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BRIEF19

A daily review of covid-19 research and policy.

RESEARCH BRIEFING

Technical Review: COVID-19 Lung Injury is not High Altitude Pulmonary Edema. Written by critical care physicians, a new paper attempts to refute the theory behind a viral internet craze initiated by a video suggesting that covid-19 does not cause acute respiratory distress syndrome (ARDS), but, rather, a condition known as High Altitude Pulmonary Edema (HAPE). HAPE is a life-threatening condition in which fluid fills the lungs of healthy people when they travel to high altitudes. The condition can cause distress and respiratory failure. A new article appearing in the journal *High Altitude Medicine and Biology* describes HAPE as excessive and uneven tightening of the blood vessels of the lungs ("pulmonary vasoconstriction"), which causes the heart to pump the blood it sends to the lungs at higher pressures. That high pressure blood can cause leakage in the lungs, making it hard for oxygen to get absorbed into the blood vessels. This is distinct from how ARDS damages lungs. According to the authors, covid-19 causes an inflammatory response, causing the microscopic sacs of the lungs (alveoli) to fail, as well as a mismatch between the amount of air in the lungs and the blood flow (which doctors call "V/Q mismatch"). Over time, the pressure of the blood sent to the lungs rises. Unlike HAPE, however, this process is not the cause of the increased fluid in the lung sacs. Although the symptoms of these two diseases may appear similar initially, the treatments are vastly different. HAPE is treated with oxygen (or descent to a lower altitude). Recovery occurs in a matter of hours to days. In covid-19 lung disease, supplemental oxygen may improve things, but the cause of the inflammation remains. Additionally, HAPE is sometimes treated with medications that dilate blood vessels of the lungs ("pulmonary vasodilators"), thereby decreasing the pressure of the blood from the heart that reaches the lungs (by way of the pulmonary arteries). In ARDS, these medications can potentially worsen the oxygen-blood flow mismatch and cause dangerously low blood pressures. Overall, this paper serves as an important reminder that we must understand the principles of known diseases more completely, before confidently advancing unproven hypotheses about new and incompletely understood diseases.

--Christopher Sampson, MD, FACEP

Headline misleads on remdesivir data. Two patients in study died. Was that more or less than expected? An "exclusive" article in the medicine and health publication STAT News states that data from patients with severe covid-19 "suggests" that patients are "responding" to remdesivir, an anti-viral medication made by Gilead that inhibits some viruses from replicating. The news item is based on a video describing of some of the findings of an ongoing study, which has no control group which was obtained by STAT. In the video, the lead physician overseeing the study at the University of Chicago states that thus far only two patients have died, out of 113 severe cases. However, in a previous study in China, zero patients with "severe" illness died (all deaths came from cases classified as "critical"). From that perspective, the news out of Gilead could equally be spun as concerning instead of "encouraging," as some experts have stated. Additionally, it is unclear just how "severe" these patients' illnesses are. The study does not include patients with multiple organ failure, the need for mechanical ventilation at the time of screening or for 5 or more days, lung bypass ("ECMO"), high levels of two important liver

enzymes, and/or moderate to severe kidney disease. Severe patients are defined in this study as having oxygen saturations (measured "peripherally," using probes on the finger) of 94% or less, or requiring supplemental oxygen at time of screening. For context, many patients with emphysema routinely have oxygen saturations in the 88-95% and are able to function normally. Finally, as the study in question has no control group, medical scientists will not be able to consider the emerging data as informative. However, randomized controlled trial data is expected to provide better information and may identify which, if any, patients benefit from the drug.

--Jeremy Samuel Faust MD, MS

POLICY BRIEFING

Governors prevail, Federalism is alive and well. Yesterday the Trump administration conceded that the decision about when states should open again for business is a decision that will be made by governors. This comes after President Trump announced earlier in the week that his administration would be the arbiter of that question. The administration shared guidelines it thinks governors should use in determining when to open up for business. These guidelines are less restrictive than guidelines shared by health policy experts. For example, Dr. Aaron Carroll has suggested other criteria, including the ability for the healthcare system to test anyone with symptoms. Such information could be helpful because it would guide individuals behaviors of people who might not otherwise realize they have SARS-CoV-2. The administration guidelines by comparison only set the ability to test symptomatic healthcare workers as a criterion. Yesterday, New York Governor Andrew Cuomo announced a stay at home order there would be extended to May 15th. It will be interesting to see how neighboring states respond. *New York Times*.

Too little, too late, stimulus funds running out. According to US Treasury Secretary Steve Mnuchin, the recent trio of aid packages passed by Congress was supposed to sustain America for approximately 10 weeks. However, just over two weeks have passed since the CARES Act started allowing small businesses to apply for loans under the stimulus package, and already the funding has already run out. The Small Business Administration announced yesterday that 1.6 million loans have been granted and that the $350 billion fund has run dry. Congress is hoping to approve more funding for small business soon, but if the prior packages are any indications, it could be days, or weeks, until that relief materializes. *Wall Street Journal*.

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