## **BRIEF19**

A daily review of covid-19 research and policy

## RESEARCH BRIEFING

Theoretical effects of vaccines on chronic covid-19 syndromes: a preliminary analysis.

Scientists are beginning to study the impacts of vaccines on individuals with chronic symptoms stemming from covid-19. There are many terms being used to describe lasting effects of SARS-CoV-2 infection; "long covid" and "long laulers" are currently in use to describe the condition and those it affect, though the terminology will likely evolve. While data is currently lacking, and information remains mostly anecdotal, some have suggested that vaccinations may improve some of the symptoms of long covid.

But first, let's assess our early understanding of this syndrome, with the caveat that these theories are preliminary and likely to change as more information becomes available, in some cases drastically. There are currently three theoretical mechanisms thought to be responsible for a variety of ongoing symptoms reported those with longer-term symptoms.

- 1. Persistent viral reservoir. This theory implies that the virus is setting up shop somewhere in the body and evading detection.
- 2. Viral fragments or remnants of RNA and protein remain in parts of the body, driving inflammation. Some call this a "viral ghost," though a "skeleton" might be a better term.
- 3. An autoimmune response induced by the infection. In other words, our body's own immune system creates an overly aggressive response that results in persistent symptoms.

Studies have thus far demonstrated that viral particles and viral RNA can been found in non-respiratory tissues during acute infection. Infectious particles have not been recovered after the acute phase though, making the 'reservoir" theory less likely. But significant post covid-19 inflammation and diverse autoantibodies (evidence of autoimmune response) have been demonstrated in some patients as well.

If the first theory were true, vaccine-induced responses might be able to eliminate the reservoir. If the second were true, vaccine-induced immunity may be able to eliminate the "viral ghosts" if those remnants were associated with the spike protein that the vaccines are designed to mimic. If the third were true, vaccines might have the potential to divert autoimmune cells away from their usual locale.

Of course, some or all of the above could be true. People with long covid may have varying degrees of some of these mechanisms simultaneously, making the condition a *heterogeneous* disease. Of course, other yet-untheorized mechanisms may be contributing.

Indeed another <u>possible</u> way in which vaccines might alleviate long covid symptoms is via stimulation of innate immune responses (i.e. baseline immunity that responds to a variety of infections). If this is the case, the beneficial impact of vaccines would *not* be long lasting.

To determine which theory or theories are primarily responsible for vaccine-mediated improvement in <u>long covid</u>, a trial comparing various vaccine mechanisms would be useful. Ideally, such a trial would use mRNA-based vaccines that target SARS-CoV-2 specifically while others would have nonspecific targets. While we are still learning about acute and chronic covid-19 symptoms, our ability to target studies and interventions is improving. If vaccines help people with longer-term symptoms recover, we may learn something very important about not just covid-19, but the chronic effects of many other conditions as well.

—Akiko Iwasaki, PhD Brief19 Thread-of-the-Week

## **POLICY BRIEFING**

## As restrictions ease, experts' fears grow.

With the Johnson and Johnson vaccine becoming the third vaccine against SARS-CoV-2 now approved for emergency use in the United States and nearly one in five adults having already received at least one dose of a vaccine, state and local policymakers are beginning to reverse restrictions on social gatherings and local businesses in hopes of easing economic struggles. Cities large and small, including those in New York, Missouri and Massachusetts, have increased availability of indoor dining and bars. For example, Iowa's governor lifted the statewide mask mandate, and schools in Las Vegas are returning to physical classrooms, albeit only a few days a week to start.

Public health officials, however, remain concerned about these steps to return to life as normal could give the virus a chance to spread again. Director of the US Centers for Disease Control and Prevention, Dr. Rochelle Walensky, said that, "we stand to completely lose the hard-earned ground that we have gained," with such rollbacks, especially if Americans interpret these policy changes as a signal that our collective guard can finally be let down. Although reported cases and deaths have sharply declined since January, numbers remain grim overall—with around 70,000 diagnoses and 2,000 deaths daily as of late.

However, those figures have been rising slightly over the past few days, which could mark the beginning of a dangerous trend. Officials are concerned about several new variants of the virus which current vaccines may be less likely to protect against. However, leaders in many cities and states prioritizing a return to economic prosperity are willing to take the risk, hoping that the increased availability of vaccines will help to keep infection rates at least stagnant.

—Jordan M. Warchol, MD, MPH

Kimi Chernoby, MD, JD, Policy Section Founder, Joshua Niforatos, MD Research Section Editor, Frederick Milgrim, MD, Editor-at-Large, Barb Cunningham, Copy-editor, Benjy Renton, Thread-of-the-Week, Anna Fang, Week-in-Review. Megan Davis, social media. Kane Elfman PhD, Publishing and Design. Jeremy Samuel Faust MD MS, Editor-in-Chief. <a href="http://www.brief19.com/">http://www.brief19.com/</a> Twitter: <a href="http://www.brief19.com/">brief19.com/</a> Twitter: <a href="http://www.brief19.com/">brief19.com/</a> Brief19 is a daily executive summary of covid-19-related medical research, news, and public policy. It was founded and created by frontline emergency medicine physicians with expertise in medical research critique, health and public policy.