BRIEF19

A daily review of covid-19 research and policy.

RESEARCH BRIEFING

Why do children account so few cases of SARS-CoV-2?

Studies from China and the United States have found that approximately 2 percent of all diagnosed cases of SARS-CoV-2 have been in children. The reason for this is unclear. One possible answer is that children are in fact infected at much higher rates than reported but they are less likely to be tested, owing to symptom-free disease or cases that are too mild have reached testing thresholds in many areas. However, there may be a biological explanation for these lower rates of infection; some experts now believe that children may be less prone to infection due to differing concentrations of certain receptors on the surfaces of cells that line the airway. As previously covered in *Brief19*, angiotensin-converting enzyme 2 (ACE2) receptors jut out from the surface of some human cells, and it is through these receptors that the SARS-CoV-2 gains entry inside where it can reproduce. A new research letter published in JAMA assessed the differences in ACE2 expression in cells collected from inner surfaces of the nostrils of children and adults. The samples had previously been collected by asthma researchers in the Mount Sinai Health System in New York City between 2015 to 2018 among patients 4 to 60 years of age with and without a history of asthma. Researchers obtained permission to thaw the cells from -80 Celsius freezers and test the samples for levels of the ACE2 gene. The samples were categorized into age groups according to the source patients: younger children (aged <10 years), older children (aged 10-17 years), young adults (aged 18-24 years), and adults (aged ≥25 years). Samples from 305 subjects were included in the study. ACE2 gene expression levels were found to be lowest in younger children. Levels of the gene significantly rose with increasing age. This association remained significant even after researchers made statistical adjustments to account for sex and history of asthma. This is among the only known studies to demonstrate that levels of ACE2 gene expression cells lining the airway of humans differs by age. Does this explain why children seem to account for so few covid-19 cases, and equally, why most children infected with SARS-CoV-2 appear to have had less severe covid-19 disease? This study provides a biologically plausible explanation for these observations but did not test either question directly. -Joshua Niforatos, MD

An update on decreased heart attacks in the US during the pandemic:

Recently, *Brief19* covered research from the United Kingdom that described an <u>possible decrease</u> in the number of ambulance calls for patients with suspected heart attacks and strokes (the decreased number of calls did not reach "statistical significance"). Yesterday, a research letter published in *The New England Journal of Medicine* describes the rate of <u>newly diagnosed heart</u> <u>attacks</u> throughout the entire Kaiser Permanente System in Northern California before and during the covid-19 outbreak. Kaiser Permanente consists of 21 medical centers and 255 clinics and provides comprehensive care for more than 4.4 million persons throughout Northern California. The researchers assessed whether the incidence of weekly heart attacks changed before and after the first reported death from covid-19 in Northern California, which occurred on March 4, 2020. The study included two important types of heart attack (known to healthcare professionals as STEMI and NSTEMI acute myocardial infarctions, reflecting differing findings on

electrocardiograms). These data were compared to weekly rates of heart attacks from the same period in 2019. These researchers found that the weekly rates of hospitalization for heart attacks decreased by up to 48 percent after March 4th. When compared to the similar time period in 2019, the numbers after March 4th were also lower. Also reported in the study is that patients diagnosed with heart attacks during the covid-19 period (March 4 - April 14, 2020) were healthier (i.e. had fewer pre-existing chronic medical problems) than heart attack patients who were diagnosed and treated both during the pre-covid-19 period of 2020, as well as in 2019. The authors conclude that overall there were fewer heart attacks diagnosed during the covid-19 pandemic than would be expected, even after considering typical seasonal variations. The large question is whether decreases in usual medical care for life-threatening conditions including major heart attacks have been significant contributors to the increases in the total number of deaths (from all causes combined) that have been observed to have occurred during the US outbreak. The numbers in this study suggest that this is currently unlikely, as only a relatively modest percent of short-term deaths from all heart attacks can be prevented by emergency care.

—Joshua Niforatos, MD

POLICY BRIEFING

Alabama opened on April 30th. Now intense care units are full.

After being one of the last states to close in an effort to flatten the covid-19 curve, doing so on April 1st, Alabama's stay-at-home order expired on April 30th. Since then, 5,000 new cases have been recorded, and the number of deaths statewide have nearly doubled. Yesterday, Steven Reed, the mayor of Montgomery (the capital and 2nd largest city in the state) said that intensive care units in the city were running out of beds. The three worst days in terms of new cases and deaths have all occurred since May 5th. Washington Post.

—Jeremy Samuel Faust MD, MS

Trump attacks Michigan over mail voting.

Earlier this week, Michigan Secretary of State Jocelyn Benson announced that all residents would receive an application by mail for absentee voting. Several states have taken similar steps, in order to reduce the risk that people will be exposed to the coronavirus by voting in person. President Trump, however, has made clear his opposition to mail voting. Yesterday, he tweeted that Michigan had sent out ballots -- which was not true -- and that doing so was illegal and a step towards voter fraud. Mr. Trump's statements come as Republicans are spending millions of dollars to oppose Democratic efforts around the country to make it easier to vote. New York Times.

—Kimi Chernoby, MD, JD

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