

Dengue Fever (DF) and Dengue Hemorrhagic Fever (DHF)

Kay M. Tomashek

Infectious Agent

- Four immunologically related, single positive-stranded RNA viruses known as dengue viruses (DENV-1 through DENV-4) of the genus *Flavivirus*, family *Flaviviridae*, are responsible for causing dengue fever (DF) and dengue hemorrhagic fever (DHF).
- Infection with one DENV produces lifelong immunity against reinfection with that one virus and short-term (≤ 9 months), partial cross-protection against the other three dengue viruses. An individual may be infected up to four times during his or her lifetime.

Mode of Transmission

- Transmission occurs from the bite of an infected *Aedes aegypti* (rarely *Aedes albopictus*) mosquito. Mosquitoes first become infected with DENV by feeding on the blood of a dengue-infected person. After the virus replicates for 8–12 days in the mosquito, the mosquito can transmit DENV to many other people.
- Direct person-to-person transmission has not been documented. A few case reports have been published of transmission of DENV through exposure to: dengue-infected blood, organs, or other tissues from blood transfusions; solid organ or bone marrow transplants; needlestick injuries; and mucous membrane contact with dengue-infected blood.

Occurrence

- Dengue infections have been reported in over 100 countries and are widespread in most tropical countries of the South Pacific, Asia, the Caribbean, the Americas, and Africa (Maps 5-1 and 5-2). The geographic spread of dengue infections is similar to that of malaria, but unlike malaria, dengue infections are often found in the urban areas of tropical nations, including Thailand, Singapore, Taiwan, Indonesia, Philippines, India, and Brazil. Because the main risk of exposure for the traveler is in populated urban and residential areas, travelers are advised to consult CDC (www.cdc.gov/ncidod/dvbid/dengue) and WHO (www.who.int/topics/dengue/en) websites for outbreak information.
- Recently, locally acquired dengue infections have been reported in Texas, Hawaii, and the Middle East.

Risk for Travelers

- Cases of DF and DHF are confirmed every year among travelers returning to the United States. Infection rates (based on antidengue serology) among febrile travelers returning from dengue-endemic areas in the tropics range from 2.9% to 8.0%.
- Dengue was the leading cause of systemic febrile illness among travelers returning from the Caribbean, South America, South Central Asia, and Southeast Asia in a recent study of 17,353 ill travelers seen at GeoSentinel surveillance network clinics. In some case studies, dengue is the second most common cause of hospitalization (malaria is the most common) among travelers returning from the tropics.

- The bite of one infected mosquito can result in infection. The risk of being bitten is highest during the early morning, several hours after daybreak, and in the late afternoon several hours before sunset, because the female mosquito typically feeds (bites) during these hours. However, mosquitoes may feed at any time during the day.
- Published data are limited on the health outcomes associated with dengue infection among pregnant women and the effects of maternal dengue infection on a developing fetus. However, if a pregnant woman has dengue at the time of delivery, the infant can be born with dengue infection or acquire dengue during labor and delivery and then develop the clinical manifestations of DF or DHF. Transplacental transfer of maternal antidengue antibodies (from a previous maternal infection) may place infants at greater risk for DHF with their first dengue infection.

Clinical Presentation

- Dengue should be considered in the differential diagnosis of febrile patients with a history of travel to the tropics in the 2 weeks prior to symptom onset. The incubation period is typically 4–7 days (range 3–14 days).
- Many travelers infected with DENV are asymptomatic, as are about half of people infected with DENV who live in areas where the virus is widespread.
- The clinical manifestations of symptomatic illness range from mild, undifferentiated febrile illness to classic DF or DHF. DF is defined clinically by an acute febrile illness with two or more of the following symptoms: headache, retro-orbital pain, muscle or joint pain, rash, hemorrhagic manifestation, or leucopenia. The rash usually appears as the fever subsides and lasts 2–4 days. The rash is either macular or maculopapular and generalized, often confluent with small patches of normal skin, and it may become scaly and itchy. Other signs and symptoms include flushed facies (usually during the first 24–48 hours), nausea, and vomiting. Approximately 1% of patients with DF develop DHF as the fever subsides (usually 3–7 days following the onset of fever).
- The hallmark of DHF is evidence of vascular leakage. DHF is defined by the presence of all the following symptoms:
 - fever or recent history of fever lasting 2–7 days,
 - any hemorrhagic manifestation,
 - thrombocytopenia (i.e., platelet count $<100,000/\text{mm}^3$), and
 - evidence of increased vascular permeability (i.e., hemoconcentration, pleural or abdominal effusion, hypoalbuminemia, or hypoproteinemia).
- Thrombocytopenia can occur with classic DF and does not by itself indicate DHF.
- Dengue Shock Syndrome (DSS) is defined as a syndrome in any case patient who meets the criteria for DHF and has hypotension, narrow pulse pressure (≤ 20 mm Hg), or frank shock.

This section has been updated as of August 24, 2009.

Map 5-1. Distribution of dengue, Western Hemisphere



Map 5-2. Distribution of dengue, Eastern Hemisphere



Diagnosis

- A suspected case of dengue infection can be laboratory confirmed by one of the following means:

- identification of DENV from serum or autopsy tissue samples by reverse transcriptase-polymerase chain reaction (RT-PCR),
 - seroconversion from negative to positive or a four-fold or greater change in anti-dengue antibody titer in paired serum samples taken in the acute- (<6 days after illness onset) and convalescent-phase (6–30 days after onset) of the illness, or
 - dengue viral antigen identification in autopsy tissue samples by immunofluorescence or immunohistochemical analysis.
- In combination with a compatible travel history and symptom profile, anti-dengue IgM positivity in a single serum sample suggests a probable, recent dengue infection. However, anti-dengue IgG positivity in a single serum sample may only indicate infection at an indeterminate time in the past. Caution should be exercised when using anti-dengue IgM or IgG antibody positivity from a single sample for diagnosis because there is cross-reactivity between anti-dengue IgM and IgG antibodies with antibodies from other flaviviruses such as the West Nile, yellow fever, and Japanese encephalitis viruses. Previous infection or vaccination with another flavivirus may also result in false-positive anti-dengue antibody results.
 - If testing at CDC is requested, acute- and convalescent-phase serum samples should be sent through state or territorial health department laboratories to CDC's Dengue Branch at 1324 Calle Cañada, San Juan, Puerto Rico 00920-3860. Serum samples should be accompanied by clinical and epidemiologic information, including the date of disease onset and sample collection and the patient's detailed recent travel history. For additional information, the Dengue Branch can be contacted by telephone 787-706-2399; fax 787-706-2496; or CDC website at www.cdc.gov/ncidod/dvbid/misc/contactus.htm.

Treatment

- No specific therapeutic agents exist for dengue infections.
- Encourage bed rest and maintenance of fluids to prevent dehydration.
- Control fever with acetaminophen. Headache, back pain and muscle aching may be so severe as to require narcotics. Aspirin (acetylsalicylic acid), aspirin-containing drugs, and other nonsteroidal anti-inflammatory drugs (e.g., ibuprofen) should be avoided because of their anticoagulant properties. Aspirin and other salicylates should be especially avoided in children due to the association with Reye syndrome.
- Ask patients to watch for warning signs of DHF or DSS as fever declines 3–7 days after onset of symptoms. Instruct patients to go to the hospital if they have any of the following warning signs: abrupt change from fever to hypothermia, severe abdominal pain, persistent vomiting, bleeding, difficulties breathing, or altered mental status (e.g., irritability, confusion, lethargy).
- Prompt and judicious administration of intravenous fluids in patients with DHF or DSS can improve outcomes. In patients with DHF or DSS, hospitalization with close monitoring of vital signs, fluid balance, and hematologic parameters (i.e., hematocrit, platelet count) is indicated, as well as additional supportive measures.

Preventive Measures for Travelers

- Neither vaccine nor drugs for preventing infection are available.
- Travelers should be advised to take measures to avoid being bitten by *Aedes* mosquitoes. These preventive measures include the following:
 - Select accommodations with well-screened windows or air-conditioning when possible. *Aedes* mosquitoes typically live indoors and are often found in dark, cool places such as

in closets, under beds, behind curtains, and in bathrooms. A traveler should be advised to use insecticides to get rid of mosquitoes in these areas.

- Wear clothing that adequately covers the arms and legs, especially during the early morning and late afternoon.
- Apply insect repellent to both skin and clothing (e.g., permethrin). The most effective repellents contain DEET (N,N-diethylmetatoluamide) (see the [Protection Against Mosquitoes, Ticks, and Other Insects and Arthropods](#) section in Chapter 2).
- For long-term travelers, empty and clean or cover any standing water that can be mosquito-breeding sites in your accommodation (e.g., water storage barrels).

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