

Ongoing 'immune injuries' might cause persistent breathlessness after COVID-19

March 9 2022, by Emily Head



Credit: Nataliya Vaitkevich from Pexels

Long-lasting immune activity in the airways might be the cause of persistent breathlessness following COVID-19.

This is according to a new study of 38 people who were previously hospitalized with severe COVID-19.

The results, published in *Immunity*, suggest these patients have an altered landscape of [immune cells](#) in their airways and signs of ongoing lung damage. However, the preliminary results hint that this might improve over time.

The researchers say that their findings need to be confirmed by a larger study, but suggest that recovery from COVID-19 might be accelerated by treatments that dampen the [immune system](#) and reduce inflammation.

Joint lead author, Dr. James Harker, from Imperial's National Heart & Lung Institute, said: "Our study found that many months after SARS-CoV-2 infection, there were still abnormal immune cells in the airways of patients with persistent breathlessness. We also identified a protein 'signature' in the lungs indicating ongoing injury to the airways."

Joint senior author, Professor Pallav Shah, also from Imperial's National Heart & Lung Institute, said: "These findings suggest that persistent breathlessness in our group of COVID-19 patients is being caused by failure to turn off the immune response, which leads to airway inflammation and injury. The next steps of our research will be to see if there are treatments that can reduce the [immune activity](#) and whether they help to reduce the persistent breathlessness some patients experience."

Previous studies have examined the causes of post-COVID-19 breathlessness by looking at markers in the blood, but the new study looks directly at which immune cells are active in the lungs too.

Lung scan discovery

The researchers studied CT scans of the lungs and how well the lungs functioned, as well as analyzing samples of fluid from within the lungs and blood samples to determine the presence of nearly 500 proteins.

Overall, the study included 38 post-COVID-19 patients three to six months after they left hospital and 29 healthy volunteers (who had no underlying diseases and had not had COVID-19) to compare against.

At three to six months, the researchers found that there were more immune cells in the lungs of the post-COVID-19 participants than in the healthy controls. However, there appeared to be no difference in the immune cells seen in the blood of the post-COVID-19 and the healthy participants.

Co-author, Dr. Bavithra Vijayakumar, also from Imperial's National Heart & Lung Institute, said: "Other research has found that the immediate response to COVID-19 involves an uptick in various types of immune cells in the blood and in the lungs to fight the virus. For severe infections, like those seen in our study participants, there also tends to be heightened signs of inflammation.

"However, after three to six months, it appears that these signs in the blood return to normal, while those in the lungs take longer to resolve. Our finding that the [immune response](#) in the blood doesn't appear to match that of the lungs emphasizes the importance of assessing airway immunity in order to better understand persistent respiratory symptoms post COVID-19."

Although the immune cells in the lungs varied for each post-COVID-19 patient, they all tended to have higher levels of immune cells linked to cell death, epithelial damage and tissue repair.

There also appeared to be distinct roles for the different immune cells in

the lungs. For example, higher numbers of cytotoxic T cells led to damage to the lung tissue and greater [airway](#) dysfunction, while having more B cells was associated with greater signs of lung abnormalities on CT scans (such as scarring and physical changes in the lung tissue).

A group of 17 post-COVID-19 participants were re-assessed a year after they had left hospital, and 14 of them saw improvements in their symptoms and fewer lung abnormalities on CT scans. The other three participants still showed [lung](#) abnormalities on CT scans, but the numbers of immune cells present in their airways was greatly reduced compared to their earlier assessments. The researchers say that this suggests that these immune responses may improve over time.

Unclear impact for less severe disease

The authors note that their study includes patients who had severe COVID-19 disease (requiring hospitalization and ongoing monitoring) and it is unclear if their results would apply to people with less severe disease. They were only able to study the participants' lungs after COVID-19, and so are unable to determine if any of the signs they discovered were present before infection.

They note that the participants of their study had COVID-19 before vaccines were available.

More information: Bavithra Vijayakumar et al, Immuno-proteomic profiling reveals aberrant immune cell regulation in the airways of individuals with ongoing post-COVID-19 respiratory disease, *Immunity* (2022). [DOI: 10.1016/j.immuni.2022.01.017](https://doi.org/10.1016/j.immuni.2022.01.017)

Provided by Imperial College London

Citation: Ongoing 'immune injuries' might cause persistent breathlessness after COVID-19 (2022, March 9) retrieved 26 April 2024 from <https://medicalxpress.com/news/2022-03-ongoing-immune-injuries-persistent-breathlessness.html>

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