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[Dengue could be the surprise culprit making Zika worse, researchers say](#)

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Felipe Dana/AP

Angelica Pereira feeds her daughter, who was born with microcephaly, in Santa Cruz do Capibaribe, Brazil.

By [Helen Branswell](#) [@HelenBranswell](#)

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A surge in the number of [Zika virus](#) cases in tandem with a rise in cases of a severe birth defect is leading scientists to consider an intriguing possibility: Perhaps it's not just one causing the other.

Instead, some researchers are theorizing that Zika is contributing to an unexpectedly [high rate of side effects](#) because it is spreading in a population in which a large number of people have been previously infected with a closely related virus, dengue.

The theory — and it's only that right now — is that prior infection with one or more of the four dengue viruses may be contributing to a spike in Brazil's cases of neurological complications among some adults infected with Zika and cases of [microcephaly](#) — underdeveloped heads and brains — in some infants born to women infected with the virus during pregnancy.

Dengue — which, like Zika, is primarily transmitted by mosquitoes — is common in Brazil and other countries where Zika outbreaks have been occurring in the past couple of years.

Read more: [What you should know about the birth defect tied to Zika virus](#)

"It's an idea that's on the table at the moment. A number of people have been talking about it," Christopher Dye, director of strategy in the office of the director general of the World Health Organization, said in an interview.

Dr. Michael Diamond, an expert on viral immunology, told STAT that dengue experts are focused on the theory that the disease could be playing a role in Zika's apparent change in behavior. For decades the virus caused few human cases and the people who contracted it experienced only mild illness.

"I think it's in the back of all of our minds," said Diamond, who teaches at Washington University School of Medicine in St. Louis. "We don't know. But I think those of us in the field think it could."

A soon-to-be published study from French Polynesia, which [had a Zika outbreak in 2013-14](#), may support the idea. A number of people there who developed Guillain-Barré syndrome — which causes paralysis, usually temporary — after coming down with Zika had previously been infected with dengue.

Still, experts caution that the theory is only one of several. Others have mused that Zika virus has simply mutated over the past couple of years, causing it to behave differently than it has in the past.

Read more: [Can scientists outsmart the mosquitoes carrying Zika virus?](#)

Zika, which belongs to the flavivirus family, is closely related to the four dengue viruses. (The four dengue viruses are called serotypes.) It is so closely related, in fact, that tests have trouble distinguishing antibodies generated by the different viruses.

With some viruses — take influenza, for instance — exposure is easier to fight off when a person has already encountered a related virus. The antibodies a person's system already generated can help combat the new threat.

Dengue is a different beast. Infection with one of the types of virus will render a person immune against that type for life — but will offer no protection against the others. In fact, getting infected with a second type of dengue raises the risk that a person will develop severe disease — dengue hemorrhagic fever — which can be life-threatening.

The phenomenon is called antibody-dependent enhancement. Antibodies to the first dengue strain that a person encounters actually help a second dengue virus trigger worse disease.

If a person has the enormous bad fortune of experiencing three or four dengue infections, the risk starts to decline again. Diamond said the greatest risk of enhanced disease is seen with the second infection.

He outlined how this still-hypothetical scenario might work: Women with antibodies to dengue viruses might develop higher levels of virus in the blood if they contract Zika virus. Those higher levels of virus in the blood might allow Zika to occasionally cross the placenta into the fetus, and trigger infection that damages its developing brain.

"Certainly what we know about the interactions between dengue serotypes suggests that this kind of thing is not impossible in a virus of this sort," the WHO's Dye said.

Read more: [Scientists on remote island unravel Zika's mysteries](#)

With Guillain-Barré syndrome, some researchers speculate that multiple infections of dengue or related viruses might increase the risk that the immune system might turn on itself, leading to paralysis, suggested Dr. Carlos Pardo-Villamizar, a neurologist at Johns Hopkins School of Medicine in Baltimore, who has been working in Colombia on the Zika response there.

Diamond wonders whether the phenomenon might work in reverse — whether people who have contracted Zika and then go on to be infected with dengue might be at higher risk of having severe dengue infections.

If the theory about dengue compounding Zika's side effects turns out to be true, it will be good news for places — such as most of the continental US — where dengue viruses have not circulated. It would mean the risk posed by Zika might be lower than currently expected.

Public health authorities in the US have said local spread of Zika virus could occur in parts of the country where the right type of mosquitoes circulate. But they do not currently expect the large explosive type of outbreak being experienced across South and Central America and the Caribbean.



Alex Hogan/STAT

Zika virus, which can be transmitted by mosquitoes, has exploded onto the world stage.

Karen Weintraub contributed reporting.

Helen Branswell can be reached at helen.branswell@statnews.com
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