

Researchers outline strategy for testing ketone bodies against COVID-19

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Given the disproportionate impact that COVID-19 has on older adults in terms of death and lasting disability, and the impact of common aging-related comorbidities like diabetes and cardiovascular disease, Buck

Institute professor and practicing geriatrician John Newman, MD, Ph.D., can make a compelling argument that those infected with the SARS-CoV2 virus are suffering from an aging-related disease, no matter how old they are when they get infected. In a review published in *Med*, a Cell Press journal, Newman and a consortium of colleagues encourage researchers studying aging, metabolism, and immunity to turn their attention to ketone bodies, which are being widely studied for their roles in aging and aging-related diseases. The research team views ketone bodies as a possible therapeutic against COVID-19, seasonal flu and other respiratory infections.

Ketone bodies are compounds naturally produced during fat metabolism. They provide energy to cells and can also reprogram cellular functions. Eating a [ketogenic diet](#)—which is high fat, low protein, and low carbohydrates—ramps up the production of the primary ketone beta-hydroxybutyrate acid (BHB).

While the purported and reported benefits of eating the strictly controlled diet have made ketogenic-related food products and supplements wildly popular, Newman, senior author of the review, is quick to point out that there is much unknown about the biology of BHB and the physiology of how it impacts various systems in the body. "I want to be clear that there is no evidence that a ketogenic diet is protective in any way against COVID-19," he said. "In fact there may be instances where BHB could promote viral replication of SARS-CoV2, the specific virus that causes the disease. But given the promise that BHB shows against many of the age-related risk factors for COVID-19 such as heart disease and diabetes we want to take advantage of this unique opportunity to bring geroscience to the fight against COVID-19."

Small [clinical trials](#) in humans have shown proof-of-concept that BHB can improve cardiac function in those with heart failure and improve key

aspects of cognitive health. In the laboratory setting BHB shows promise against type 2 diabetes and dampens harmful inflammation. Elevation of blood ketones has been shown to be broadly protective against hypoxia-related tissue damage, which occurs in severe respiratory infections.

Doctors at Johns Hopkins University plan on testing a ketogenic diet on a small group of intubated patients suffering from COVID-19. The hope is that the diet will improve oxygen exchange, reduce the duration of time on ventilators and perhaps most importantly, reduce the systemic inflammation that leads to the cytokine storm that often proceeds the development of acute respiratory distress syndrome.

"Basic research shows that BHB directly inhibits the activation of the pro-inflammatory pathway NLRP3, which is central to the disease pathogenesis of COVID-19 and is a likely contributor to the cytokine storm," said Brianna Stubbs, Ph.D., a Buck researcher with expertise in ketone biology and lead author of the review. "Understanding how BHB impacts innate immunity following infection is one of the key preclinical questions we hope researchers will be eager to tackle."

"Dying is not the only bad outcome from COVID-19," says Newman. "Some survivors are presenting with long-term severe memory impairments, extreme exhaustion and weakness from muscle wasting following an extended time in the hospital." Pointing out the fact that BHB and other ketones act on multiple systems in the body, the authors are hoping for [clinical studies](#) that test ketone supplementation as a way to bolster muscle function and attenuate or avoid delirium among those who have been infected. Key preclinical and clinical questions are included in the review and are detailed at www.impactmetabolism.org.

"Age-related risk factors are putting [older adults](#) at particular peril for COVID-19. Those that survive it, no matter what their age, can emerge with symptoms that are associated with aging," said Newman. "Studying [ketone bodies](#) in this current environment not only holds promise in the

fight against COVID-19, but the research is also likely to yield results that could help all of us live better longer in the absence of a pandemic."

More information: Brianna J. Stubbs et al, Investigating Ketone Bodies as Immunometabolic Countermeasures against Respiratory Viral Infections, *Med* (2020). [DOI: 10.1016/j.medj.2020.06.008](https://doi.org/10.1016/j.medj.2020.06.008)

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