# Study uncovers two phases of infection in patients with severe COVID-19 pneumonia

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What does SARS-CoV-2, the virus that causes COVID-19, do once it enters a person's airways, and how does infection in lung cells affect patients' immune responses? New research led by investigators at

Massachusetts General Hospital (MGH) and published in *Nature Communications* provides insights that could help improve treatment strategies for infected patients.

To analyze SARS-CoV-2 at the tissue level, the scientists examined autopsied material from 24 patients who succumbed to COVID-19. "We used a method called RNA in situ hybridization to visualize the actual SARS-CoV-2 virus in human lung specimens. This assay is now a clinical test being used at MGH to understand what tissues can be infected by the virus," explains co-author David T. Ting, MD, associate clinical director for Innovation at the Mass General Cancer Center and an assistant professor of Medicine at Harvard Medical School.

The analyses revealed two phases of infection in patients with severe COVID-19 pneumonia. The early phase is defined by high levels of virus in the lungs that trigger patients' cells to express genes involved with the interferon pathway, a critical part of the immune response. In the later phase, virus is no longer present, but the damage to the lungs is too severe for recovery.

"The interferon response to SARS-CoV-2 indicates that people's immune systems are able to attack SARS-CoV-2, but the response is variable between patients and even in different parts of the lung of the same patient, making a 'one drug fits all' therapy approach difficult," says Ting. Also, treatments that target viral replication, such as remdesivir, may only be effective in the early phase of infection.

The team also found that there is surprisingly very little viral replication in the lungs, which suggests that the virus is mostly replicating in the nasal passages and then dropping into the lungs, where it can cause pneumonia and other complications.

It will be important to conduct additional autopsy analyses to better

understand the extent and timing of SARS-CoV-2 infection in the lungs and other tissues, which could lead to improved treatment strategies for patients with COVID-19.

**More information:** Niyati Desai et al, Temporal and spatial heterogeneity of host response to SARS-CoV-2 pulmonary infection, *Nature Communications* (2020). DOI: 10.1038/s41467-020-20139-7

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