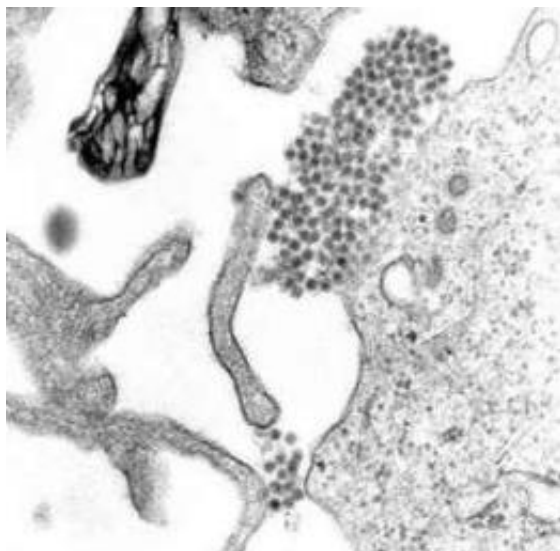


New evidence shows second dengue infection can be more severe due to antibody levels

3 November 2017, by Bob Yirka



A TEM micrograph showing Dengue virus virions (the cluster of dark dots near the center). Image: CDC

(Medical Xpress)—A team of researchers from the U.S. and Nicaragua has found evidence that suggests people infected a second time by the dengue virus may experience a more severe form of dengue fever if their antibody levels are at a certain level. In their paper published in the journal *Science*, the team describes their study of the disease in children in Nicaragua over the course of 12 years and what they found.

Dengue fever is a malady caused by infection of the [dengue virus](#). On first infection, most people have relatively minor symptoms—fever and muscle and joint pain. For many people, a second infection is similar to the first, but for a third group, a second infection can cause what has come to be known as [dengue hemorrhagic fever](#) or [dengue shock syndrome](#) (DHF/DSS). This form is much worse for the patient, as symptoms include loss of bodily fluid due to blood leaking from vessels, which in

turn can lead to organ failure and possibly death. Health scientists have had difficulty agreeing on the cause of DHF/DSS, though some suggested it relates to the level of antibodies produced and maintained after the initial infection. In this new effort, the researchers have found evidence supporting this theory.

Antibodies are blood proteins that the body produces to battle specific antigens. To determine if, indeed, they play a role in dengue infections, the researchers took blood samples from 8,000 children ages two to 14 every year over the course of 12 years in Managua—each sample was tested for antibody levels. This allowed the researchers to monitor levels in children who were not infected, children who were, and children who were infected more than once. By comparing antibody levels in children that developed DHF/DSS to those who did not, the researchers were able to spot a trend—those children who had neither high nor low antibody levels did not develop the more severe reaction—it was those children who had medium levels. In fact, for this group, levels were approximately 7.64 times higher.

The researchers acknowledge that their results are just a first step in proving that [antibody levels](#) are the true cause of more severe bouts of [dengue fever](#), but also suggest their findings may soon lead to requirements that new vaccines not be given to [children](#) with medium levels of antibodies for fear that the shot might set off DHF/DSS.

More information: Leah C. Katzelnick et al. Antibody-dependent enhancement of severe dengue disease in humans, *Science* (2017). DOI: [10.1126/science.aan6836](https://doi.org/10.1126/science.aan6836)

Abstract

For dengue viruses (DENV1-4), a specific range of

antibody titer has been shown to enhance viral replication in vitro and severe disease in animal models. Although suspected, such antibody-dependent enhancement (ADE) of severe disease has not been shown to occur in humans. Using multiple statistical approaches to study a long-term pediatric cohort in Nicaragua, we show that risk of severe dengue disease is highest within a narrow range of pre-existing anti-DENV antibody titers. By contrast, we observe protection from all symptomatic dengue disease at high antibody titers. Thus, immune correlates of severe dengue must be evaluated separately from correlates of protection against symptomatic disease. These results have implications for studies of dengue pathogenesis and for vaccine development, because enhancement, not just lack of protection, is of concern.

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APA citation: New evidence shows second dengue infection can be more severe due to antibody levels (2017, November 3) retrieved 6 August 2022 from <https://medicalxpress.com/news/2017-11-evidence-dengue-infection-severe-due.html>

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