Zika—Not the Only Mosquito-Borne Virus to Worry About

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As the spread of the Zika virus continues to garner attention in the national spotlight, two other mosquito-borne viral infections pose a potential threat to the United States: dengue fever and chikungunya.

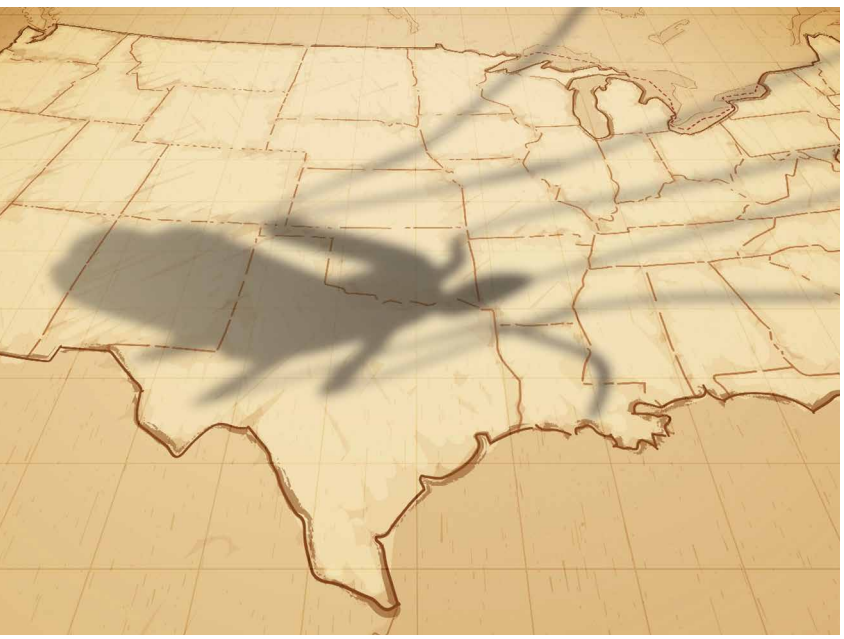
At the annual meeting of the Pacific Dermatologic Association, Iris Z. Ahronowitz, MD, shared tips on how to spot and diagnose patients with these viral infections.

"You really need to use all the data at your disposal, including a thorough symptom history, a thorough exposure history, and of course, our most important tool in all of this: our eyes," said Dr Ahronowitz, a dermatologist at the University of Southern California, Los Angeles. Reaching a diagnosis involves asking about epidemiologic exposure, symptoms, morphology, and performing confirmatory testing by polymerase chain reaction (PCR) and/or enzyme-linked immunosorbent assay (ELISA). "Unfortunately we are not getting these results very quickly," she said. "Sometimes the turnaround time can be 3 weeks or longer."

She discussed the case of a 32-year-old woman who had returned from travel to Central Mexico. Two days later, the patient developed fever, fatigue, and retro-orbital headache, as well as flushing macular erythema over the chest. Three days later, she developed a generalized morbilliform eruption. Her white blood cell count was 1.5 x 10^9/L, platelet count was 37 x 10^9/L, aspartate aminotransferase (AST) was 124 U/L, and alanine aminotransferase (ALT) was 87 U/L.

The differential diagnosis for morbilliform eruption plus fever in a returning traveler is extensive, Dr Ahronowitz said. It includes measles, chikungunya, West Nile virus, O'nyong-nyong virus, Mayaro virus, Sindbis virus, Ross river disease, Ebola/Marburg, dengue, and Zika. Bacterial/rickettsial possibilities include typhoid fever, typhus, and leptospirosis.

The patient was ultimately diagnosed with dengue virus, a mosquito-borne flavivirus. Five serotypes have been identified, the most recent in 2013. According to Dr Ahronowitz, dengue ranks as the most common febrile illness in travelers returning from the Caribbean, South America, and Southeast Asia. "There are up to 100 million cases every year, 40% of the world population is at risk, and an estimated 80% of people are asymptomatic carriers, which is facilitating the spread of this disease," she said. The most common vector is *Aedes aegypti*, a daytime biting mosquito that is endemic to the tropics and subtropics. But a new vector is emerging, *Aedes albopictus*, which is common in temperate areas. "Both types of mosquitoes are in the United States, and they're spreading rapidly," she said. "This is probably due to a combination of climate change and international travel."



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Dengue classically presents with sudden onset of fever, headache, retro-orbital pain, and severe myalgia; 50% to 82% of cases develop a distinctive rash. "While most viruses have nonspecific lab abnormalities, one that can be very helpful to you with suspected dengue is thrombocytopenia," she said. "The incubation period ranges from 3 to 14 days."

Rashes associated with dengue are classically biphasic and sequential. The initial rash occurs within 24 to 48 hours of symptom onset and is often mistaken for sunburn, with a flushing erythema of the face, neck, and chest. Three to 5 days later, a subsequent rash devel-

ops that starts out as a generalized morbilliform eruption but becomes confluent with petechiae and islands of sparing. "It's been described as 'white islands in a sea of red,'" Dr Ahronowitz said.

A more severe form of the disease, dengue hemorrhagic fever, is characterized by extensive purpura and bleeding from mucosa, gastrointestinal tract, and injection sites. "The patients who get this have prior immunity to a different serotype," she said. "This is thought to be due to a phenomenon called antibody-dependent enhancement, whereby the presence of preexisting antibodies facilitates entry of the virus and produces a more robust inflammatory response. Most of these patients, even the ones with severe dengue, recover fully. The most common long-term sequela we're seeing is chronic fatigue."

The diagnosis is made with viral PCR from serum less than 7 days from onset of symptoms, or immunoglobulin M (IgM) ELISA more than 4 days from onset of symptoms. The treatment is supportive care with fluid resuscitation and analgesia; there is no specific treatment. "Do not give nonsteroidal anti-inflammatory drugs (NSAIDs) which can potentiate hemorrhage; give acetaminophen for pain and fevers," she advised. "A tetravalent vaccine is now available for dengue. Prevention is so important because there is no treatment."

Next, Dr Ahronowitz discussed the case of a 38-year-old man who returned from travel to Bangladesh. Two days after returning he developed fever to 104˚F, headache, and cervical lymphadenopathy. Three days after returning, he developed severe pain in the wrist, knees, and ankles, and a rash. "This rash was not specific; it was a morbilliform eruption primarily on the chest," she said.

The patient was ultimately diagnosed with chikungunya, a single-strand RNA mosquito-borne virus with the same vectors as dengue. "This has been wreaking havoc across the Caribbean in the past few years," Dr Ahronowitz said. "Chikungunya was first identified in the Americas in 2013, and there have been hundreds of thousands of cases in the Caribbean." The first case acquired in the United States occurred in Florida in the summer of 2014. As of January 2016 there were 679 imported cases of the infection in the United States. "Fortunately, this most recent epidemic is slowing down a bit, but it's important to be aware of," she said.

Clinical presentation of chikungunya includes an incubation period of 3 to 7 days, acute onset of high fevers, chills, and myalgia. Nonspecific exanthem around 3 days occurs in 40% to 75% of cases, and symmetric polyarthralgias are common in the fingers, wrists, and ankles. Labs may reveal lymphopenia, acute kidney injury, and elevated AST and ALT levels. Acute symptoms resolve within 7 to 10 days.

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Besides the rash, other cutaneous signs of the disease include aphthous-like ulcers and anogenital ulcers, particularly around the scrotum. Other patients may present with facial hyperpigmentation, also known as "brownie nose," that appears with the rash. In babies, bullous lesions can occur. More than 20% of patients who acquire chikungunya still have severe joint pain 1 year after initial presentation. "This can be really debilitating," she said. "A subset of patients will develop an inflammatory seronegative rheumatoid-like arthritis. It's generally not a fatal condition except in the extremes of age and in people with a lot of comorbidities. Most people recover fully."

As in dengue, clinicians can diagnose chikungunya by viral culture in the first 3 days of illness, and by reverse transcription PCR in the first 8 days of illness. On serology, IgM is positive by 5 days of symptom onset.

"If testing is not available locally, contact the Centers for Disease Control and Prevention," Dr Ahronowitz said. "Treatment is supportive. Evaluate for and treat potential coinfections, including dengue, malaria, and bacterial infections. If dengue is in the differential diagnosis, avoid NSAIDs." A new vaccine for chikungunya is currently in phase II trials.