

## **DENGUE FEVER**

(Breakbone Fever, Dandy Fever)

### **REPORTING INFORMATION**

- **Class B1:** Report by the end of the next business day in which the case or suspected case presents and/or a positive laboratory result to the local public health department where the patient resides. If patient residence is unknown, report to the local public health department in which the reporting health care provider or laboratory is located.
- Reporting Form(s) and/or Mechanism:
  - [Ohio Confidential Reportable Disease form](#) (HEA 3334, rev. 1/09), [Positive Laboratory Findings for Reportable Disease form](#) (HEA 3333, rev. 8/05), the local public health department via the Ohio Disease Reporting System (ODRS) or telephone.
  - The Centers for Disease Control and Prevention (CDC) [Mosquito borne Illness Case Investigation worksheet](#) is available for use to assist in local disease investigation. Information collected from the form should be entered into ODRS and not sent to the Ohio Department of Health (ODH), unless otherwise requested. If requested, the mailing address for this form is: Ohio Department of Health, Outbreak Response and Bioterrorism Investigation Team, 246 North High Street, Columbus, Ohio 43215.

### **AGENT**

Dengue viruses 1, 2, 3 and 4: flaviviruses. There is substantial serologic cross-reaction with other flaviviruses (e.g. St. Louis encephalitis, yellow fever, Japanese B encephalitis, West Nile virus).

#### **Infectious Dose**

One bite of an infectious mosquito is sufficient.

### **CASE DEFINITION**

#### **Clinical Description**

- Dengue fever (DF): 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). Anorexia, nausea, abdominal pain and persistent vomiting may also occur but are not case-defining criteria for dengue fever.
- Dengue hemorrhagic fever (DHF): 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  $\text{mm}^3$ ) and
  - 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, ascites or hypoproteinemia.
- Dengue shock syndrome (DSS): all of criteria for DHF plus circulatory failure as evidenced by:
  - Rapid and weak pulse and narrow pulse pressure ( $< 20$  mm Hg) or
  - Age-specific hypotension and cold, clammy skin and restlessness.

#### **Laboratory Criteria for Diagnosis**

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**

Suspect: 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.

### **Comments**

*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.

## **SIGNS AND SYMPTOMS**

Dengue is characterized by a sudden onset of high fever (103-106°F), severe headache, backache, intense pain in joints and muscles, retro-orbital pain, nausea and vomiting and a generalized erythematous rash. Minor bleeding phenomenon such as petechiae, epistaxis or gum bleeding may occur during the febrile phase of illness. Generally, younger children have a milder illness than older children and adults. Remission usually develops on day

three, lasting 2-3 days. Fever and pains recur for about 1-2 days. Eruption recurs. Hemorrhagic symptoms are thought to result upon second encounter with a dengue virus of a different serotype.

## **DIAGNOSIS**

The CDC in San Juan, Puerto Rico can perform ELISA-IgM and virus isolation on the acute serum. A convalescent serum should be obtained two weeks later and also sent to CDC.

Proper protocol is to send the sample(s) to the CDC Dengue Laboratory via the ODH Laboratory. Contact the ODH Laboratory at (614) 728-0544 (Monday- Friday; 8 AM-5 PM) for CDC specimen criteria.

The diagnosis of dengue fever can be confirmed by isolating dengue virus from the acute blood sample, by demonstrating specific IgM antibody in appropriately timed serum sample(s) (obtained  $\leq 5$  and 6-60 days after onset of illness) or by demonstrating a 4-fold or greater change in IgG antibody titer to dengue virus in a serum pair. Individuals who have had one or more flavivirus infections, including yellow fever immunization, may produce heterologous antibodies to a wide range of flavivirus antigens. A specific dengue diagnosis can still be made, however, by virus isolation or inferred from epidemiologic associations.

## **EPIDEMIOLOGY**

### **Source**

Humans are the vertebrate reservoir, with monkeys possibly being involved. The principal vector is the *Aedes aegypti* mosquito, and transmission usually occurs in tropical and subtropical areas.

### **Occurrence**

Dengue is endemic in tropical Asia, East and West Africa, Polynesia, Micronesia and Tahiti. Dengue is also endemic in the Caribbean, northern South America and Central America. Dengue is periodically epidemic in the Western Hemisphere, with thousands of cases diagnosed. Travelers are always at risk when visiting endemic countries. About 10 imported cases are identified annually in Ohio.

### **Mode of Transmission**

The virus is transmitted only by *Aedes* species of mosquitoes. *Aedes aegypti* is endemic to the southeastern Atlantic and Gulf Coast states in the United States. Two potential dengue vectors might occur in Ohio. *Aedes aegypti* probably cannot become established in Ohio due to severity of winters. *Aedes albopictus*, the Asian vector of dengue, has recently become established in Ohio. Since 1987, it has spread throughout Ohio. The spread of *Aedes albopictus* is due primarily to commerce in used tires, in which it breeds.

### **Period of Communicability**

Humans are infectious to biting *Aedes aegypti* or *Aedes albopictus* from the day prior to onset of symptoms to day five of illness. No human-to-human transmission occurs.

### **Incubation Period**

3-14 days, usually 4-7 days.

## **PUBLIC HEALTH MANAGEMENT**

### **Case**

#### Investigation

A complete travel history for 15 days prior to onset for the patient must be obtained. Determine the patient's yellow fever vaccine status.

#### Treatment

There is no specific medication for treatment of a dengue infection. 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.

#### Isolation and Follow-up Specimens

No specific isolation procedures are indicated for the acute dengue patient in Ohio. A convalescent serum sample should be obtained 2 weeks after the acute sample. If a convalescent serum sample was not obtained, a late convalescent sample should be obtained. Autopsy blood and/or tissue samples may also be taken. Proper protocol is to send the sample(s) to the CDC Dengue Laboratory via the ODHL (See **DIAGNOSIS**, above).

#### Public Health Significance

High in endemic areas.

#### Special Information

There is a low probability of endemic transmission occurring in Ohio because of the low prevalence of the vector mosquito.

#### **Contacts**

No prophylaxis is indicated. There is no vaccine available.

#### **Prevention and Control**

##### Follow-up Specimens

Does not apply if dengue has been laboratory confirmed.

##### Travelers

Travelers entering endemic areas should be warned to avoid mosquitoes, use mosquito repellants, occupy screened quarters and use mosquito netting over beds.

##### Vaccination

There is no vaccine available.

##### Vector Investigation

A survey should be performed by the local health department to determine if *Aedes aegypti* or *Aedes albopictus* mosquitoes are present near the patient's home or travel sites in Ohio. For advice on vector assessment, contact the Zoonotic Disease Program at (614) 752-1029 and select option #2 or via the ODH website [www.odh.oh.gov](http://www.odh.oh.gov).

#### **SPECIAL INFORMATION**

Accurate travel history and confirmation are desirable to document importation of dengue infections from endemic areas into the United States. Note if travelers had spent any time in the southeastern Atlantic or Gulf Coastal states, where *Aedes aegypti* or *Aedes albopictus* is endemic, before returning to Ohio. The CDC Dengue Branch may be contacted at 787-766-5181 for special consultation.

**What is dengue fever?**

Dengue fever is also known as break-bone fever or dandy fever. It is caused by one of four very similar viruses.

Each year, millions of cases of dengue fever occur worldwide. It is commonly found in the tropical and sub-tropical environments of Asia, East and West Africa, Polynesia, Micronesia and Tahiti. It may also be found in the Caribbean, northern South America and Central America.

Although there are two types of mosquitoes capable of transmitting dengue fever found in some Ohio counties, the virus is not endemic in the state. A few (two to three) human cases are reported in Ohio each year, but most have a history of travel to infected areas.

**How is dengue fever transmitted?**

Dengue fever is transmitted through the bite of an infected mosquito, most often *Aedes aegypti*. No transmission occurs directly from person to person.

**What are the symptoms of dengue fever?**

Patients typically develop a high fever, severe headache, pain behind the eyes, painful joints and muscles, nausea, vomiting, and often a rash. These symptoms last about one week, but weakness and tiredness may persist for several weeks. Young, healthy people often have no or mild symptoms.

Some patients with dengue fever go on to develop dengue hemorrhagic fever (DHF), a severe and sometimes fatal form of the disease. About the time the fever begins to subside, the patient may display problems with blood circulation. These can include abnormal bruising, blood in the urine or stool, bloody nose and/or bleeding gums. If untreated, these symptoms may lead to death.

**How long after exposure before symptoms appear?**

Symptoms typically develop within 3 to 14 days, usually in 4 or 7.

**How is dengue fever diagnosed?**

The virus can be isolated in a lab. or a test for specific antibodies can be performed on blood or other tissues.

**Can dengue fever be treated?**

There is no cure for the virus, so treatment is aimed at treating the symptoms. Fluids to maintain hydration and medications to reduce fever and eliminate pain are often prescribed. Aspirin should be avoided because it can decrease the blood's ability to clot. Severe cases and those that progress to dengue hemorrhagic fever require hospitalization with intensive monitoring and treatment.

**How can I prevent dengue fever?**

Prevent mosquito bites especially when traveling to areas where dengue fever is common. It only takes one bite from an infected mosquito to transmit disease.

Avoid mosquito bites.

- Avoid areas where mosquitoes are active.
- Avoid outdoor activities during the peak mosquito biting times of dawn, dusk and early evening.
- When outdoors, apply mosquito repellent as directed to clothing and exposed skin.
- Reapply mosquito repellent as needed especially if swimming or sweating.

- Clothing will help protect you from mosquito bites. If weather permits, wear long pants, long sleeves, and/or socks.
- Install or repair window and door screens to keep mosquitoes outside.

Eliminate mosquito breeding sites.

- At least once or twice a week, empty water from flower pots, pet food and water dishes, birdbaths, swimming pool covers, buckets, barrels, and cans.
- Check for clogged rain gutters and clean them out.
- Remove discarded tires and other items that could collect water.
- Be sure to check for containers or trash in places that may be hard to see, such as under bushes or under your home.

**For more information please visit these websites:**

CDC dengue fever fact sheet

<http://www.cdc.gov/Dengue/faqFacts/fact.html>

CDC dengue fever information for health care providers

<http://www.cdc.gov/dengue/clinicalLab/clinical.html>

CDC insect repellent use and safety

[http://www.cdc.gov/ncidod/dvbid/westnile/qa/insect\\_repellent.htm](http://www.cdc.gov/ncidod/dvbid/westnile/qa/insect_repellent.htm)