

In battle against Zika, researchers seek foolproof test for infection

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Transmission electron microscope image of negative-stained, Fortaleza-strain Zika virus (red), isolated from a microcephaly case in Brazil. The virus is associated with cellular membranes in the center. Credit: NIAID

The Zika virus has struck fear throughout the Americas, but determining whether people have been infected can be difficult.

Here's why: Most infected people don't display symptoms or they choose to tough out what may seem like nothing more than influenza instead of seeking medical help. Moreover, infected people don't have much detectable virus, and what's in the body doesn't linger.

There is no commercial [test](#) approved by the Food and Drug Administration to detect Zika infections, but the agency has given emergency-use authorization for 10 tests to be used by health officials in the meantime. But processing these tests takes time because they must be shipped to laboratories. In addition, there are concerns about accuracy - one test, developed by the federal Centers for Disease Control and Prevention, which looks for antibodies to the virus, has been plagued by false-positives. It often shows infection by the Zika virus when the culprit is really a closely related microorganism from the same family.

Researchers are seeking to streamline the process. Among them is Robert Garry, a Tulane University virologist who has been working for the past six months to develop a test that doesn't look for the virus but, like the CDC-developed process, searches for the immune system's reaction to it. Unlike the existing procedures, he said, "we're trying to put together a test that anybody could use" and process within 20 minutes without having to use a lab.

The procedure Garry and his colleagues want to develop will look for antibodies because, Garry said, they stay in the body longer, especially in urine.

"The virus goes away quickly, but the damage can be done," said Garry, a professor of microbiology and immunology.

According to the CDC, Zika antibodies show up in the blood four to five days after the onset of illness and can last 12 weeks - or longer.

Garry said the CDC's test looks for immunoglobulin M, or IgM, antibodies that show up relatively early in an infection.

"They wouldn't detect a longer-term infection," said Garry, adding that the test he and his colleagues want to develop would find antibodies that appear later.

The Zika virus, which now has a foothold in the United States after sweeping through Brazil and other Latin American countries, is most commonly spread by mosquitoes but can also be transmitted via blood, sexual contact and by mother to fetus.

The CDC has logged more than 2,900 cases in the United States and since July reported cases in Florida that were likely caused locally by mosquito bites. Nearly 16,000 cases have been reported in U.S. territories, primarily Puerto Rico.

Symptoms can include fever, rash, joint and muscle pain, and nausea, but most [infected people](#) may not realize they have the virus. There is no specific medicine or vaccine. The CDC recommends rest and plenty of fluids.

The virus is most dangerous when transmitted to a pregnant woman because it can cause microcephaly, a condition in which the brain does not develop properly in the fetus, resulting in a smaller-than-normal head.

In addition to the CDC's antibody-detection test, which is known as Zika MAC-ELISA, another test from the CDC is designed to distinguish the Zika virus from closely related microorganisms that cause dengue and

chikungunya.

In both, a specimen of blood, urine or other fluid from the body is put onto a plastic plate and subjected to several hours of incubation and washing, followed by the addition of a reagent that will produce a color pattern. An instrument that measures colors is then used to confirm the presence of the virus, said Randall Kincaid, the senior scientific officer at the National Institute of Allergy and Infectious Diseases.

The turnaround time on each should be about a day, he said.

"It isn't my favorite or anyone's favorite type of an assay," Kincaid said, "but it's what the CDC had available as a template for evaluating infections by endemic virus."

Acknowledging that this takes time, Kincaid said, "If your concern is knowing that you've been infected, you're willing to sacrifice a day to get the most reliable answer."

The other procedures also use blood and other body fluids to look for the Zika virus's RNA, a molecule that is important to genetic expression. Each test, Kincaid said, teases out the virus - if it's there. The result should be available within hours.

The confidence in these tests is "quite different, based on the virological truths that underlie these tests," Kincaid said.

The research is still relatively new, Garry said, so it may take time for articles to appear in peer-reviewed journals.

Like other Zika-detection tests, Garry said the device he is working on would be similar to a pregnancy test. Blood or urine would be put on a plastic sheet or in a cassette that would show the results.

Results would be ready within 20 minutes without resorting to a lab, he said.

So far, results have been "promising," according to Garry, but he and his colleagues are still working to rule out what is known as cross-reactivity, in which the test reacts to a virus similar to the one that causes Zika.

The Zika virus is a flavivirus, a member of a gene that includes the viruses that cause West Nile fever, dengue fever and yellow fever.

Garry said he hopes to have a test ready in a few months and then apply for emergency-use authorization from the FDA.

He said he is aiming for a test that would provide results quickly and could be used in what he called "low-resource settings," where a clinic or laboratory might not be available.

"That's something we'd love to have access to in the best of worlds," Kincaid said, because it would become easier to administer the tests in areas where the virus is endemic but access to health care is, at best, scarce.

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