Week in Review: 1 – 5 March 2021

BRIEF19

A daily review of covid-19 research and policy.

RESEARCH BRIEFING

Johnson & Johnson vaccine approved over the weekend. A look at the data.

On Saturday, the Food and Drug Administration officially granted Emergency Use Authorization (EUA) for the Janssen Ad26.COV2.S vaccine. The pharmaceutical company, Janssen (owned by Johnson & Johnson), is now cleared to start distributing its single dose vaccine in the US at a time when covid-19 numbers seem to have plateaued after a sharp drop that seemed to coincide with the distribution of Pfizer and Moderna's shots. Although Janssen's vaccine is not noted to be quite as effective as those two in the initial weeks, it eventually has similarly favorable outcomes when it comes to hospitalization and death.

The Johnson & Johnson (J&J) vaccine offers new hope for reaching the light at the end of the long coronavirus tunnel, as it provides a handful of various advantages. Not only will the single dose regimen allow for more efficient inoculation, its ability to be refrigerated at normal temperatures for months will make it easier for community and rural doctors offices to carry the shot. It is also based on a technology that has been used before.

With respect to its efficacy, data from Phase 3 clinical trials released in early February suggested that the J&J vaccine was 72 percent effective at preventing moderate and severe disease 28 days after the shot in the US. More promising was the 85 percent global prevention of *severe* disease at day 28, and the fact that there were *no severe cases* at day 49. With its EUA request, submitted on February 4th, J&J and Janssen submitted more safety and efficacy data from their Phase 3 trial, which was a randomized, double-blind and placebo controlled study. In addition to the aforementioned figures, we now know that the shot was found to be around 66 percent effective (across the globe) at day 14 and 28, which suggests that just two weeks after the shot, it is already doing its job. Other encouraging news included the fact that after 28 days, not a single vaccinated participant died, or was even hospitalized. For anyone wondering if the J&J vaccine is "as good" as the Pfizer and Moderna options, we note that both of those vaccines were not even considered to be fully effective until 7 or 14 days after that, as they require a booster at 3 or 4 weeks.

Furthermore, the J&J safety profile was quite good. Similar to its competitors, the primary side effects noted after the shot were injection site pain (49 percent), fatigue (38 percent), myalgias (33 percent), headaches (29 percent), nausea (14 percent) and fever (9 percent). While the Pfizer vaccine quickly developed a reputation for causing hypersensitivity reactions such as anaphylaxis (albeit, exceedingly rarely), it seems J&J has avoided this, with only one documented case of hypersensitivity (which was *not* classified as anaphylaxis).

A note on pregnancy—while no pregnant women were included in the trials, eight women did get pregnant after enrolling (four each in the placebo and vaccine groups), which doesn't provide sufficient data to draw conclusions. However, a study performed in rats in which pregnant females were injected with a double dose of vaccine showed no adverse events.

With SARS-CoV-2 variants replicating rapidly, now is the time to build herd immunity across the globe, and the Johnson & Johnson vaccine provides a third tool in the US to make this a reality. The company has pledged to get 100 million doses to the US by June, and shipments are expected to begin today and arrive by tomorrow. *1 March 2021*. *—Fred Milgrim, MD*

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 possible 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 long covid, 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. *2 March 2021*.

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

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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 policy, and public policy.