

New perspective on stress pandemics and human resilience from the analysis of COVID-19

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A new analysis of the effects of SARS-CoV-2, the virus causing the current pandemic, on the human body has provided novel insights into the nature of resilience and how we deal with stressful situations. Using COVID-19 as an example, the findings provide a new framework that may be central to managing this disease, minimize the likelihood of ferocious viral outbreaks in the future and deal with other major stresses.

"COVID-19 has been a huge burden on society at all levels. Whilst the prospects are improving in countries with efficient vaccination schemes like the UK, the virus is still present, and new variants continue to pose considerable risks. Moreover, there are sustained effects such as Long COVID and the mental health burden of the pandemic to overcome," Martin Feelisch, Professor of Experimental Medicine and Integrative Biology at the University of Southampton explained.

"By analyzing and re-ordering the information available in the literature we aimed to offer a systems-level view on the disease within a single

framework that provides a coherent picture about the way this infection stresses the [human body](#)."

The research team involving physicians, chemical biologists and an authority on [human nutrition](#), looked at COVID from a higher level than just a disease affecting the lungs and considered how the whole body deals with the various stresses the virus causes when viewed through the lens of electron exchange (also known as 'redox') processes. Electron exchange reactions are the foundation of all Life on Earth, underpinning human physiology and our ability to react to changes in demand and environmental conditions. While change is healthy in principle, some people experience unfavorable consequences when a major stress such as a viral infection is added to the stresses of daily life. What happens when such stresses act together is not yet fully understood, and COVID-19 was used as an example to look at the consequences of those interactions.

"COVID can present as a severe lung infection in one person while producing only minor symptoms in others, although it may have affected several other organs by then already. Arriving at a better understanding of how the body deals with different stresses while maintaining an appropriate redox balance would put us in a better position to treat patients acutely, protect the rest of the population and control disease spread. While the current vaccination success story is encouraging, emerging virus mutants show the threat continues, and we need to be better prepared in the future," Prof Feelisch continued.

Their analysis, published in the leading journal *Antioxidants & Redox Signaling*, revealed three key areas in the body's ability to cope with the stress of viral infections:

Firstly, nutrition emerges to be of utmost importance in maintaining the necessary redox balance and provide one's metabolism with the flexibility to adjust and combat the damaging effects of viral infection on cells and tissues. It also explains the greater susceptibility to disease in more deprived areas of the country because low income increases the risk for poor nutrition.

The second key finding was the importance of the endothelium—the inner lining of blood vessels that provides organs with oxygen and nutrients—in particular, a highly fragile layer on its surface that regulates nutrient/fluid exchange and protects blood cells from coming into close contact with the vessel wall. The research team have found that the crucial regulatory function performed by the endothelium has not been fully recognized in existing research and may also be essential to understanding the effects of Long COVID, where the body does not get back to its normal balance. They advise that routine monitoring of this cell layer in a non-invasive fashion, such as from under the tongue, may provide valuable insight into this and other stressful process and guide therapeutic approaches.

The final key observation was the role played by [small molecules](#) known as 'gasotransmitters.' These are used by all cells to sense changes in their environment and adapt. These molecules are part of a body-wide system that uses circulating blood as a communication highway to inform other organs how to best respond to the mixture of stresses experienced by other parts of the body, for example how to ramp up the metabolism in the liver to deal with an infection of the lung. Of all the molecules involved, nitric oxide appears to be fundamental in protecting the overall redox system.

Professor Feelisch concluded, "We need to make best use of the opportunity the current crisis has given us to learn more about how the body and individual cells deal with stresses. Our holistic framework should be interpreted as a 'call to action' and encourage investigators around the world to study whole-body redox regulation, find ways to monitor redox status and identify factors that are critical for health and resilience. The next pandemic could be just around the corner and if we do not

learn from current events, chances are we will face the same problems all over again."

More information: Andrew F Cumpstey et al, COVID-19 – A Redox Disease What a Stress Pandemic Can Teach Us About Resilience and What We May Learn from the Reactive Species Interactome About its Treatment, *Antioxidants & Redox Signaling* (2021). [DOI: 10.1089/ars.2021.0017](https://doi.org/10.1089/ars.2021.0017)

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