

Outbreak of paralyzing disease linked to non-polio enterovirus

January 22 2019

The Translational Genomics Research Institute (TGen), an affiliate of City of Hope, has identified a polio-like virus as a potential cause of an outbreak of a disease known as Acute Flaccid Myelitis (AFM), a crippling condition that causes muscle weakness and paralysis usually among children.

At the request of Arizona and Maricopa County health officials, TGen was tasked with trying to identify the microbial cause of the outbreak of AFM among as many as 11 patients at a Phoenix-area hospital in September 2016.

Using multiple genomic sequencing tests, TGen identified a specific non-polio enterovirus—EV-D68—among at least four of the children, according to a study published today in the scientific journal *mBio*. The finding is significant because AFM cases are continuing to increase and there has been no official recognition that this disease is being caused by EV-D68, which limits the research community's ability to develop preventative measures, such as new vaccines.

"We clearly identified the presence of EV-D68 virus in the confirmed AFM patients," said Dr. David Engelthaler, Co-Director of TGen's Flagstaff-based Pathogen and Microbiome Division, TGen North, and the study's senior author.

Since there are no available tests for diagnosing EV-D68, TGen needed to apply numerous cutting-edge genomic analyses to different samples to

help unravel the mystery.

"The results of this investigation significantly add to the growing body of evidence that AFM is associated with EV-D68 infection," Dr. Engelthaler said.

AFM is a neuromuscular disorder that involves the spinal cord and messaging signals between the brain and muscle nerve cells. Symptoms include loss of muscle reflexes in arms and legs, resulting in a polio-like paralysis, but also include face drooping and respiratory failure.

Outbreaks of AFM in the U.S. since 2014 have come as the U.S. Centers for Disease Control and Prevention (CDC), and the World Health Organization (WHO), are on the verge of eradicating poliovirus. In the early 1950s, polio afflicted as many as 15,000 children a year in the U.S.

Since the first polio vaccines were developed in 1955, the number of polio cases in the U.S. has dropped to zero. And, once numbering in the hundreds of thousands, the number of cases worldwide has dropped dramatically to the point that the disease has nearly been wiped out. Only 22 cases were reported worldwide in 2017, and the virus is now only found in two countries.

"The impending eradication of polio is one of the great achievements of human history," Dr. Engelthaler said. "The current AFM outbreaks are a stark reminder, however, of the need for ongoing excellence in public health, medicine and research."

For AFM, there is no confirmed cause, no vaccine and limited ways to diagnose or treat the disease. According to the CDC, it is unknown why most children recover from enteroviruses, yet a small number develop AFM. The CDC has definitively ruled out the poliovirus as the cause of AFM. And, AFM remains rare, annually affecting fewer than 1 in 1

million children in the U.S.

"As a result of this study, we developed novel EV-D68 tests that now can be used for other investigations, and for larger-scale surveillance to better understand the spread of EV-D68 and its linkage to AFM," said Dr. Jolene Bowers, a Research Assistant Professor at TGen North, and the study's lead author.

Also contributing to this study were: Northern Arizona University, the Maricopa County Department of Public Health, and the Arizona Department of Health Services.

More information: Jolene R. Bowers et al, Genomic Analyses of Acute Flaccid Myelitis Cases among a Cluster in Arizona Provide Further Evidence of Enterovirus D68 Role, *mBio* (2019). [DOI: 10.1128/mBio.02262-18](https://doi.org/10.1128/mBio.02262-18)

Provided by The Translational Genomics Research Institute

Citation: Outbreak of paralyzing disease linked to non-polio enterovirus (2019, January 22) retrieved 18 April 2024 from <https://medicalxpress.com/news/2019-01-outbreak-paralyzing-disease-linked-non-polio.html>

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