Mosquitoes that spread Zika virus could simultaneously transmit other viruses

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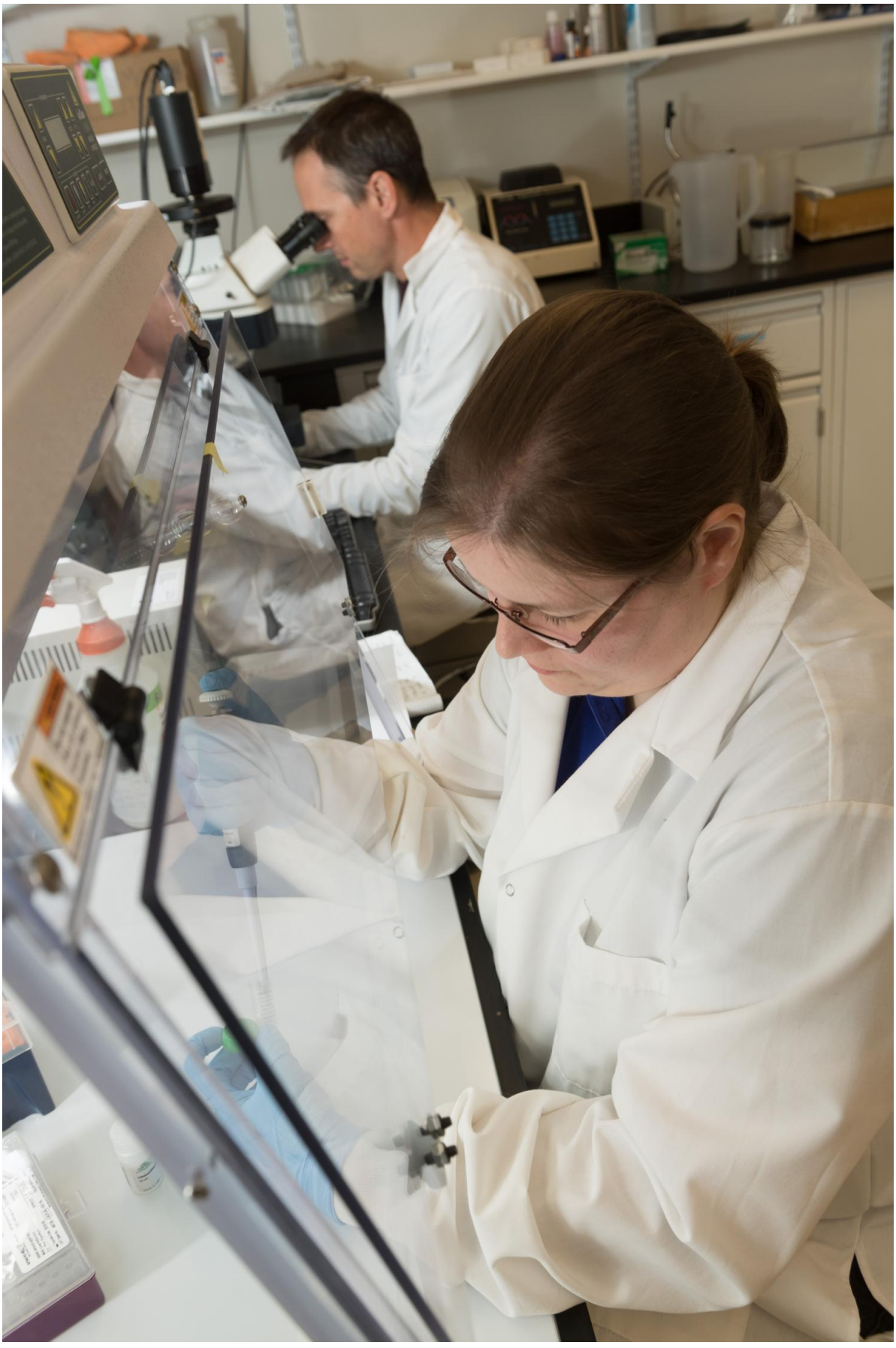


Researchers at Colorado State University infected mosquitoes in the lab with multiple kinds of viruses to learn more about the transmission of more than one infection from a single mosquito bite. Credit: John Eisele/CSU Photography

A new study led by Colorado State University researchers found that Aedes aegypti, the primary mosquito that carries Zika virus, might also transmit chikungunya and dengue viruses with one bite. The findings shed new light on what's known as a coinfection, which scientists said is not yet fully understood and may be fairly common in areas experiencing outbreaks.

"A mosquito, in theory, could give you multiple viruses at once," said Claudia Ruckert, post-doctoral researcher in CSU's Arthropod-borne and Infectious Diseases Laboratory.

Ruckert presented initial findings from the study last fall at the annual meeting of the American Society of Tropical Medicine & Hygiene in Atlanta, Georgia. The research team's paper was published May 19 in *Nature Communications.*

The CSU team infected mosquitoes in the lab with multiple kinds of viruses to learn more about the transmission of more than one infection from a single mosquito bite. While they described the lab results as surprising, researchers said there's no reason to believe that these coinfections are more severe than being infected with one virus at a time. Existing research on coinfections is sparse, and the findings are contradictory.

One, two, three viruses in one mosquito

Chikungunya, dengue and Zika viruses are transmitted to humans by Aedes aegypti mosquitoes, which live in tropical, subtropical, and in some temperate climates. As the viruses continue to emerge into new regions, the likelihood of coinfection by multiple viruses may be increasing. At the same time, the frequency of coinfection and its clinical and epidemiologic implications are poorly understood.

The first report of chikungunya and dengue virus coinfection occurred in 1967, according to the study. More recently, coinfections of Zika and dengue viruses, Zika and chikungunya, and all three viruses have been reported during various outbreaks, including the recent outbreak of Zika virus in North and South America.

Ruckert said the research team found that mosquitoes in the lab can transmit all three viruses simultaneously, although this is likely to be extremely rare in nature.

"Dual infections in humans, however, are fairly common, or more common than we would have thought," she said.

CSU researchers had expected to find that one virus would prove to be dominant and outcompete the others in the midgut of the mosquito where the infections establish and replicate before being transmitted to humans.

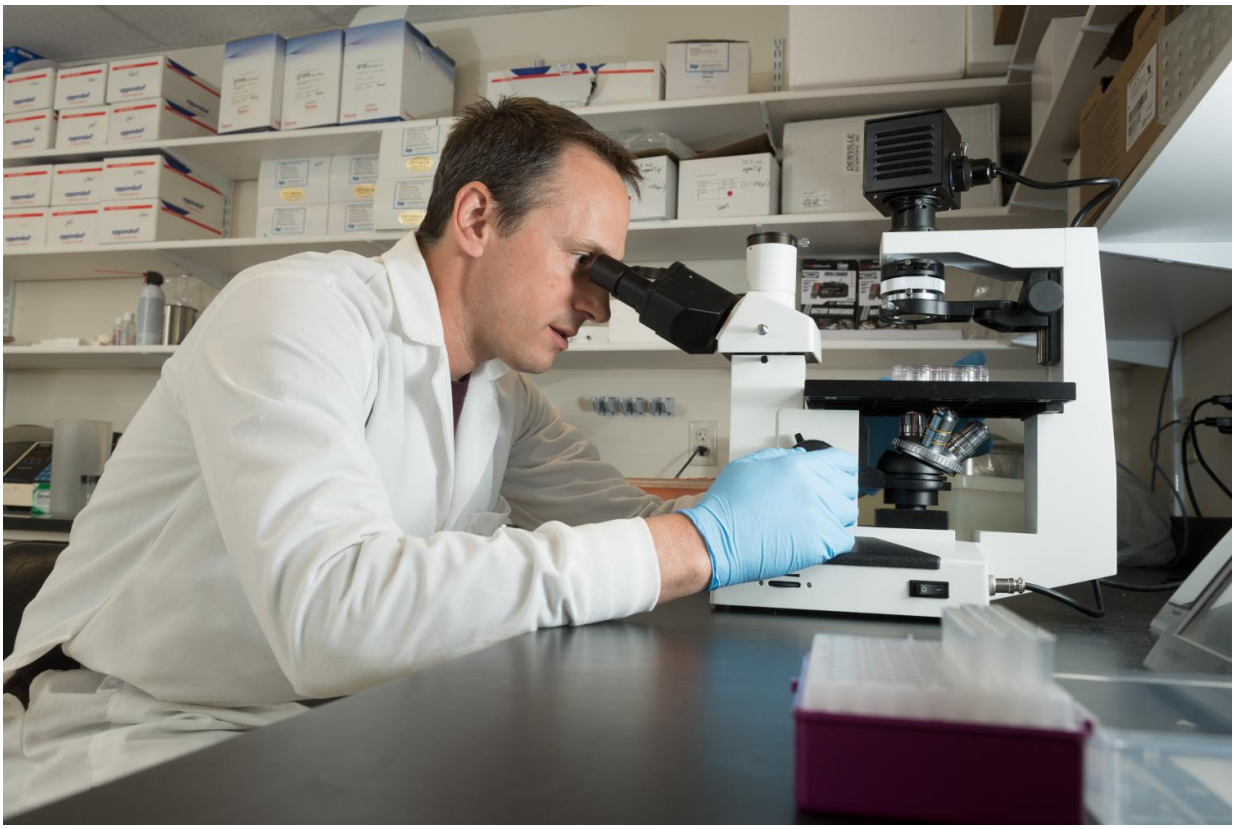
"It's interesting that all three replicate in a really small area in the mosquito's body," Ruckert said. "When these mosquitoes get infected with two or three different viruses, there's almost no effect that the viruses have on each other in the same mosquito."

Greg Ebel, director of the Arthropod-borne and Infectious Diseases Laboratory and co-author of the study, said the results were surprising.

"Based on what I know as a virologist, epidemiologist and entomologist, I thought that the viruses would either compete or enhance each other in some way," he said. "On the one hand, all of these viruses have mechanisms to suppress mosquito immunity, which could lead to synergy. On the other hand, they all likely require similar resources within infected cells, which could lead to competition. We didn't see much evidence of either one of these things in mosquitoes that were infected in the lab by multiple viruses."

Three viruses, similar symptoms

Zika virus typically results in symptoms similar to the flu and may be accompanied by a skin rash. Last year, however, concerns about the virus skyrocketed following the link between Zika virus infection with microcephaly in Brazil. Microcephaly is when a baby is born with a small head and incomplete brain development.



CSU's Greg Ebel said he thought that the viruses would either compete or enhance each other in some way, but that wasn't the case. Credit: John Eisele/CSU Photography

Concerns about Zika virus were also heightened following news that the virus could be transmitted sexually in addition to being spread by mosquitoes. Brian Foy, CSU associate professor in the Arthropod-borne and Infectious Diseases Laboratory, made that connection in 2008.

Dengue and chikungunya virus symptoms are similar to an infection with Zika virus, and can also include joint and bone pain, nose or gum bleeding and bruising.

No strong evidence coinfection poses serious threat to humans

What is the threat for people diagnosed with a coinfection?

"There's no strong evidence that coinfection of humans results in infections that are clinically more severe," Ruckert said.

But findings are contradictory. A team in Nicaragua looked at a large number of coinfection cases in one study, but saw no changes in hospitalization or clinical care. But other studies found a possible link between neurological complications and coinfection.

"There might be some indications, but it is still fairly unknown what the effect is from coinfection," said Ruckert.

It is also likely that coinfections in humans are significantly underdiagnosed.

"Depending on what diagnostics are used, and depending on what the clinicians think, they might not notice there's another virus," Ruckert said. "It could definitely lead to misinterpretation of disease severity."

Next steps for coinfection research

Ruckert and the team in the Ebel Lab are now taking a closer look at what happens when mosquitoes are infected with multiple viruses. They'll explore how a coinfection affects the evolution of viruses within the mosquito.

"We will study how these virus-mosquito interactions change when there are two viruses, what gets transmitted from a coinfected mosquito, and

how that differs from a mosquito infected with one virus," Ruckert said.

The team is also interested in learning more about where the viruses replicate in mosquitoes, and by potentially examining yellow fever, a fourth virus that is carried by Aedes aegypti, as a possibility for coinfection with chikungunya, dengue or Zika viruses.

Yellow fever virus is found in tropical and subtropical areas in South America and Africa. The Brazilian Ministry of Health reported an ongoing outbreak in December 2016.

It is a very rare cause of illness in U.S. travelers, according to the Centers for Disease Control and Prevention. But between 20 percent and 50 percent of people who develop severe illness related to yellow fever virus may die.

"A large urban outbreak of yellow fever virus in a tropical megacity is a terrifying prospect," said Ebel.

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