*14 August 2020*

# ***BRIEF19***

*A daily review of covid-19 research and policy.*

## ***RESEARCH BRIEFING***

**Experiments with Icatibant show promise in treating covid-19 lung disease.**

As the U.S. awaits a safe and effective vaccine to combat SARS-CoV-2, researchers have continued to explore the use of pre-existing medications to treat the virus. A group of scientists in the Netherlands have conducted one such trial to explore whether Icatibant, a drug approved in 2011 by the FDA to treat hereditary angioedema would be successful in reducing fluid accumulation in the lungs of patients suffering from covid-19.

Hereditary angioedema is a genetic condition in which those affected lack or have dramatically decreased activity of an enzyme called C1 esterase *inhibitor*. When C1 esterase inhibitor is offline, C1 esterase runs overtime, leading to a buildup of two other chemicals, bradykinin and kallikrein. These chemicals cause remarkable and even life-threatening swelling, most notably in the mouth, throat and areas lined with mucosa, including the intestines and parts of the lungs.

Meanwhile, ACE2 receptors promote the degradation of bradykinin and kallikrein. SARS-CoV-2 uses this very same receptor to enter human cells, thereby preventing the ACE2 receptors from carrying out their usual functions. Because of this connection, researchers hypothesized that Icatibant might be able to reduce lung swelling in covid-19 patients by compensating for the loss of ACE2 function. They gave one dose of Icatibant to nine patients requiring oxygen support and found that four out of nine patients needed less supplemental oxygen. However, of those four, the improvement in two lasted only a few hours.

In sum, this trial hints that Icatibant may help patients in covid-19 whose disease involves swelling of and accumulation of fluid in lung tissue. But it is not a large enough of a study to provide strong evidence. There is still much to be learned, including how exactly the mechanism of Icatibant may work for these patients and whether there is true statistical significance.

*—Michael Chary, MD PhD*

**Covid-19 versus 1918 H1N1 "Spanish flu." They belong in the same conversation.**

**Editor's brief.** In research published in *JAMA Network Open,* Carlos del Rio (Emory), Zhenqiu Lin (Yale), and I found that the first 61 days of the covid-19 outbreak in New York City was more than 70% as deadly as the worst 61 days of 1918 H1N1 ("Spanish flu") in that city. Given that 21st century pre-pandemic baseline mortality rates (2017-2019) were around half that of 20th century baseline pre-pandemic rates (1914-1917), covid-19 actually represents a larger deviation from normal expectations. In fact, New York City residents were more than twice as likely to die during the first two months of the covid-19 outbreak than New Yorkers were between 1914-1917 (the pre-Spanish flu baseline period). We assessed all-cause mortality in each era, in order to remove subjectivity; while even we do not have ample SARS-CoV-2 testing, our predecessors had virtually no way to test for H1N1. Our findings suggest that the current pandemic has the potential to have a similar final death toll as 1918 H1N1, depending on factors in the coming months. While some of these are beyond our control (such as how this virus spread in the Fall and Winter), other factors are modifiable, including how much we slow down the spread of the virus while a vaccine is developed and tested in large human trials.

*—Jeremy Samuel Faust, MD MS*

## ***POLICY BRIEFING***

**Georgia ICE facility reports another covid-19-related death.**

A 70-year-old man with diabetes has become the second detainee at a Georgia Immigration and Customs Enforcement detention center to die due to complications from covid-19. The man, originally from Costa Rica, had been hospitalized since the beginning of August and was awaiting deportation. The facility in Lumpkin, GA has had 154 cases of covid-19 among its detainees in custody, including a 34-year-old man who also succumbed to the illness in May. The two fatalities are the most of any ICE detention facility in the United States and bring the total number of deaths of detainees in custody there to six in the past three years. Critics of the agency have previously demanded that all detainees in a category considered high-risk for complications related to coronavirus infection be released due to the difficulty enacting safety measures such as social distancing. ICE reports having released over 900 such people since the covid-19 pandemic began. The now deceased detainee had been in the U.S. since 1999 and was transferred to the Stewart Detention Center from prison where he was serving a 20-year sentence for statutory rape and indecent liberties with a child. *AP*

*—Jordan M. Warchol, MD, MPH*

**New Zealand Responds to the Return of Covid-19.**

As *Brief19* reported on Wednesday, New Zealand recently announced its first coronavirus infection in 102 days. The country has been widely regarded as one of the best in its initial response to the pandemic, becoming the only nation to eliminate the disease entirely. However, after the emergence of four new cases within the same family, Prime Minister Jacinda Ardern has reimposed strict guidelines in the city of Auckland. With 1.5 million people, Auckland is New Zealand's largest city, and is now in the second most restrictive category of the country's four-tiered coronavirus containment strategy. Residents were advised to stay home and nonessential businesses, including restaurants, were closed for 3 days. No long-term closures or other restrictions have as of yet been announced. It is not known how the new cases of covid-19 were transmitted as the family had not traveled outside of New Zealand. Contact tracing is now being used to attempt to identify and quarantine any persons who may have contracted the virus from the infected family. Other parts of the country have also ramped up protective measures against spread of the novel coronavirus, though those restrictions are less severe than in Auckland. *WSJ*

*—Jordan M. Warchol, MD, MPH*