Dengue Fever in the United States


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In the United States during 1981, fourteen state health departments reported a total of 44 imported cases of dengue fever. Most originated in the Caribbean, where dengue type 4 has reached pandemic proportions. Because the mosquito vector for dengue is abundant throughout the southeast and imported cases continue to occur, the possibility exists for indigenous dengue transmission. We report a cluster of imported dengue type 1 cases in Florida, discuss the clinical, epidemiologic, and public health aspects of the disease, and make recommendations as to how clinicians can assist public health officials in minimizing the risk of indigenous dengue transmission in the United States.

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DENGUE fever is an acute febrile illness caused by a mosquito-borne virus. The disease has long been present in the western hemisphere; however, the last major outbreak in the United States was reported in 1945. Since then, the only known indigenous transmission within the United States was reported in southern Texas during August 1980 and probably was a result of introduction from Mexico. The first case in the Texas outbreak was identified by a clinic participating in a dengue surveillance program. Neighborhood campaigns to eliminate vector breeding sites were initiated and may have been responsible for limiting the outbreak to a few sporadic cases.

Texas is unique in its proximity to a country with endemic dengue, and extra precautions are required to deal with the potential introduction of infected vector mosquitoes. Many states besides Texas, however, have an abundance of native vector mosquitoes (Fig 1) and have potential sources of dengue virus introduced each year by infected tourists returning from endemic-epidemic areas of the world. In 1981, for example, 44 serologically confirmed imported cases of dengue were reported to the Centers for Disease Control by 14 state health departments. Most originated in the Caribbean, where both endemic and epidemic dengue have been major health problems in recent years. Given the widespread occurrence of dengue throughout the Caribbean basin (Fig 2), especially in areas frequented by American tourists, the flow of imported cases seems likely to continue.

This article briefly reviews the clinical, epidemiologic, and public health aspects of dengue, and brings into focus the clinician’s role in keeping the risk of indigenous dengue transmission at a minimum.

REPORT OF A CLUSTER OF IMPORTED CASES

On July 7, 1981, fever, chills, myalgias, retro-orbital headaches, and a rash developed in a 24-year-old woman from Broward County, Florida. She consulted her physician the following day because of worsening myalgias and headaches and was admitted to a hospital for evaluation. Findings on physical examination were unremarkable except for an oral temperature of 39.8°C and a maculopapular rash that was confined to the lower abdomen and back. Routine laboratory studies showed a total WBC count of 1.3×10⁹/cu mm with 41% polymorphonuclear leukocytes, 13% lymphocytes, 16% atypical lymphocytes, 9% band forms, 3% monocytes, and 1% basophils. The platelet count was 62×10⁹/cu mm. Her hemoglobin level was 11.7 g/dL, with a hematocrit reading of 35%. No tourniquet test was done. Because the patient volunteered a recent travel history to the Caribbean, her physician obtained an acute-phase serum specimen for dengue titers. The patient’s condition improved over the next several days, and she was discharged when her WBC and platelet counts returned to normal. She had no signs of hemorrhagic diathesis of circulatory failure. A convalescent-phase serum specimen was obtained two weeks after onset and tests on the paired serum specimens showed a greater than fourfold rise in hemagglutination-inhibiting (HI) and complement-fixing (CF) antibodies with monotypic patterns compatible with recent dengue type 1 infection.

An epidemiologic investigation disclosed that the patient had vacationed with nine other family members in St Thomas, Virgin Islands, from June 26 to July 2. She had not traveled previously to other areas where dengue is endemic. An exposure period was calculated from the onset date of symptoms and the incubation period for
Fig 1.—Seasonal distribution of *Aedes aegypti* in the United States.

Fig 2.—Dengue in the Caribbean—1981.
dengue virus, and implicated St Thomas as the place where the patient most likely acquired dengue. The other family members were interviewed, and four were found to have had dengue-like symptoms. Three had returned to Volusia County, Florida, and one was still in St Thomas. All had onset dates within a week of one another, and the exposure periods overlapped during a time when the family was vacationing together in St Thomas (Fig 3). Paired serum specimens were collected on all symptomatic family member and showed a greater than fourfold rise in CF titers to dengue type I. When the symptomatic family members returned to Florida, all were either hospitalized or living in air-conditioned, screened houses; thus, while they were viremic, vector mosquitoes had minimal exposure to these potential sources of infection.

No further cases were detected from surveillance of clinics, physicians, and emergency rooms serving the communities where affected family members reside.

**EPIDEMIOLOGY**

Dengue is caused by a flavivirus (group B arbovirus); there are four distinct serotypes (types 1 through 4). All show a degree of cross-reactivity in serological testing with other flaviviruses such as yellow fever, Japanese encephalitis, and St Louis encephalitis.

The *Aedes aegypti* mosquito is the only known vector of dengue in the new world, although other species are important in Asia and the Pacific. *Aedes aegypti* mosquitoes are usually daytime biters and have a short flight range. They breed almost exclusively in artificial water reservoirs (ie, planters, gutters, old tires, etc) in and around human habitations. The eggs are quite hardy and can resist drying for several months.

The cycle of transmission begins when a female *A aegypti* mosquito bites an infected human during a four- to five-day period of viremia that probably begins just before the onset of symptoms. After a ten- to 14-day extrinsic incubation period within the vector, the mosquito is capable of transmitting the virus for life. Clinical symptoms appear three to 15 days after an infected vector mosquito bites a susceptible human host.

**CLINICAL FEATURES**

Dengue virus infection produces a spectrum of illness ranging from asymptomatic infection to hemorrhage, shock, and death. Classically, patients complain of abrupt onset of fever, chills, retro-orbital headache, anorexia, nausea and vomiting, myalgias, and arthralgias. Fever generally lasts from three to seven days; the fever curve may be biphasic. Flushing of the face and neck is sometimes noticeable during the early stages of illness, and an erythematous macular or maculopapular rash often appears after two or three days of fever. Characteristically, the rash begins on the trunk and spreads to the extremities and face. Toward the end of the febrile period, petechiae sometimes occur, especially on the lower extremities; desquamation and pruritus may follow. Most patients recover completely, but convalescence may be prolonged, accompanied by weakness and depression. Dengue may also present as an undifferentiated febrile illness, especially in children. During the acute phase of the illness, laboratory examination typically reveals neutropenia with a predominance of lymphocytes, often atypical, and various degrees of thrombocytopenia. Serum transaminase levels are sometimes slightly elevated.

Recent observations suggest that dengue infection may also be associated with encephalopathic signs in both fatal and nonfatal cases. To date, however, dengue virus has not been isolated from brain tissue or spinal fluid, and histopathologic findings of encephalitis have not been found in fatal cases.

The frequency and severity of hemorrhagic manifestations associated with dengue infection varies from outbreak to outbreak. The most common features are epistaxis, gingival bleeding, gastrointestinal tract hemorrhages, menorrhagia, hematuria, and extensive petechiae or purpura. Life-threatening shock occurs in a small percentage of persons with dengue (<1%). If shock occurs, it usually develops around the time of deferred vescence, and patients who survive

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**Table:** World Health Organization Criteria for Grading Dengue Hemorrhagic Fever (DHF) and Dengue Shock Syndrome (DSS)

| Grade I (DHF) | Fever accompanied by nonspecific constitutional symptoms; the only hemorrhagic manifestation is a positive tourniquet test result |
| Grade II (DHF) | The additional manifestation to those of grade I is spontaneous bleeding—skin or other hemorrhages or both |
| Grade III (DHF/DSS) | Circulatory failure manifested by rapid and weak pulse, narrowing of pulse pressure (<20 mm Hg) or hypotension, with the presence of cold clammy skin and restlessness |
| Grade IV (DHF/DSS) | Profound shock with undetectable BP and pulse |

*Adapted from WHO Guide for Diagnosis, Treatment, and Control of Dengue Hemorrhagic Fever, 1980.* The presence of thrombocytopenia with concurrent hemoconcentration will differentiate grade I and II DHF from classic dengue fever.
more than 48 hours usually recover completely. Loss of plasma from the vascular compartment (indicated by hemoconcentration and hypoalbuminemia) accompanies shock in some patients, while massive blood loss leads to shock in others. The former pathophysiological picture is defined by the World Health Organization as a distinct clinical syndrome, dengue hemorrhagic fever/dengue shock syndrome (DHF/DSS), which requires hemoconcentration and thrombocytopenia for diagnosis (Table). It should be noted, however, that in some patients with dengue shock develops secondary to severe hemorrhage, and these patients may not have hemoconcentration and therefore would not meet the WHO criteria for DHF/DSS. At present, there is no reliable basis for predicting accurately in which patients these more severe manifestations of dengue will develop; however, abdominal pain, restlessness, and an increasing hematocrit reading often are signs of incipient circulatory failure.

In Asia, DHF and DSS occur preponderantly in children younger than 15 years. However, in other parts of the world, a number of adult cases also have been reported. 

Differences in the proportion of adult and pediatric cases may be related to differences in the immune backgrounds of various populations. The hypotheses that the risk of development of DHF/DSS is greater among those patients who have secondary infections, or among those who are infected with a particularly virulent strain of dengue virus, require further investigation.

TREATMENT

Therapy for dengue and DHF/DSS is symptomatic and supportive. Aspirin is not recommended as an antipyretic because it could compound hemorrhagic manifestations. Mortality rates for DHF/DSS once as high as 50% have been reduced to less than 1% by close monitoring of vital signs and hematocrit reading in order to evaluate plasma loss or hemorrhage. If shock develops, aggressive fluid therapy should be started in an intensive care setting.

Patients with severe hemorrhage will require transfusion, preferable with whole blood, whereas patients with DSS (hemoconcentration) without severe hemorrhage may require only fluid replacement therapy.

LABORATORY DIAGNOSIS

Laboratory confirmation of dengue is established by demonstrating a fourfold rise in HI, CF, or neutralizing antibody titers between acute- and convalescent-phase serum specimens collected approximately two weeks apart. The isolation of dengue virus from an acute-phase serum specimen is also diagnostic; mosquito-cell culture and mosquito inoculation are the most commonly used isolation techniques.

RECENT DEVELOPMENTS IN THE CARIBBEAN

In 1981, there were two important dengue-related events in the Caribbean. In April, dengue type 4 was confirmed in the Leeward Islands of St Barthelemy and St Martin. This was the first documentation of this subtype in the Caribbean. In the ensuing spring and summer months, dengue type 4 outbreaks were reported in Dominica, Guadeloupe, Curacao, and St Thomas. Cases of dengue type 4 were also confirmed in Belize, Haiti, Puerto Rico, and Jamaica. The second notable event was a major epidemic of dengue in Cuba during June-August 1981. More than 300,000 cases and 149 deaths from DHF were reported. The serotype was reported to be type 2; however, there has been no laboratory confirmation outside Cuba. Epidemic DHF has been a major cause of morbidity and mortality in Southeast Asia for more than 25 years, but has not previously been seen in the western hemisphere.

COMMENT

All four dengue serotypes have now been reported from the Caribbean. Types 2 and 3 were first documented in the Caribbean in the 1960s. Type 1 reached pandemic levels in 1977 and was the predominant serotype until the last part of 1981, when the type 4 pandemic began. In 1981, both types 1 and 4 were imported into areas in the United States populated by Aedes aegypti mosquitoes; however, no indigenous transmission was reported. Two factors may have contributed to this. First, in the United States, persons ill with dengue are likely to remain in screened or air-conditioned housing. This minimizes the exposure of vector mosquitoes to potential sources of dengue virus. Second, there is some evidence to suggest that geographically distinct vector mosquito populations have genetically predetermined differences in susceptibility to dengue virus infection. Thus, the vector mosquito population in the United States may be biologically less efficient at transmitting dengue virus than those found elsewhere in the world. Further investigation is currently under way to confirm this hypothesis.

RECOMMENDATIONS

At present, the greatest risk of introducing dengue into the United States seems to come from travelers returning to, or entering from, endemic-epidemic areas within the Caribbean, Central America, and northern South America. Physicians should advise patients who expect to travel in these endemic areas to use mosquito repellants, netting, or protective clothing whenever possible and feasible. Spraying hotel rooms with commercially available insecticides may be advisable if the mosquito population is heavy or if window screens are in disrepair or nonexistent. Patients should be instructed to recognize the symptoms of dengue and of the need to bring such symptoms to the attention of a physician promptly.

The diagnosis of dengue should be considered in any patient who has fever, myalgias and rash, and who has traveled to an area where dengue is endemic. In the southeastern United States, such patients should be kept indoors in screened housing that has been rid of mosquitoes by household insecticide spray. Physicians may wish to hospitalize patients with hemorrhagic manifestations until the need for fluid replacement therapy can be ruled out. Serum specimens should be collected from all suspected dengue patients and submitted to the appropriate state or federal laboratories for serologic testing and virus isolation. An acute-phase serum specimen should be obtained as soon as possible after onset of symptoms and shipped on dry ice. If the convalescent-phase speci...
CONCLUSION

Although the risk of indigenous dengue transmission in the United States is probably small, the possibility exists since the mosquito vector is abundant in the southeast and sporadic, imported cases continue to occur. Clinicians play a critical role in keeping this risk at a minimum by (1) advising their patients traveling to endemic areas on ways to avoid infection; (2) including dengue in the differential diagnosis of patients returning from endemic areas; (3) confirming the diagnosis with appropriate laboratory testing; (4) isolating suspect cases from potential vector mosquitoes; and (5) promptly reporting any suspected cases to the local county health department.

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References