

Commentary

The Dengue Threat to the United States

Crystal Franco, Noreen A. Hynes, Nidhi Bouri, and D. A. Henderson

Over the past 3 decades, dengue has spread rapidly and has emerged as one of the world's most common mosquito-borne viral diseases. Although often found in tropical and semitropical areas, dengue is capable of being transmitted in temperate climates as well. Dengue is currently endemic to Mexico, most other Latin American countries, and parts of the Caribbean, and it has the potential to become reestablished as an endemic disease in the United States. In fact, sustained transmission of dengue has occurred in Florida within the past year. Conditions exist in the U.S. that could facilitate sustained dengue transmission, including environmental factors, competent mosquito vectors, limited vector and dengue surveillance, increased domestic outdoor daytime activities in warmer months, and low public awareness of the disease. If dengue were to be reestablished in the U.S., it could have significant medical, public health, and economic consequences for the country. The impact of dengue as a public health threat could be lessened through enhanced awareness and reporting of cases, increased support for vector surveillance and control programs, and a greater focus on vaccine development.

Conditions in the United States are favorable to support dengue transmission, and, with the disease far more prevalent in popular tourist destinations than ever before, opportunities for reintroduction through international travel are much greater. Confirmation of sustained endemic dengue virus transmission in Key West, Florida, in 2009¹ has heightened concern that dengue could reemerge as an endemic disease elsewhere in the U.S.² Although the multiple dengue cases reported in July 2010 from Marion and Orange counties in Florida were likely the result of travel to nearby Haiti and Puerto Rico and were not locally acquired, public health officials in those counties have responded by issuing health advisories about dengue and implementing limited mosquito control programs.³

Dengue is currently endemic in more than 100 tropical and semitropical countries, and frequent large outbreaks threaten approximately 2.5 billion people around the world.⁴ In 2008, almost 1 million cases of dengue fever (DF) and 25,000 cases of a severe form of the infection—dengue hemorrhagic fever (DHF)—were reported in Mexico, the Caribbean, and Central and South America alone.⁵

Dengue, although thought of as a tropical disease unique to the developing world, was once endemic in the United States.⁶ Currently, almost all reported cases in the U.S. have been among travelers returning from endemic areas. However, in the past decade, a number of U.S. outbreaks of dengue with locally sustained transmission have occurred in

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Texas,⁷ Hawaii,⁸ and, most recently, Florida.¹ The mosquito vectors that transmit dengue, *Aedes aegypti* and *Aedes albopictus*, are present in large numbers throughout southern and central portions of the U.S., and dengue is already well established in neighboring Mexico and the Caribbean (including the U.S. territory of Puerto Rico).

Risk factors for establishing endemic foci of dengue virus in the U.S. include delayed diagnosis of the disease, sub-optimal epidemiologic and vector surveillance, urban population growth, air travel from endemic areas, degradation of public health infrastructure, and a spreading prevalence of competent mosquito vectors.⁹ Given these risk factors, it is apparent that the threat of dengue to the U.S. is current and real. If dengue is reestablished in the U.S., it could have significant medical, public health, and economic consequences.

What Is Dengue?

Dengue infection is caused by 4 closely related but distinct viruses or serotypes, which are transmitted to humans through the bite of an infected mosquito but not directly from person to person.¹⁰ Infection with one serotype results in lifelong immunity to that dengue type but continued susceptibility to the other 3 types. In fact, some individuals with antibodies to one dengue virus type are more likely to develop severe disease if infected with a different dengue type.¹¹

The mosquitoes that carry dengue are *Aedes aegypti* and *Aedes albopictus*. Both species are day-biting mosquitoes that reproduce in clean standing water. *Ae. aegypti* is the more efficient vector for dengue, as it preferentially bites humans and breeds almost exclusively in densely populated urban areas. *Ae. albopictus* is somewhat less discriminating in its species choice for biting and feeding, and it can breed in both urban and rural settings. As a result, *Ae. albopictus* has fewer opportunities to be infected with dengue and to transmit the virus to humans.¹⁰ However, this species is the dominant vector in some areas of the world. Sustained transmission of dengue virus among humans occurs primarily in densely populated, urban areas. Temperature and humidity affect the survival and biting patterns of these mosquitoes and thus affect the transmission and spread of the dengue viruses. Temperatures above 20°C (68°F),¹² as are found in the southern U.S. for most of the year and in some northern locations in summer, seem to best support disease transmission.^{13,14}

All 4 dengue virus strains cause similar types of illness, ranging from asymptomatic infection, to classic dengue fever, to severe dengue. Most dengue patients experience influenzalike symptoms that are often mistaken for the flu or other febrile illnesses. Classic dengue fever is characterized by high fever, headache, pain behind the eyes, rash, mild bleeding of the nose or gums, easy bruising, and body aches.¹⁰ The more severe cases of classic dengue experience

excruciating bone, joint, and muscle pain. Thus, dengue is also referred to as the “break bone fever.”¹⁵ The most severe cases of dengue experience capillary leakage, which can lead to shock (dengue shock syndrome), or accumulation of fluids causing respiratory distress, severe bleeding (dengue hemorrhagic fever), and severe dysfunction in major organs of the body including the liver, central nervous system, and heart. Severe dengue can result in circulatory system failure, shock, and occasionally death. There is no specific treatment for dengue or severe dengue and no licensed vaccine to prevent the disease. However, supportive therapy, including fluid replacement therapy, can be life-saving if severe dengue is detected early.¹⁶

Although a vaccine has not yet been licensed for dengue, vaccine research is ongoing, and 2 vaccine candidates—made by Sanofi-Aventis and GlaxoSmithKline (GSK)—have progressed to Phase II clinical trials.¹⁷⁻¹⁹ As an indication of the global need for a dengue vaccine, Sanofi-Aventis is also investing in the construction of a €350 million dengue vaccine manufacturing plant in France. The Sanofi-Aventis plant is scheduled to be operational in 2013.²⁰

Risk Factors for Reintroduction of Dengue in the U.S.

Lack of Dengue Awareness

Dengue was only recently added (in 2010) to the list of Nationally Notifiable Infectious Conditions.²¹ Awareness of dengue is low among medical and public health practitioners, most of whom have had limited training or experience with the disease.²² This low level of awareness, along with failure of diagnosis and reporting of dengue, may lead to delayed identification of possible outbreaks when virus introduction occurs.

Increased Travel

Increasing numbers of dengue-infected travelers make outbreaks in the U.S. more likely. Reports of travel-related introductions of dengue to the U.S. rose from 336 suspected and confirmed cases from 2001 to 2004²³ to 574 suspected and confirmed cases in 2006 to 2008.²⁴ These case numbers were compiled in the years before dengue became a Nationally Notifiable disease and unquestionably understate the number of cases that have actually occurred.

Expanded Mosquito Range and Numbers

Both types of dengue mosquito vectors are abundant in the United States. *Ae. aegypti* is present throughout the southern U.S., and *Ae. albopictus*, although less efficient in transmitting dengue infection to humans, continues to

increase its range and is now found in the southern U.S., the eastern seaboard up to southern New England, and the Mississippi River area and its watershed up to Chicago. It is predicted that the ranges of both types of mosquitoes will expand in coming years due to travel, shipping, and a reduction of vector control measures.²⁵

Loss of Funding

With recent local, state, and national public health budget cuts, vector surveillance and control programs have suffered, and some have been eliminated entirely.²⁶ For the coming year, the U.S. Centers for Disease Control and Prevention (CDC) FY2011 budget proposes to eliminate all funding for the CDC vectorborne diseases division and cut funding in half for the CDC Dengue Branch.^{27,28} If funding is eliminated, vector surveillance will be greatly reduced, as will our ability to respond to dengue in the U.S.

Recommendations

Medical and public health practitioners need to be aware of the symptoms and risks of dengue for individuals and communities. Dengue should be considered as a possible diagnosis in travelers with fever and aching pains who have returned from endemic areas in the past 2 to 7 days. Serological confirmatory testing should be sought if dengue is suspected.^{16,29,30} Clinicians and public health professionals should also advise travelers to use repellents and wear appropriate clothing when visiting endemic areas, in order to diminish their exposure to mosquitoes.

Medical and public health practitioners should report all suspected and confirmed cases of dengue to state public health officials and from state public health to the CDC. Reporting of cases is critical to enable prevention strategies to be implemented and to avert sustained transmission through introduction of the virus in domestic locations with competent vectors.

Vector control programs must be funded, and studies of vector distributions in the U.S. need to be greatly strengthened. Without an accurate assessment of the distribution of dengue mosquitoes in the U.S. and without programs aimed at reducing vector populations, it will be very difficult to prevent reintroduction of dengue—and even more difficult to interrupt transmission if an epidemic should occur.

Vaccine development should be continued for dengue. Vaccine development for dengue is under way in both the public and private sectors. Because vector control for dengue can be difficult, and sometimes impossible, a vaccine is needed to prevent cases and reduce the impact of dengue globally. Manufacturers should be encouraged to seek vaccine licensure in the U.S.

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Note: An especially useful, comprehensive document on dengue, titled *Dengue: Guidelines for Diagnosis, Treatment, Prevention, and Control*, was issued in 2009 by the World Health Organization (WHO). The document can be found at: http://whqlibdoc.who.int/publications/2009/9789241547871_eng.pdf.

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