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Dengue Virus

<u>Case Definition</u> – https://ndc.services.cdc.gov/case-definitions/dengue-virus-infections-2015/

Overview

- Agent Dengue virus is caused by infection from flaviviruses. There are four serotypes associated with human infection: DENV-1, -2, -3, -4. All 4 DENV serotypes can cause dengue and have been associated with severe dengue with a fatal outcome. It is important to note, however, that the majority (75%) of DENV infections are asymptomatic. Infection by one serotype is thought to provide lifelong immunity against that particular serotype (homotypic immunity). While a brief period of cross-protection to other serotypes has been observed, individuals remain at risk for infections with other serotypes. Infection with additional serotypes can predispose an individual to more severe disease. Dengue-endemic areas may have more than one serotype circulating.
- **Reservoir** Where endemic, DENV is maintained in a human-*Aedes* mosquito cycle, in which human infections are either with or without symptoms. Humans are the primary amplifying host of dengue virus and the main source of virus for *Aedes* mosquitoes. There is also a sylvatic monkey-mosquito cycle in Asia and Africa, but this rarely impacts humans.
- *Occurrence* DENV is endemic throughout the tropical and subtropical regions of the world which includes nearly 130 countries. Currently, Asia carries the largest disease burden followed by the Americas and Africa.
- *Risk Factors* Individuals residing in or traveling to dengue-endemic areas are at an increased risk of infection. In endemic areas, transmission of DENV can occur year-round but peak transmission generally occurs during the rainy season.
- Mode of Transmission DENV is primarily transmitted through the bite of an infected
 mosquito. Other possible, though rare, modes include vertical transmission (mother to baby
 during pregnancy); transmission via breastfeeding, blood, or organ donation; sexual
 transmission; or healthcare-associated transmission via needlestick or mucocutaneous
 exposures.
- *Incubation Period* 3-14 days. DENV can be transmitted from people, both symptomatic and asymptomatic, 1-2 days before symptoms develop and throughout the approximately 7-day viremic period.
- Clinical Illness The majority of people who become infected are asymptomatic. If symptoms develop, they can range from mild febrile illness to severe illness and even death. Commonly reported symptoms are non-specific, acute febrile illness with severe headache, pain behind the eyes, joint pain, muscle and bone/joint pain, rash, plasma leakage, and in severe dengue cases there can also be mucosal bleeding, vomiting, difficulty breathing, signs of shock, and a rapid decline in platelet count with an increase in hematocrit.
- *Laboratory Testing* Testing for DENV is available through many commercial laboratories. There are a variety of test types available, including RT-PCR, NS1 antigen, and IgM serology. Some commercial laboratories will report an identified DENV serotype (1-4) with



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the positive RT-PCR result. Serotype may not be available with NS1 antigen or IgM serology testing. The Missouri State Public Health Laboratory (MSPHL) does not currently conduct dengue virus testing. In special cases, arrangements can be made to send specimens to CDC for testing, but this requires pre-approval. Requests for testing through CDC should be coordinated through the Bureau of Communicable Disease Control and Prevention (BCDCP) Zoonotic Disease Program.

- *Treatment* No specific antiviral therapy exists for dengue virus infection. Recommended supportive care measures include keeping patient hydrated and avoiding the use of aspirin and aspirin-containing drugs as well as other nonsteroidal anti-inflammatory medications, to minimize the risk of bleeding in patients with dengue virus infections. Early recognition of symptoms of shock and initiation of intensive supportive therapy can reduce the risk of death if severe dengue symptoms develop.
- Priority High; Dengue virus infection should be reported to DHSS within 1 day.

Quick References / Factsheets

- Health Professionals:
 - o <u>Dengue Clinical Management Pocket Guide</u> (07/25)
 - o <u>Dengue Clinical Management Course</u> (07/25)
- Public Health Professionals:
 - o Reviewing Dengue Medical Records: Job Aid (07/25)
 - o Response to Dengue Cases in Non-Endemic Areas of the United States (07/25)

Forms

- Disease Case Report (CD-1)
- CDC Dengue Case Investigation Form
- Missouri Outbreak Report Form (MORF)

Notifications

• If dengue virus infection is suspected, the local public health agency (LPHA) should notify the <u>District Epidemiologists</u> or the Missouri Department of Health and Senior Services (MDHSS) Bureau of Communicable Disease Control and Prevention (BCDCP), phone (573) 751-6113, Fax (573) 526-0235.

Reporting Requirements

- Dengue is a Category 2 (A) disease and shall be reported to the LPHA or to the Missouri Department of Health and Senior Services (MDHSS) within one (1) calendar day of first knowledge or suspicion by telephone, fax, or other rapid communication.
 - 1. For confirmed and probable cases, complete a <u>Disease Case Report</u> (CD-1) and a CDC Dengue Case Investigation Form.
 - 2. Entry of the completed CD-1 into the ShowMe World Care (SMWC) database negates the need for the paper CD-1 to be forwarded to the District Office.



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- 3. All outbreaks or "suspected" outbreaks must be reported as soon as possible (by phone, fax, or e-mail) to the District Communicable Disease Coordinator. This can be accomplished by completing the Missouri Outbreak Report Form (MORF).
- 4. Within 90 days from the conclusion of an outbreak, submit the final outbreak report to the <u>District Communicable Disease Coordinator</u>.

Laboratory Testing and Diagnosis

Testing for DENV is available through many commercial laboratories. There are a variety of test types available including RT-PCR, NS1 antigen, and IgM serology. Clinicians should consider DENV in patients with fever who live in or recently traveled to areas with risk of DENV. Patient medical history, active CDC travel notices for DENV outbreaks for area of residence/travel, and patient vaccination status for DENV, yellow fever, and Japanese encephalitis are also important factors to consider.

The Missouri State Public Health Laboratory (MSPHL) does not currently conduct DENV testing. In special cases, arrangements can be made to send specimens to CDC, but this requires pre-approval. Requests for testing through CDC should be coordinated through the Bureau of Communicable Disease Control and Prevention (BCDCP) Zoonotic Disease Program.

For acute dengue diagnosis (Day 0-7 from onset), clinicians should order RT-PCR or NAAT and IgM tests or NS1 ELISA and IgM tests. After Day 7 from onset, IgM serology testing is the recommended test type. IgM antibodies can be detected reliably for 3 months or longer after DENV infection. Although IgG testing may be available, use of this test type with a single specimen is not recommended for the diagnosis of acute dengue in patients, as these tests may detect antibodies from dengue infections or other flavivirus infections that occurred in the past. Serum is the preferred specimen type for DENV testing, but whole blood and plasma may also be tested. If dengue is suspected, clinicians should provide appropriate management without waiting for diagnostic test results.

Conducting the Investigation

- Verify the diagnosis. Obtain demographic, clinical and laboratory information on the case from the health care provider, hospital, and/or laboratory. Does the laboratory test result provide evidence of a recent DENV infection? Obtain other epidemiological information necessary to complete the Disease Case Report (CD-1) and the CDC Dengue Case Investigation Form from the patient or a knowledgeable family member.
- Establish the extent of illness. Determine if household, traveling companions or other close contacts are, or have been, ill by contacting the health care provider, patient, or family members. Strongly urge persons with a dengue-like illness to contact their physician for a medical evaluation. These persons should also be watched for warning signs of severe dengue infection 3 to 7 days after symptoms initially begin. Persons with a dengue-like illness should go immediately to an emergency room or the closest health care provider if any of the following warning signs appear: severe abdominal pain or persistent vomiting,



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mucosal bleeding, difficulty breathing, early signs of shock, or a rapid decline in platelet count with an increase in hematocrit.

- **Establish the source of infection.** For all cases, please obtain the following information from the patient, patient's family, or health care provider:
 - Travel history:
 - Determine the start and end dates of the trip and the location(s) of travel.
 Start and end dates will be requested for all locations if patient visited multiple cities or countries.
 - o If there is no history of foreign travel consistent with exposure to DENV, please contact your <u>District Epidemiology team</u> and/or the Zoonotic Disease Program. Sporadic outbreaks of DENV have occurred in Florida, Texas, California, and Hawaii in recent years. Cases that are suspected to have been acquired within the U.S. need to be promptly reported.
 - Do any of the following situations apply for the case:
 - o Works in a laboratory or clinical setting?
 - Lives, works or has visited international airports, shipyards or other areas in which shipments from international sources may have been located?
 - Pregnant or breastfeeding at time of exposure/onset?
 - o Known to have contacts with a similar illness or a similar illness reported in the area of exposure?
 - Known to be a recent organ, tissue, bone marrow, or blood donor or recipient?
 - If yes, the blood or tissue bank will need to be notified and asked to determine if any donated blood components or tissues remain and whether any products have been disseminated to other individuals.
 - Identification of other possibly exposed patients through these routes will be required.
 - If assistance is needed with this tracing process, please reach out to the Zoonotic Disease Program for guidance.
 - Known to be previously vaccinated for DENV, yellow fever, or Japanese encephalitis?
 - There is only one licensed vaccine to prevent DENV infection in the U.S. As of May 2025, this vaccine product (Dengvaxia) is in the process of being discontinued.
 - ☐ Dengvaxia was limited to use in children aged 9-16 years who had a prior laboratory-confirmed DENV infection and were living in a dengue-endemic area.
 - ☐ Within the U.S., dengue-endemic areas include the U.S. territories of American Samoa, Puerto Rico, the U.S. Virgin



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Islands, and freely associated states including the Federated States of Micronesia, the Republic of Marshall Islands, and the Republic of Palau.

 Vaccination for yellow fever or Japanese encephalitis will not protect against infection with DENV, but these vaccines can create potential challenges interpreting DENV test results due to crossreactivity.

Control Measures

There is only one licensed vaccine to prevent DENV infection in the U.S. As of May 2025, this vaccine product (Dengvaxia) is in the process of being discontinued.

Efforts should be made to promote DENV awareness among international travelers and persons visiting family and friends in other countries. For more information about international travel and DENV risk, visit CDC's pages about <u>Travel Health Notices</u> and <u>Areas with Risk of Dengue</u>. For awareness, CDC does not generally issue Travel Health Notices for the U.S. or U.S. territories.

There are no specific medications to treat DENV infections. This makes personal protective behaviors to avoid mosquito bites the most important prevention measure. Key prevention measures include the following:

- <u>Protect your home against mosquitoes</u>! Identify and eliminate sources of standing water that mosquitoes need in order to reproduce.
- Avoid mosquito-prone areas and all mosquito bites for 2 weeks following return from international travel to dengue-endemic areas.
 - Be aware of peak mosquito exposure times (typically around dawn and dusk).
 - The *Aedes* mosquitoes that transmit DENV are known to be daytime biters and can be active all day long.
- Apply insect repellent to all exposed skin when planning to spend time outdoors.
 - The American Academy of Pediatrics has recommended that repellents containing up to 30% DEET are safe to use on children over 2 months of age.
 - For other active repellent ingredients, check the product label for minimum age requirements before applying to children.
 - EPA offers an <u>insect repellent search tool</u> that the public can use to identify repellent products that work best for their needs.
- Wear long sleeves and pants when weather permits to help reduce the amount of exposed skin and easy places for mosquitoes to bite.
- Consider the use of bed nets and/or choose accommodations that have air conditioning or tight, well-fitting window and door screens to prevent mosquitoes from getting into sleeping or living areas.
- Mosquito control measures may need to be considered, especially if a locally acquired case of DENV infection is identified. Vector control activities are the



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responsibility of the county, city, or municipal jurisdiction. For more information about this, please reach out to the Zoonotic Disease Program.

Resources

- 1. American Academy of Pediatrics. [Dengue]. In: Kimberlin DW, Barnett, ED, Lynfield, R, Sawyer, MH, eds. *Red Book: 2021 Report of the Committee on Infectious Diseases*. 32nd ed. Itasca, IL: American Academy of Pediatrics; 2021: [301-304].
- 2. American Public Health Association. [Dengue]. In: Heymann DL, ed. *Control of Communicable Diseases Manual*. 21st ed. Washington, DC: American Public Health Association; 2022 [147-154].
- 3. Centers for Disease Control and Prevention. Dengue. https://www.cdc.gov/dengue/index.html (07/25)
- 4. Centers for Disease Control and Prevention. Areas with Risk of Dengue. https://www.cdc.gov/dengue/areas-with-risk/index.html (07/25)
- 5. Centers for Disease Control and Prevention. Clinical Testing Guidance for Dengue. https://www.cdc.gov/dengue/hcp/diagnosis-testing/index.html (07/25)
- 6. Centers for Disease Control and Prevention. Response to Dengue Cases in Non-Endemic Areas of the United States. https://www.cdc.gov/dengue/media/pdfs/2024/08/response to dengue.pdf (07/25)