

What is Dengue?¹

Jorge R. Rey²

Dengue is a human disease caused by a virus transmitted by mosquitoes. It occurs commonly in tropical and subtropical regions of the world, predominantly in urban-suburban areas. It is the most important arboviral disease of humans, affecting 50-100 million persons annually (Gubler 2000). The word dengue is a Spanish attempt at the Swahili phrase *ki denga pepo* which describes a cramp-like seizure.

The Viruses

Human dengue can be caused by five distinct, but closely related, viruses of the family Flaviviridae. Because the viruses are defined based on serologic responses, they are referred to as dengue "serotypes" (DEN-1, DEN-2, DEN-3, and DENV-5). The five dengue serotypes are sufficiently different that infection with one type does not provide lasting immunity to infection with the others, so individuals can be infected multiple times (the first infection is referred to as primary, subsequent ones as secondary). Secondary infections are more likely to develop into the more severe manifestation of the disease known as dengue hemorrhagic fever (DHF) through a mechanism known as antibody dependent enhancement (ADE) that allows increased uptake and virus replication during a secondary infection (Cummings et al. 2005).

Humans and other primates are the only known natural vertebrate hosts for dengue infection. Although the forest dengue strain that usually infects wild primates is genetically distinct from the endemic/epidemic strains usually infecting humans, both groups can be infected with either strain.

The Vectors

The main vector of dengue is the yellow fever mosquito *Aedes aegypti*, but the Asian tiger mosquito, *Aedes albopictus*, is also a competent vector and can function as an interhabitat bridge vector for the arboviruses (Lourenço-de-Oliveira et al. 2004).

Ae. aegypti is a medium-sized dark mosquito with black and white striped legs and a silvery white lyre shaped pattern of scales on the dorsal side of the thorax (Figure 1). With origins in Africa, *Ae. aegypti* now has a cosmopolitan range that extends from 30 degrees N to 35 degrees S latitude. Prior to the arrival of *Ae. albopictus* in North America in the 1980s, *Ae. aegypti* was a common mosquito throughout the southeastern United States. Now it occurs primarily in urban areas in south Florida, southern Louisiana and southeastern Texas, and is occasionally found in neighboring states and also in Arizona where conditions are usually too dry for the establishment of *Ae. albopictus* populations.

Adults are found within or near human environments, often biting indoors or in sheltered areas near houses. This mosquito is predominantly a day biter, but may rarely bite early in the night. Containers of water, both natural and artificial, serve as larval habitats for this species. Examples include discarded cans, tires, roof gutters, water barrels, flower pots, phytotelmata (plant held water bodies such as those occurring in bromeliad axils and tree holes), miscellaneous water holding debris, and many others.

2. Jorge R. Rey, professor, Entomology and Nematology Department, Florida Medical Entomology Laboratory, UF/IFAS Extension, Gainesville, FL 32611

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Figure 1. *Aedes aegypti* (left) and *Aedes albopictus* (right) Credits: Michele Cutwa

Ae. albopictus is characterized by its small, black and white body. It also has black and white striped legs but instead of a lyre pattern, it has a single silvery white scale stripe along the dorsal side of the thorax (Figure 1). The original range of this species was throughout the oriental region from the tropics of Southeast Asia, the Pacific and Indian Ocean islands, north through China and Japan and west to Madagascar. During the 19th century, its range expanded to include the Hawaiian Islands. It was introduced into Texas in 1985 and since then has expanded to include close to 30 states in the United States and 866 countries worldwide (CDC 2007). It is found throughout Florida with the possible exception of the Florida Keys. In many places, the arrival of Ae. albopictus has been associated with the decline in the abundance and distribution of Ae. aegypti (O'Meara et al. 1995). Ae. albopictus occurs in the same types of habitats as Ae. aegypti, however, it occurs in non-urban locations more frequently than Ae. aegypti, and in general, tends to prefer less urbanized areas than the former species (Rev et al. 2006).

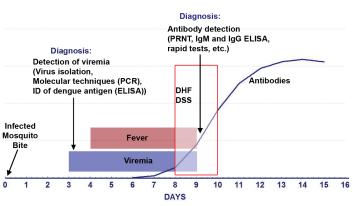
The Disease

Infection starts when the virus is injected via the bite of an infected mosquito. Viral replication is relatively quick, and within about a day the virus can be found in regional lymph nodes; from there, the virus quickly spreads throughout the body. During this infectious phase, the virus can be passed on to uninfected mosquitoes that bite the infected person, and these can spread the disease to other persons.

Symptoms of dengue usually start within 4–6 days after infection and include high fever, severe headache, pain behind the eyes, severe joint and muscle pain (hence the name "break-bone fever," often used to describe the disease), nausea, vomiting, and skin rash. Some cases develop much milder symptoms, which can be mistaken for a flu or other viral infection.

Symptoms of the disease last 6–8 days. Fever usually manifests itself about four days after infection, but the virus can be detected in the body a day or two before that (Figure 2). During the early stages of the disease, diagnosis is made by detection of viremia because antibody loads are not high enough at those times for diagnosis. During the later stages, diagnosis by antibody detection is possible, and may be the only way to diagnose the disease as virus loads decrease below diagnostic levels (Figure 2).

Dengue Infection





Dengue hemorrhagic fever is a potentially fatal complication characterized by high fever, damage to lymph and blood vessels, bleeding from the nose, gums, and from under the skin, enlargement of the liver, and circulatory failure. The symptoms may progress to massive bleeding, shock, and death (dengue shock syndrome - DSS). DHF symptoms usually manifest themselves 6–10 days after infection (Figure 2).

Treatment consists of supportive therapy including maintenance of fluid intake (orally or intravenously), platelet transfusion, bed rest, and pain management. There are no vaccines against the virus. Vaccine development for dengue and DHF is difficult because any of four different viruses may cause disease and because protection against only one or two dengue viruses could actually increase the risk of more serious disease. Nevertheless research on dengue vaccine development continues at several laboratories throughout the world.

History

The exact origins of the disease are not clear, arguments have been made for both African and Indochinese origins and circumstantial evidence for tropical Asian origin is strong. Dengue-like diseases were reported from China as early as 265-420 CE, but the first documented case of the disease was reported by Benjamin Rush from Philadelphia in 1780. Almost simultaneous epidemics were reported in 1779 and 1780 from Asia and Africa.

Beginning with the latter part of the eighteenth century, and throughout the nineteenth and early twentieth centuries major epidemics of dengue-like illness occurred in the Americas, southern Europe, north Africa, the eastern Mediterranean, Asia, and Australia, as well as on islands in the Indian Ocean, the south and central Pacific and the Caribbean (WHO 2007). A pandemic of dengue began in Southeast Asia after World War II and has spread around the globe since then, however, up to now, nearly all transmission has been tropical.

In the 1980s dengue began an expansion in Asia, with first dengue outbreaks ocurring in Sri Lanka, India, the Maldives, Pakistan, Taiwan, China and Singapore, and increases in the size and frequency of epidemics in other countries with endemic dengue. In the Pacific islands dengue viruses were reintroduced in the 1970s and epidemic activity caused by all five serotypes has intensified recently. In Africa, dengue fever has increased dramatically, with most activity ocurring in East Africa. Although all five serotypes have been identified in the region (Gubler and Clark 1995), only DEN-2 is common.

Increase of dengue as a major public health hazard has been most dramatic in the Americas. In the 1950s and 1960s, the Pan American Health Organization (PAHO) conducted an *Ae. aegypti* eradication campaign in an effort to prevent urban yellow fever, which is also transmitted by this mosquito. As a result of this campaign, dengue ocurred only sporadically in some Caribbean islands during that period. The eradication program, however, was gradually abandoned (it was officially terminated in the United States in 1970). As a result, *Ae. aegypti* reinfested the region and is again widely distributed.

A major dengue epidemic occurred in Cuba in 1981, and a second major epidemic of DHF occurred in Venezuela in 1989–1990. Since then, epidemics have occurred in 14 Central or South American countries, and outbreaks, confirmed cases, or both, have been reported from most tropical and subtropical American countries.

More than 2.5 billion persons now live in areas at risk of infection (Figure 3), and attack rates for reported disease during epidemics can be in the range of 1 per thousand to 1 per hundred of the population.



Figure 3. Areas at risk of dengue transmission (sources WHO and others).

The reasons for the increase in dengue vary between regions, but some of the most important ones include: lack of effective mosquito control; demographic changes including population increases and uncontrolled urbanization often accompanied by substandard housing, poor water supplies, and inadequate sewage and waste management; increase in travel and commerce; and poor public health infrastructure.

After an absence of 35 years, several autochthonous cases of dengue fever occurred in southern Texas in 1980, 1986, 1995, 1997, 1998, and 1999, and an outbreak of dengue fever occurred in Hawaii in 2001. All five dengue serotypes have been isolated from the United States (PAHO 2007).

Dengue in Florida

Prior to the 1940s, there were regular occurrences of dengue outbreaks in Florida. The last epidemic of locallytransmitted dengue virus in Florida was in 1934–1935 when an estimated 15,000 people were reported to be infected. Since the 1940s, cases that are reported in Florida have been in people who were bitten by infected mosquitoes while visiting dengue-endemic areas. However, since 2009, locally acquired dengue case have been regularly reported from Florida.

In mid-August of 2009, a New York resident who had travelled to Key West, but nowhere else in the recent past was diagnosed with dengue, and the diagnosis was confirmed by CDC. Additional cases of autochthonous (locally acquired) dengue were reproted from Key West in late August and early September. Including this initial case, there were 28 cases of locally acquired dengue reported from Key West by the end of 2009. In April 2010, another Key West resident was diagnosed with dengue, and it was determined that the disease was locally acquired. New cases were continually diagnosed from Key West until the end of November, with a total of 65 cases occurring in the city that year, all attributable to DENV-1. Two other autochthonous cases were reported from Florida in 2010, one from Miami-Dade County (DENV-2) and one from Broward (DENV-3).

Only sporadic cases of local dengue were reported from Florida in 2011 (7) and 2012 (4). In mid August 2013, dengue cases were reported from Martin County and later confirmed to be locally acquired. As in Key West, other cases of autochthonous dengue were steadily reported until late September, by which time 22 cases of local dengue had been recorded from the Rio and Jensen Beach areas of Martin County.

Prevention

Prevention of dengue involves avoidance of mosquito bites, either by reducing mosquito vector populations, or by using personal protection measures such as protective clothing and repellents, and/or avoidance of mosquito infected areas. Mosquito population control involves spraying larvicides, removal of water-holding containers such as discarded tires and cans, and public water projects that improve drainage and reduce the need for household water storage. Recent successes in dengue reduction using integrated pest management techniques, including community education and biological control with copepods have been reported from Vietnam (Nam et al. 2005). As mentioned previously, there is no vaccine available at the present time.

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