq 20\%$  above average for age or a decrease in hematocrit  $\geq 20\%$  of baseline following fluid replacement therapy), OR pleural effusion, or ascites or hypoproteinemia.

## **Dengue Shock Syndrome (2010)**

### **Clinical Description**

Dengue shock syndrome (DSS) has all of criteria for DHF plus circulatory failure as evidenced by

- Rapid and weak pulse and narrow pulse pressure ( $< 20\text{mm Hg}$ ), OR
- Age-specific hypotension and cold, clammy skin and restlessness

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### **Comment**

#### ***Asymptomatic Blood or Tissue Donor***

Dengue virus - specific viral antigen or genomic sequences demonstrated in donated blood or organs during screening and confirmatory testing in the absence of symptoms in the donor.

Dengue viruses are members of the Flaviviridae and have sufficient antigenic similarity to yellow fever virus, Japanese encephalitis virus, and West Nile virus that previous infection or vaccination may raise cross-reactive serum antibodies. After a primary infection with a heterologous flavivirus, subsequent antibody testing by ELISA may produce false positive results for a different flavivirus. PRNT can often resolve cross-reactive serum antibodies in this situation and identify the infecting virus. However, high-titered cross-reactive antibody levels produced from multiple previous flavivirus infections cannot be resolved by PRNT. This demonstrates the complexity inherent in serological diagnosis and differentiation in populations living in regions where more than one flavivirus co-circulates. However, only a small proportion of the US population has evidence of previous flavivirus infection (or vaccination) so that cross-reactive flavivirus antibodies should not be a significant limitation to dengue diagnosis among most US travelers. Among US residents, most testing for dengue is done through private clinical laboratories using IgM or IgG detection techniques.

### **Case Investigation Process:**

- Fill out morbidity form
- Verify case status.
- Fill out 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 will be defined as: a larger than normal number of cases by county, or one case of an unusual or exotic arboviral etiology.

### **Identification of case contacts:**

This disease is not spread person to person.

### **Case contact management:**

None

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