Travel-related health risks are of concern to all members of the healthcare community—both as business and recreational travelers ourselves and as professionals charged with caring for our patients who travel abroad. Many of our patients will come to us for necessary vaccinations, pre-travel checkups and prescription renewals before they embark on their journeys. These visits provide a good opportunity to offer guidance, advice and important medical information that can guard health and support a carefree vacation.

Part 1 of this three-part series presented a discussion of the occurrence and prevention of non-infectious health risks that occur due to travel-related injury as well as from complications from underlying health problems. Part 2 of this series now looks at emerging mosquito-borne infectious illnesses, specifically chikungunya fever (endemic in areas of tropical Africa, India and Southeast Asia) and dengue fever (originating in the South Pacific, Asia, Caribbean, Mexico, South and Central America and Africa). Although considered “tropical” illness, travelers visiting many other parts of the world, including Europe and even parts of the United States, have been infected with these illnesses by the bite of infected mosquitoes. It is important for all healthcare professionals to be familiar with the methods of prevention as well as the diagnosis and treatment of these illnesses.

CHIKUNGUNYA FEVER

Chikungunya fever is an acute febrile illness, caused by the chikungunya virus, a member of the genus Alphavirus, that is transmitted by the bite of an infected Aedes mosquito. The virus was named chikungunya from the Makonde word meaning "that which bends up," after the virus was first isolated from both patients and mosquitoes during an epidemic on the Makonde plateau in Tanzania in 1952. Subsequently, this virus has been isolated frequently from humans and mosquitoes in tropical Africa, India and Southeast Asia.

* This is the second of a three-part series on travel-related health risks. The third and final installment will explore non-mosquito-borne infectious illnesses.
Starting in 2004, a massive outbreak of chikungunya fever swept over the islands on the western rim of the Indian Ocean (the Comoros, Lamu, Mauritius, the Seychelles, Madagascar, Mayotte and Reunion). In Reunion (an overseas department of France, with a population of 770,000, where the medical system and accessibility to medical care are said to be no different from that in mainland France), there were 265,000 clinical cases (an incidence of 34 percent). A seroprevalence study done at the time in Reunion revealed that approximately 38 percent of the population was infected, with very few asymptomatic cases. Attack rates observed in the Kenyan island of Lamu (75 percent) and the Grande Comoro Island (63 percent) were even higher than that reported from Reunion. Large outbreaks of chikungunya fever also occurred in India (where over 1.25 million people were reported infected, with attack rates in some areas as high as 45 percent), the Maldives, Sri Lanka and countries in Southeast Asia (Malaysia, Singapore, Indonesia and Thailand).

Several European countries and the United States have reported imported chikungunya infections among travelers returning from the Indian Ocean region where the virus was spreading rapidly. According to Eurostat, over 1.4 million people travelled from Madagascar, Mauritius, Mayotte, Reunion Island and the Seychelles to the European continent in 2004. Because viral loads are very high during the first seven days of illness—frequently above 10⁹ virus particles per milliliter of serum—acutely infected people can disseminate the virus to local mosquitoes in countries where competent vectors reside.

**Chikungunya Fever Transmission and Manifestations:** Chikungunya virus is transmitted to humans by infected *Aedes* mosquitoes, particularly *Aedes aegypti* and *Aedes albopictus* (the Asian tiger mosquito). *Ae. aegypti*, the classical vector of chikungunya, was involved in the initial 2004 Kenyan and Comorian outbreaks. However, sometime during 2005, a chikungunya virus was selected that had a single amino acid change in the envelope glycoprotein, which allows efficient viral replication in *Aedes albopictus*, the predominant mosquito in Reunion. *Aedes albopictus* has also contributed to the spread of chikungunya in Sri Lanka and Southeast Asia where this mosquito species is abundant. To further complicate matters, not only is *Aedes albopictus* now a good host for chikungunya virus, but this mosquito is spreading across the globe from eastern Asia to Europe and the United States. The mosquito was first found in the U.S. in 1985 when it was isolated in Houston, Texas, having arrived there from Asia in ships carrying scrap tires.

An outbreak of locally acquired chikungunya fever occurred in Ravenna, Italy, in 2007—the first ever in Europe, which ultimately involved more than 217 confirmed cases. The outbreak was started by an infected traveler from Kerala, India, who transmitted the virus to local *Aedes albopictus* mosquitoes. The first indigenous cases of chikungunya fever in France were reported in 2010. Moreover, as a direct consequence of the high viremia in patients, direct human-to-human nosocomial transmission has occurred by exposure to infected blood, and there is the possibility of transmission by blood transfusion or organ transplantation from unsuspected viremic donors.

Chikungunya is characterized by sudden onset of high fever (typically greater than 102°F) and severe, sometimes persistent, joint pain. Because of the short incubation period of two to four days from mosquito bite to onset of symptoms, the traveler will likely become sick while still away from home. The ankles and wrists are most commonly involved; intense pain caused by pressure on the wrist is a strong diagnostic sign of the disease. Arthritis with effusion is rare in patients with chikungunya. After two to five days, a maculopapular rash is common on the trunk and extremities, but can also include the palms, soles and face. Other symptoms include headache, fatigue, nausea, vomiting and myalgias. Hemorrhagic signs are rarely reported in chikungunya.

Lymphopenia is a common hematologic abnormality in the acute phase of chikungunya fever. Laboratory abnormalities may also include moderately low platelet counts and elevated liver enzymes. Previously undescribed, severe clinical
forms of the illness were reported during the large outbreaks in Reunion and India, including cases of myocarditis, ocular disease (uveitis, retinitis), hepatitis and neuroinvasive disease, such as meningoencephalitis, Guillain–Barré syndrome, paresis or palsies. Peripartum transmission from mother to infant has been reported and can result in complications for the baby, including neurologic disease, hemorrhagic symptoms and myocardial disease.

Chikungunya fever is usually not life-threatening. However, with such large numbers of infected individuals in Reunion, chikungunya was implicated in 237 deaths\(^1\) that appear to be associated with increased age and underlying illnesses. Chikungunya virus infection (whether clinically apparent or silent) is thought to confer life-long immunity.

**Chikungunya Fever Diagnosis and Treatment:** Preliminary diagnosis of chikungunya fever is based on the patient’s clinical features, as well as places and dates of travel and activities. Laboratory diagnosis is generally accomplished by RT-PCR, seroconversion on paired serum specimens or positive IgM serologic test results.

However, chikungunya fever may be difficult to distinguish clinically from several other febrile illnesses without localizing findings that travelers may acquire abroad, namely dengue, malaria, leptospirosis, scrub typhus, rickettsial infections and typhoid fever. Often, specific laboratory investigations are required to exclude these conditions. Diagnosis of dengue is based on a positive IgM capture ELISA test; malaria on demonstration of malarial parasites on peripheral blood smear or a positive rapid diagnostic assay for malaria; leptospirosis on a positive leptospira IgM ELISA test; scrub and murine typhus is diagnosed by a 4-fold increase in antibody titers between acute and convalescent serum specimens using the immunofluorescent assay (IFA); and typhoid fever on blood culture. Healthcare providers should contact their state or local health department or Centers for Disease Control and Prevention for assistance with diagnostic testing.

Anti-inflammatory drugs are used to relieve joint pain and fever of chikungunya fever. While recovery from chikungunya is the expected outcome, convalescence can be prolonged (up to a year or more), and persistent joint pain may require analgesic medication.

**Dengue Fever**

Dengue fever is the most common arbovirus infection worldwide, affecting up to 100 million people annually. In a recent prospective study from the Netherlands, the frequency of dengue fever in tourists was projected to be as high as four infections per every 1,000 travelers to high-risk countries.\(^{10}\) Dengue fever has an incubation period of three to 14 days. Sick travelers with flu-like symptoms should consider dengue infection if their travel history includes a dengue endemic region within the previous two weeks.

Dengue viruses are endemic in the South Pacific, Asia, Caribbean, Mexico, South and Central America and Africa. There is also a small but significant risk of dengue transmission in the United States. A small dengue outbreak occurred in Hawaii in 2001\(^{11}\) and Key West, Florida, in 2009.\(^{12}\) However, most dengue cases in U.S. citizens occur in inhabitants of Puerto Rico, the U.S. Virgin Islands, Samoa and Guam, where dengue is endemic.\(^{13}\)

**Dengue Fever Transmission and Manifestations:** Although the virus that causes dengue (a flavivirus) is very different from that which causes chikungunya, both infections are transmitted by the same mosquito species. In areas where both viruses co-circulate, they can be transmitted together. There are many similarities in the clinical
manifestations of chikungunya and dengue, also known as breakbone fever. However, unlike dengue, joint pains tend to be disabling in chikungunya, and hemorrhagic manifestations are more prominent in dengue. In a small proportion of dengue cases, the disease develops into life-threatening dengue hemorrhagic fever/DHF (evidence of increased vascular permeability, e.g., hemoconcentration [hematocrit increased by >20 percent from baseline], pleural or abdominal effusions, or hypoproteinemia, bleeding and thrombocytopenia) or dengue shock syndrome/DSS (circulatory failure). In rare cases, dengue can be transmitted in organ transplants or blood transfusions from infected donors, and there is evidence of transmission from an infected pregnant mother to her fetus.

There are four different types of dengue virus; infection with one type usually gives lifelong immunity to that type, but only short-term immunity to the others. Subsequent infection with a different type is believed to increase the risk of dengue hemorrhagic fever and dengue shock syndrome. Dengue fever is usually self-limited with fever lasting three to seven days, while the fatality rate of patients with DSS can be as high as 44 percent.14

**Dengue Fever Diagnosis and Treatment:** Diagnosis of dengue is based on a positive IgM capture ELISA test. Treatment of dengue is primarily supportive. Aggressive intravenous fluid replacement is essential in patients with DHF/DSS. Aspirin should be avoided because of potential bleeding diathesis and the increased risk of Reye’s syndrome associated with dengue.

**PREVENTION OF CHIKUNGUNYA AND DENGUE FEVERS**

No vaccines are available against chikungunya or dengue—or malaria for that matter. However, while drugs can prevent malaria, there is no such option available to prevent chikungunya or dengue. Prevention of chikungunya and dengue depends entirely upon taking steps to avoid Aedes mosquito bites and to eliminate their breeding sites. Aedes aegypti mosquitoes prefer to lay eggs in artificial water containers and tend to live in close proximity to humans in highly urbanized areas. In Asia, Ae. albopictus is primarily a woodland species that breeds in tree holes that periodically fill with water. This species, however, has adapted to suburban and vegetated urban environments, where it breeds in tires and other discarded water-holding containers that are common both outside and inside human dwellings.

Breeding sites can be eliminated by draining water from coolers, tanks, barrels, drums and buckets, etc., by changing the water in pet dishes and replacing the water in birdbaths weekly, by drilling holes in tire swings so water drains out and by keeping children’s wading pools empty and on their sides when they aren’t being used.

In addition, the same preventive steps taken to avoid bites by the Anopheles mosquito, which bites at night and transmits malaria, are effective against the Aedes mosquitoes, which are aggressive daytime biters. To avoid Aedes mosquito bites, travelers should do the following:
• Wear full-length clothing that cover the limbs.
• Apply an insect repellent containing 20 to 30 percent DEET on exposed skin, particularly in the morning and early evening hours when the mosquitoes bite the most (products containing DEET can be used in pregnancy without adverse effects).
• Secure screens on windows and doors to keep mosquitoes out if the building is not air-conditioned.
• Use permethrin-impregnated mosquito nets to protect babies, the elderly and others who may rest indoors during the daytime.

Because mosquitoes become infected when they bite viremic people who are infected with chikungunya and dengue, these people should use mosquito repellents when outdoors, or they should stay indoors; if the building is not air-conditioned, they should stay in areas with screens or under a mosquito net. Because of the risk of mother-to-child transmission for chikungunya, dengue and malaria, pregnant women need to take special care to protect themselves from mosquito bites.

While these preventive methods are quite effective in helping travelers avoid mosquito-borne infectious illnesses, other non-mosquito borne illnesses are not as easily avoided. The final third part of this series will discuss the prevalence, transmission, diagnosis and treatment of the travel-related non-mosquito infectious illnesses of leptospirosis, norovirus, legionellosis and Pontiac fever.

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