NIAID Pandemic Autopsy Study Fosters Long COVID Treatment Trial

Early findings of widespread, long-lasting virus helps inform long COVID research.

December 14, 2022 By National Institute of Allergy and Infectious Diseases

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Autopsies of 44 people who died from COVID-19 in the first year of the pandemic showed researchers that disease-causing SARS-CoV-2 virus spread throughout the body – beyond just a respiratory disease – and remained in tissue for months.

The study, from the National Institutes of Health and published in Nature, helped scientists broaden their perspectives on where SARS-CoV-2 could cause infection and persist, including the brain. The work also supported the rationale for a clinical trial evaluating the antiviral drug Paxlovid for the treatment of post-acute sequelae of COVID-19, also known as Long COVID.

Findings from the autopsies, which took place between April 2020 and March 2021, confirmed that SARS-CoV-2 primarily infected and damaged the airway and lungs. But scientists also found virus fragments (viral RNA) in 79 of 85 body locations, with some virus found up to 230 days after patient's symptoms began. Scientists found virus in cardiovascular, lymphoid, gastrointestinal, renal, endocrine, reproductive, muscle, brain and other tissue – although none of these areas sustained significant inflammation compared to what they found in the respiratory tract.

Scientists from NIH's National Institute of Allergy and Infectious Diseases and Clinical Center led the work, closely collaborating with National Cancer Institute (NCI) pathologists, four other NIH institutes, the University of Maryland, and Maryland health care facilities in Salisbury and Towson.

"We show SARS-CoV-2 disseminates across the human body and brain early in infection at high levels and provide evidence of virus replication at multiple extrapulmonary sites during the first two weeks following symptom onset," their study states. Virus can spread throughout the body and viral RNA may remain detectable for months even in cases with mild or no symptoms, they say.

Senior study author Dr. Daniel Chertow said prior to the work, "the thinking in the field was that SARS-CoV-2 was predominantly a respiratory virus." Finding the viral fragments in tissue throughout the body – and sharing those findings with colleagues a year ago – helped scientists explore a relationship between the viral fragments and long COVID.

Long COVID gets its name from the persistent symptoms some people experience after having COVID-19; symptoms can be debilitating, and the cause is not known. Though the study in Nature did not specifically explore long COVID, finding the viral RNA throughout the body raised speculation that those fragments might contribute to the persistent symptoms, according to Dr. Chertow. Treating people with an effective COVID-19 antiviral such as Paxlovid could, therefore, eliminate the persistent symptoms.

The Paxlovid trial, now underway at Duke University, is part of the NIH-funded RECOVER project – Researching COVID to Enhance Recovery – and includes an extension of the autopsy work, according Dr. Stephen Hewitt of NCI, who collaborated on the paper in Nature, and serves on a steering committee for the RECOVER project.

He said one branch of RECOVER includes tissue pathology studies, and obtaining material from autopsies is in progress; these autopsies include people who both were vaccinated and infected with variants of concern – data not available in the earlier study that Dr. Chertow's group led.

"We're hoping to replicate the data on viral persistence and study the relationship with Long COVID," Dr. Hewitt said, adding that the project is scheduled to last four years. "Less than a year in we have about 85 cases, and we are working to expand these efforts."

This blog post was originally published by the National Institute of Allergy and Infectious Diseases on December 14, 2022.
