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BRIEF19

A daily review of covid-19 research and policy.

RESEARCH BRIEFING

Can alpha-1 adrenergic receptor antagonists prevent covid-19 cytokine storm? A preprint published in [arXiv](#) looked at the use of drugs known as “alpha-1 adrenergic receptor antagonists” (α 1-AR antagonists) to prevent the massive inflammation that seems to evolve in covid-19 patients who develop acute respiratory distress syndrome. Previous research in mice suggests that α 1-AR antagonists can prevent these “cytokine storms” and death. The authors of this paper conducted a retrospective study in human patients with acute respiratory distress or pneumonia. Patients taking α 1-AR antagonists for other conditions were 35 percent less likely to require mechanical ventilation, and were 56 percent less likely to experience mechanical ventilation *and* death (the researchers combined these two outcomes into a composite, which occurred in 56% fewer patients than patients not on these drugs). Analysis: should we use α 1-AR antagonists for patients with covid-19? This retrospective study of medications that have not been shown to improve outcomes in humans (but have shown possible benefit in mice) does not provide the answer. The medical literature is rife with studies that were promising in mice but that failed in humans. Treatments that work in both mice and humans are the exception, not the rule. Prospective controlled trials that investigate both whether these medications prevent cytokine storms in a clinically meaningful way and if that leads to better clinical outcomes in covid-19 may provide the answers.

News leak from the CORIMUNO-TOCI clinical trial. Patients with covid-19 and acute respiratory distress syndrome (ARDS) can develop an enormous immune response called “cytokine storm syndrome.” The presence of that syndrome indicates an increased in the risk of death. One marker of this “hyperinflammation” is a cytokine known as interleukin-6 (IL-6). Many hospitals are now testing patients with severe/critical covid-19 for IL-6 labs. They are also following how these levels change over time. However, IL-6 levels are what scientists call “surrogate markers” of disease. They indicate internal activity in the body, but not whether that activity has any clinical effect or relevance. The medication tocilizumab is a “humanized monoclonal antibody” and was previously approved by the FDA for use in cytokine storm syndrome. On April 27, 2020 the largest hospital system in Europe [released](#) a statement claiming that Tocilizumab “improves significantly clinical outcomes of patients with moderate or severe COVID-19 pneumonia.” The claim is based on results of the CORIMUNO-TOCI trial, which is controlled (i.e. some patients in the trial did not receive the drug) but is not blinded (“open-label.”) Patients with moderate or severe covid-19 pneumonia but who did *not* require intensive care at the time of hospitalization were included. The primary outcome was need for ventilation (non-invasive or mechanical) or death by day 14. A total of 129 patients were enrolled, of which around half received the drug. The statement reports that “a significantly lower proportion of patients reached the primary outcome in the tocilizumab arm.” These data have not been published in a peer-review medical journal. When that happens, information on dosing, statistics, which patients were excluded, side effects, and other key information will be available. Until then, the strength of these findings cannot be assessed.

–Joshua Niforatos, MD, Research Section Editor

POLICY BRIEFING

Advanced service payments coming to a halt. In late March, as hospitals, clinics and doctors' offices saw their revenue plummet as a result of the coronavirus pandemic, the Centers for Medicare and Medicaid Services (CMS) expanded its Accelerated Payment Program and Advance Payment Program, programs that allow healthcare entities to apply for payment in advance of anticipated services rendered. On Sunday CMS [announced](#) that, after paying out \$100 billion through these programs since March 28, it was re-evaluating the amounts that would be paid under the Accelerated Payment Program and would not be accepting any new applications under the Advance Payment Program. CMS said it was making these changes in light of funding for healthcare providers in the subsequent federal stimulus packages. *The Centers for Medicare and Medicaid Services.* –Joshua Lesko, MD

States stockpile hydroxychloroquine despite FDA recommendations. State and local governments have acquired about [30 millions doses](#) of hydroxychloroquine, despite concerns about dangerous side effects and a warning from the FDA that doctors should not prescribe it to coronavirus patients outside of hospitals or research settings. Some states and cities have received donations of the drug from pharmaceutical companies or received shipments of it from FEMA. Others have purchased the drug with taxpayer dollars. Hydroxychloroquine has FDA approval for use in treating malaria, lupus, and rheumatoid arthritis, but is known to have serious side effects including abnormal heart rhythms that can result in death. While there have been anecdotal reports and preliminary findings in clinical trials that the drug may be effective against SARS-CoV-2 infection, robust clinical evidence is still lacking. *AP.*

–Jordan M. Warchol, MD, MPH

Trump says meat processing plants must stay open. Seeking to prevent shortages of meat, President Trump yesterday declared meat processing plants “[critical infrastructure](#)” and said his administration would “take all appropriate action” to keep them open. The administration also suggested it would seek to prevent state and local authorities from forcing plants to close. Union and labor advocates said the president was putting workers at risk and called for steps including giving workers protective gear and paid sick leave, enforcing social distancing inside plants, and making daily testing available. More than a dozen food processing or meatpacking plants have closed because of covid-19 outbreaks. Thousands of workers have fallen ill, and more than twenty have died. *New York Times.* –Kimi Chernoby, MD, JD, Policy Section Editor

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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.