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BRIEF19

A daily review of covid-19 research and policy

RESEARCH BRIEFING

Exposure to other coronaviruses does not give immunity against SARS-CoV-2.

There are many coronaviruses. Most cause symptoms of the common cold. Occasionally, a nasty one, like SARS and SAR-CoV-2 causes far worse illness. Coronaviruses are actually common causes of the common cold. Therefore, many people are in fact walking around with antibodies from previous infections of run-of-the-mill coronaviruses. The question has therefore arisen: might antibodies from previous common coronavirus infections help people fight off the novel SARS-CoV-2 coronavirus? The idea is all the more enticing because some of these antibodies can indeed cross-react with parts of SARS-CoV-2.

The authors of a new study appearing in the journal *Cell* tested the blood collected back in 2017 from 263 children (under 18 years of age) and 168 adults as part of the Penn Medicine Biobank at the University of Pennsylvania. The scientists tested the blood for any ability to bind to the entire SARS-CoV-2 Spike protein, the receptor binding domain, and the nucleocapsid protein. The Moderna and Pfizer vaccines are directed against the spike protein, making it an attractive target. The receptor binding domain is the portion of the novel virus that is most unique to SARS-CoV-2, and it is believed to account for its virulence and, possibly, its potential to elicit counterproductive inflammation, including so-called cytokine storms. For its part, the nucleocapsid protein provides a resting place, tethered to the inner barrier of the virus for the viral genome to nestle in.

Of the samples tested, 4.2 reacted to the SARS-CoV-2 full length spike protein, 0.93 percent to the receptor binding domain, and 16.2 percent to the SARS-CoV-2 nucleocapsid protein. But binding to these proteins is *not* the same as inactivating them. These pre-existing antibodies that bound to SARS-CoV-2 did not stop the virus from infecting cells when put to the test in laboratory experiments, nor did people who had antibodies to other milder coronaviruses experience less severe illness than those without evidence of cross-reactive antibodies.

The bottom line is that antibodies against old and novel coronavirus infections may cross-react, but this cross-reactivity provides no direct clinical protection. The only mildly reduced efficacy of vaccines in the face of the British and South American variants suggests that the response to vaccines will be at least somewhat effective against other variants of SARS-CoV-2, though, unless those variants dramatically alter the structure of function of the receptor binding domain. If that happens, a race to tweak the viruses will intensify.

—Michael Chary, MD PhD

The frozen fish theory thaws. Understanding the WHO investigation and its limitations.

A theory has been going around that frozen fish delivered to China was the original source of SARS-CoV-2. While to date, no transmission has been linked to food packaging despite multiple shipments of frozen food in multiple countries testing positive for the presence of SARS-CoV-2 genetic material, it is understandable why what otherwise sounds like a far-fetched theory was not dismissed outright. The reality is that SARS-CoV-2, and therefore covid-19, likely came from a small mammal. But we truly do not know for sure.

This was the backdrop for the World Health Organization's mission to Wuhan which concluded earlier this week. At its conclusion, the team left open the possibility that the virus *may* have been transmitted to humans through frozen food. While this scenario is highly unlikely, this investigation occurred in an extremely complex political and diplomatic landscape.

Determining a virus' origin, whatever that may be, could be an extremely long process. It can take decades and sometimes definitive answers never emerge. So, pinning down the origin of SARS-CoV-2 was never going to happen in two weeks. The WHO's mission was the start of a much longer process that will likely take years.

Ebola has been around for 40+ years and while we think it circulates in bats, we still haven't proved it by isolating infectious virus. We've only just sequenced a full genome from a bat. This isn't a movie, like *Outbreak*, where scientists find the host monkey instantly end the pandemic. Nor is the WHO a law enforcement agency. They cannot simply show up to a country with a warrant and demand access to every relevant archive.

The purpose of the WHO mission is to lay the groundwork for a much longer collaboration. If the international community wants to be part of these origin studies, there must be a collaborative relationship with scientists in China and with the Chinese government. Building long-term productive collaborations requires diplomacy and trust, and the building and maintaining of productive relationships. That also requires compromise. Like it or not, China does not have to allow any investigation at all. The WHO team is there at the pleasure of the Chinese government and cannot conduct the type of forensic investigation that many inexperienced onlookers from afar have demanded. They are also not detectives by profession or hobby; rather, they are a bunch of microbiologists. In fact, these particular experts are not qualified to conduct an audit of the Wuhan Institute of Virology. If the WHO is going to investigate the lab origin hypothesis, far-fetched though it may be, they will need to assemble a team compromised actual forensic investigative skills. What this WHO mission can do, however, is to continue to study both natural zoonotic origin and the "frozen fish" theory. That is within their skill set. And as implausible as the frozen fish theory might be, investigating it might be a condition of investigating other origins as well.

—Angela Rasmussen, PhD
(Brief19 Thread-of-the-Week)

POLICY BRIEFING

New Emergency Use Authorization for covid-19 therapeutics.

On Tuesday the US Food and Drug Administration (FDA) announced an Emergency Use Authorization (EUA) for Elli Lilly's antibodies bamlanivimab and etesivimab as a therapeutic for the treatment of mild to moderate covid-19 patients who are at least twelve years old and at-risk for progression to severe disease or hospitalization. Specifically, this EUA allows for the concomitant administration of bamlanivimab and etesivimab or bamlanivimab alone; excluded are hospitalized patients, those requiring new supplemental oxygen, or an increase in a person's baseline oxygen requirement.

The EUA is based on the Phase 3 results of the BLAZE-1 Trial, which showed a seventy percent reduction in hospitalization and death for the target population, although it should be noted that the investigators changed the primary outcome of interest a few times *during* the trial, which indicates some degree of cherry-picking. *Various*

—Brief19 Policy Team

Strengthening of federal-local vaccination program.

Called the Federally Qualified Health Center program, on Tuesday the White House announced a new effort to increase community vaccination rates. Rolling out next week, the program will initially target at least one community health center in each state, allowing them to

directly order vaccines from the federal government. In the coming weeks, this number will expand to two hundred and fifty centers, with the eventual inclusion of all one thousand and three hundred centers, responsible for an estimated thirty million people nationwide. This move is in keeping with President Biden's five-part national vaccination strategy.

Additionally, to help reach the goal of one hundred million vaccinations in one hundred days, the administration will raise the number of weekly doses delivered to states, territories, and tribal lands to eleven million for at least the next three weeks, described as a 28 percent increase since initiation. This possible expansion of vaccinations will likely be a result of President Biden's invocation of the Defense Production Act (DPA) in his initial flurry of Executive Orders in the first days of his administration. *The White House.*

—Brief19 Policy Team

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