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Double Threat: Researchers Find New Evidence Mosquitoes Could Infect Humans with Zika and Chikungunya Viruses at the Same Time

Second Study Links Three Mosquito-Borne Viruses—Zika, Chikungunya and Dengue—Currently Hitting Americas to Severe Neurological Problems

ATLANTA (14 November 2016)—Mosquitoes are capable of carrying Zika and chikungunya viruses simultaneously and can secrete enough in their saliva to potentially infect humans with both viruses in a single bite, according to new research presented today at the 2016 Annual Meeting of the American Society of Tropical Medicine and Hygiene (ASTMH).

The work by scientists from Colorado State University is one of several new Zika-related studies being presented at the world's largest gathering of tropical medicine experts, including probing the implications of having three mosquito-borne viruses—dengue, Zika and chikungunya—circulating in the Americas and parts of Asia at the same time. They include a new study from researchers in northeastern Brazil who documented an intriguing—and troubling—mix of neurological problems in patients treated during a rare and unprecedented outbreak of all three diseases in 2015.

Scientists are investigating whether antibodies to dengue can either intensify or, conversely, neutralize a Zika virus infection. Zika and dengue are closely related and come from the same family of viruses, known as flaviviruses. Very little is known about Zika's possible interactions with chikungunya, however, in humans or mosquitoes.

That's why researchers at a laboratory headed by Greg Ebel, ScD, at Colorado State University, are testing what happens in the *Aedes* variety of mosquitoes responsible for transmitting the viruses when they encounter more than one virus at a time. In a contained experiment, the scientists allowed mosquitoes to feed on blood that contained dengue, chikungunya or Zika, either alone or in combination. The tests so far show strong evidence that mosquitoes can pick up and transmit Zika and chikungunya simultaneously—something that had not been confirmed before, given the recent arrival of Zika in the Americas.

"Their saliva is clearly testing positive for both, which could mean that people bitten by this type of mosquito could be infected by both viruses at once," said Claudia Rückert, PhD who is presenting the results at the ASTMH meeting.

It's not clear if mosquitoes can carry all three viruses at the same time. But a previous study, also conducted in a laboratory setting, found that *Aedes* mosquitoes can carry dengue and

chikungunya simultaneously, an observation that was confirmed by the Colorado State research team. And the real-world opportunities for mosquitoes to encounter more than one of these viruses appear to be increasing. A recent study in Nicaragua revealed that about one in five patients who tested positive for dengue, chikungunya or Zika also had a co-infection with at least one of the other two diseases. Some even tested positive for all three.

“We need to understand more about what happens in both mosquitoes and people when all of these viruses are circulating in close proximity,” Rückert said.

She said the study also suggests that co-infection with chikungunya inhibits infection of Zika virus in the *Aedes aegypti* mosquito, meaning that one virus may outcompete another in mosquitoes, which could have an impact on the epidemiology of two mosquito-borne viruses circulating at the same time.

Sorting Out Neurological Problems When Zika, Dengue, Chikungunya Hit at Once

In a second study released at the annual meeting, researchers in Brazil presented new insights from their efforts to work in real-time to untangle a web of neurological complications encountered in a group of 21 patients at the Roberto Santos General Hospital in the northeastern city of Salvador-Bahia over a four-month period in 2015 during an “unprecedented and concurrent” outbreak of Zika, dengue and chikungunya.

Thus far, their evidence indicates that each disease may be linked to severe neurological problems, including a rare disorder seen in two patients called Opsoclonus-myoclonus-ataxia syndrome or OMS. It’s sometimes referred to as “dancing eyes-dancing feet syndrome” for the chaotic eye movements and muscle contractions it causes. One of those patients tested positive for Zika and dengue. But the other patient tested positive for chikungunya and dengue, though it’s been difficult to determine whether this “co-infection” was to blame.

“Our analysis shows that each of these viruses may have the potential to cause a range of neurological complications, some very severe, and patients should be monitored for symptoms,” said Isadora Siqueira, MD, PhD, a scientist with Brazil’s Oswaldo Cruz Foundation. “What’s very difficult to determine is whether having a co-infection with two of these viruses increases the risk of neurological problems. We are still looking closely at the case of the patient who was infected with both chikungunya and dengue.”

She and her colleagues were particularly surprised to encounter OMS, which globally occurs in about one in a million people. Seeing it around the same time in two unrelated patients in the same hospital is considered unusual. Dr. Siqueira said she and her colleagues are now investigating whether the problem was the result of an auto-immune disorder sparked by one of the viruses that caused the immune system to attack nerve cells, similar to what occurs in Zika patients who develop Guillain-Barré Syndrome.

Zika already is known to occasionally cause Guillain-Barré Syndrome (GBS), which prompts the immune system to attack nerve cells and can cause paralysis and even death. But Dr. Siqueira said they also saw GBS in patients who did not have Zika— but tested positive for either chikungunya or dengue.

Dr. Siqueira said there is also interest in learning more about how the presence of dengue antibodies might affect the course of a Zika infection in patients, given that the viruses share

many similarities. She said a large majority of people in the region of Brazil where Zika exploded have been infected with dengue in the past and carry antibodies to the disease.

“This kind of clinical research is essential so that we can better understand the true public health threat of these mosquito-borne viruses,” said Stephen Higgs, PhD, president of ASTMH.

“Tropical medicine scientists must continue to be vigilant on the front-lines of these outbreaks and provide new and beneficial insights for physicians around the world. It is great to have so many of our members involved, and to see the impact of their work.”

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About the American Society of Tropical Medicine and Hygiene

The American Society of Tropical Medicine and Hygiene, founded in 1903, is the largest international scientific organization of experts dedicated to reducing the worldwide burden of tropical infectious diseases and improving global health. It accomplishes this through generating and sharing scientific evidence, informing health policies and practices, fostering career development, recognizing excellence, and advocating for investment in tropical medicine/global health research. For more information, visit astmh.org.