

Dengue Fever Is Increasing in Texas and Florida

BY DAMIAN McNAMARA
Miami Bureau

MIAMI — From 1977 to 2004, there were 3,806 suspected cases of dengue imported to the United States, according to the Centers for Disease Control and Prevention.

"Many more cases probably go unreported each year because surveillance in the United States is passive and relies on physicians to recognize the disease, inquire about the patient's travel history, obtain proper diagnostic samples, and report the case," according to the CDC.

"We are starting to see more and more cases of dengue fever," Dr. Christian C. Patrick said at a pediatric update sponsored by Miami Children's Hospital, "particularly in south Texas."

Following a case report of a woman in Brownsville, Tex., infected with dengue without traveling in July 2005 and an outbreak of 1,251 reported cases in Tamaulipas, Mexico, an investigation identified 24 additional cases in Texas, including 2 more infections not associated with travel (MMWR 2007;56:785-9). A review of hospitalization records revealed that 16 of 25 (64%) eventual infections in Texas developed the more serious dengue hemorrhagic fever, compared with 34 of 104 cases (33%) identified in Mexico.

Results of another study suggest dengue is endemic along the southern Texas-Mexico border (Emerg. Infect. Dis. 2007;13:1477-83). Investigators found 2% of Brownsville residents had serologic evidence of recent dengue infection, compared with 7.3% of residents in the bordering city of Mata-

moros in Tamaulipas in 2004. The cross-sectional survey with 600 participants also showed that 40% of Brownsville residents and 78% of Matamoros residents had a past dengue infection. Relevant mosquito larvae were found in 30% of households in both cities, they reported.

The *Aedes aegypti* mosquito that spreads this disease is now found throughout central and southern United States, he said.

Dr. David Morens and Dr. Anthony Fauci also described dengue and hemorrhagic fever as a potential public health threat to residents of the continental United States in a commentary in JAMA (2008; 299:214-6). Dr. Fauci is the director of the National Institute of Allergy and Infectious Diseases, where Dr. Morens is the dengue program officer.

"The range of *Aedes albopictus* ('Asian tiger mosquito'), a secondary dengue vector related to the classical vector, *Aedes aegypti*, has been expanding globally at an alarming rate. Since its introduction into the United States in 1985, *Aedes albopictus* has spread to 36 states," they wrote. "Worldwide, dengue is among the most important reemerging infectious diseases with an estimated 50 million to 100 million annual cases and, by WHO [World Health Organization] estimates, 22,000 deaths, mostly in children."

"We don't talk much about [dengue] in the United States, but we have it in our differential," said Dr. Patrick, chief medical officer and senior vice president for medical and academic affairs, Miami Children's Hospital.

In 1997-1998, there were 18 cases of

confirmed imported dengue reported in Florida, higher than the previously reported 10-year mean of 1.3 cases per year (MMWR 1999;48:1150-2).

The incubation period for dengue fever generally is 4-7 days after a mosquito bite (range, 3-14 days), with a characteristic high fever. "Temperature and the virus go hand in hand," Dr. Patrick said.

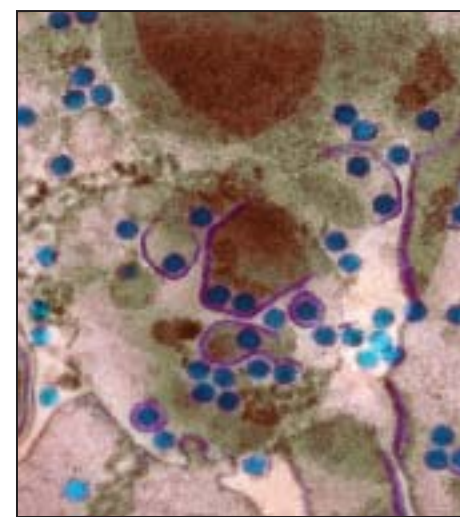
Infected patients also typically experience abrupt headaches, retrobulbar eye pain, marked muscle and joint pain, and a variety of rashes, both macular and maculopapular. Respiratory symptoms include cough, sore throat, and congestion; each is observed in approximately one-third of patients, he said.

A meeting attendee asked how Dr. Patrick would decide which patients to test. "There are a lot of patients who do not have dengue fever. But the retrobulbar pain is pretty distinctive." Epidemiology also is helpful, he said, and recommended testing any patient with a febrile illness who has traveled to a high-risk region within 2 weeks of presentation.

The differential diagnosis includes influenza, typhoid fever, malaria, measles, and rubella.

Diagnosis of dengue is mainly serology based. An IgM immunoassay is recommended, although the timing can be tricky. Most people present while acutely febrile, a time when the IgM serology usually is negative, Dr. Patrick said.

Leucopenia and thrombocytopenia also indicate dengue infection, as does transaminase values 2-5 times the upper limit of normal.



Micrograph shows dengue fever virus particles (blue) within a cell.

Dengue fever is the most common mosquito-borne viral disease. The *A. aegypti* mosquito is a daytime biter that resides near domestic areas. A secondary vector, the *A. albopictus* mosquito, is a more aggressive biter and is better adapted to colder environments. This characteristic may portend a shift in the epidemiology of dengue northward, Dr. Patrick said.

Vaccines to prevent dengue infection are in preclinical trials. Although an immunized person could have lifelong protection, dengue is an RNA virus with four distinct subtypes.

The CDC's "Protect Yourself from Mosquito Bites and Dengue" patient brochure can be downloaded free at www.cdc.gov/ncidod/dvbid/dengue.

Bubonic Plague Was Surprise Culprit

BY GREG MUIRHEAD
Contributing Writer

WAIKOLOA, HAWAII — An infamous, deadly disease that killed a large portion of the population of Europe in medieval times can still make rare and disruptive appearances in the modern emergency department.

Speaking at a symposium on emergency medicine sponsored by Stanford University, Dr. Diku P. Mandavia recalled the case of a 30-year-old woman admitted to a special part of the emergency department where very ill patients were placed.

"She's intubated," he recalled. "She's on three pressor agents. She's in frank sepsis. She's in shock. They're throwing the kitchen sink at her, as far as antibiotics—she's got four or five antibiotics. They still can't sort out what to do. Her chest and urine are clear. All the other suspects are clear."

The woman had been in the emergency department for 10 hours before she came to his attention, explained Dr. Mandavia, attending staff physician

at Cedars-Sinai Medical Center, Los Angeles. When he asked for the cause of the sepsis, a resident said that a deep abscess in the right axilla was suspected. The abscess had not yet been drained because of concerns about how deep it was, and that draining might cause injury.

Dr. Mandavia called for an axillary ultrasound to be done, after which he had the abscess drained and cultured.

"A lot of pus emerged," he remembered. "After draining, the patient went to bed in the ICU. This all happened by 3 p.m., Wednesday afternoon. At about 10:30 p.m. on Friday night, I get a phone call at home, and it's from a faculty [member] who never calls me."

The caller asked if he recalled the case of the septic woman whose abscess was drained; Dr. Mandavia said he did.

"She said, 'Guess what? You've been exposed to the plague!'" he recalled.

"You may know nothing about the plague," he said to his audience. "I knew nothing myself." Dr. Mandavia started

looking for information about it on the Internet, but "there's not a lot out there," he commented. "It's not an everyday diagnosis."

Dr. Mandavia called a couple of infectious disease experts who also didn't know much about it. Meanwhile, the hospital was in turmoil; the Centers for Disease Control and Prevention was involved, "and I'm an indexed case now," he said.

Meanwhile, Dr. Mandavia learned a crucial piece of information: There's a critical difference between the bubonic plague and the highly contagious disease it can convert to, called the pneumonic plague.

"Thank God she had the bubonic plague because if she had had the pneumonic plague, I would have been dead in 24 hours," Dr. Mandavia explained. "Everyone in the room would have been dead in 24 hours."

How did the patient get the bubonic plague? "This was a patient who had very, very poor hygiene in the house, and there were dead rodents and fleas," he explained.

Neuropsychiatric Events Added to Flu Drug's Label

BY ELIZABETH MEHCATIE
Senior Writer

Information about neuropsychiatric events associated with zanamivir in people being treated for influenza was added to the warnings and precautions section of the antiviral drug's label.

The addition reflects postmarketing reports of delirium and abnormal behavior in patients with influenza taking neuraminidase inhibitors, including zanamivir (Relenza, Glaxo-SmithKline). Some of the cases resulted in fatalities related to self-injurious behavior.

The addition is described in a Dear Healthcare Professional letter from GSK, and in a notice on the Food and Drug Administration's MedWatch site.

Most of the reports have been from Japan, primarily among pediatric patients, and events "often had an abrupt onset and rapid resolution," the revised labeling says. The label says that the contribution of zanamivir to these

events "has not been established" and points out that influenza also can be associated with various neurologic and behavioral symptoms, including seizures, hallucinations, delirium, and abnormal behavior, which in some cases can be fatal.

The incidence of these adverse events cannot be estimated because the reports were voluntary, "but they appear to be uncommon based on usage data for Relenza," the label says.

Neuropsychiatric events associated with zanamivir and the other available neuraminidase inhibitor, oseltamivir (Tamiflu), were discussed at a meeting of the FDA's Pediatric Advisory Committee, and the panel narrowly recommended revising the labeling for both drugs to include information about these events.

The letter is available at www.fda.gov/medwatch/safety/2008/safety08.htm#Relenza. Report adverse reactions to the FDA's MedWatch program at 800-332-1088 or www.fda.gov/medwatch.