

Team develops better way to detect causes of deadly childhood diarrhea

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Researchers at the University of Virginia School of Medicine have developed an important new diagnostic approach to determining the cause of diarrhea in the developing world, revealing a problem even more complex than previously appreciated. The new approach is set to have enormous impact on vaccine development and is already prompting researchers to reevaluate the effectiveness of existing vaccines.

The approach uses a panel of molecular diagnostic assays to pinpoint the cause of the all-too-common illness, the second-leading cause of death in children younger than 5 worldwide. Often, the researchers have discovered, a child's symptoms have more than one cause.

"We found [diarrhea](#) was caused by multiple infections more often than was appreciated before – often there were two, three or four infections on top of each other," said Dr. Eric Houpt, a professor of medicine in U.Va.'s Division of Infectious Diseases and International Health.

He noted that the new panel of assays offers improved diagnostic ability over the traditional approach. "The old methods missed infections a lot of times," he said. "There was more *Shigella* and toxin-producing *E. coli* than previously seen. It's as though we are now able to see with glasses."

Perhaps even more importantly, the new approach offered invaluable insights into how severe an [infection](#) needed to be to cause symptoms. "Our methods were able to not just detect infections, but quantify how much was there, and that proved to be critical," Houpt said. "In these

impoverished parts of the world, there's enormous exposure to different bacteria, viruses and parasites, and you can find low amounts with these sophisticated methods. We were able to figure out the right amount above which it becomes clinically relevant – that is, that it's the likely cause of diarrhea."

The researchers have already put their new approach to the test, deploying it across three platforms to five institutions around the world – two in Africa and three in Asia. The approach proved more sensitive and less expensive than traditional testing, while providing more holistic information about the causes of childhood diarrhea.

The new approach could be useful for other illnesses as well. "It's not just for diarrhea. We are applying it to other infectious diseases as well," said Jie Liu, an assistant professor of [infectious diseases](#) and international health and the lead author of a new paper outlining the approach and the results of its testing. "We look forward to expanding this into a bigger study."

She noted that there are already at least three studies using or planning to use the new approach to reevaluate vaccine effectiveness, as researchers may have wrongly assumed that a vaccine failed when the illness was actually being caused by another pathogen.

"With conventional methods, they all have different sensitivities and specificities. It's hard to compare the pathogens in one sample when there is a co-infection," Liu said. "With the molecular methods, it's an even playing field, so we can compare the quantities [of pathogens] to determine which is the likely cause."

The new approach has important applications in the U.S. as well, offering an easy way to detect pathogens without the need to run multiple tests for specific types.

The article has been published online by the journal *Lancet Infectious Diseases* and will appear in a forthcoming print edition.

The authors include U.Va.'s Liu, Jean Gratz, Steve M. Becker, Darwin J. Operario, Mami Taniuchi, Lalitha Janaki, James A. Platts-Mills, Doris M. Haverstick and Houpt, in collaboration with colleagues in Pakistan, Gambia, Thailand, Bangladesh and Tanzania.

Provided by University of Virginia

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