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BRIEF19

A daily review of covid-19 research and policy.

RESEARCH BRIEFING

Hydroxychloroquine ineffective in preventing SARS-CoV-2.

The question as to whether hydroxychloroquine (HCQ) can prevent coronavirus infection has been in the air since rumors and low-quality evidence trumped the scientific method and droves of Americans began taking the medication this spring. The spike in HCQ use since March occurred despite lack of proof that the drug is effective beyond its prior use for conditions including lupus and rheumatoid arthritis. While the medication is known to inhibit viral production in the cells in the research laboratory setting, it has not been shown to work in humans. Now, a new high-quality study published in *The New England Journal of Medicine* yesterday provides important insight. The upshot is that HCQ does not appear to prevent infection in persons who reported a dangerous exposure (in terms of time and distance) to someone with covid-19. This trial was randomized; around half of the volunteers received HCQ, and half received placebo pills that were similar in appearance. Neither the subjects nor the researchers were aware of which subjects were which in order to minimize bias. This was particularly important here because in this study, many of the subjects deemed to have developed covid-19 after enrolling in the trial did not have access to SARS-CoV-2 testing. Therefore, a "clinical definition" of infection was used to diagnose suspected illness in some cases (i.e. a combination of symptoms that met the "case definition" used in the United States is considered sufficient to diagnose probable infection). The subjects in the study experienced either moderate (face mask but no eye shield) or high-risk exposures (neither). Around two-thirds of the subjects were healthcare workers and approximately 30 percent had at-home exposure to the "source" patient. Possible subjects were included in the study only if they had been less than 6 feet away from the source patients for longer than 10 minutes. Impressively, the researchers sent couriers to the homes of the test subjects in order to deliver either HCQ or placebo pills. Everyone in the study began taking HCQ or placebo within 4 days, though many started within 1-2 days. Rates of infection were assessed at 5, 10, and 14 days. No difference was found, regardless of whether the medications were initiated within 24 hours or not. Side effects were more common amongst subjects taking HCQ (40 percent) versus placebo (17 percent). Nausea, vomiting, diarrhea, and other symptoms of "upset stomach" were most common. No serious side effects were reported. In a related finding, 75 percent of the subjects taking HCQ reported taking all of the prescribed doses, compared to 83 percent in the placebo arm. The most common reason given for not completing the full 5-day course of pills was side effects. Among other interesting features of this study included an inquiry as to whether subjects could correctly guess whether they were in the HCQ or placebo group of the study. Those who had side effects, regardless of which group they were in, were more likely to think they had received HCQ. Finally, it is important to note that independent data analysts monitored the study as it unfolded. It was determined by them that the study should be stopped early; a planned "interim" statistical analysis done during the study concluded that the trial had become futile because the data already collected indicated that HCQ

was extremely unlikely to eventually show any statistical benefit, even if more subjects were enrolled in the study. *–Jeremy Samuel Faust MD, MS*

Two major studies under cloud of suspicion. *The New England Journal of Medicine* and *The Lancet*, arguably the two most prestigious medical journals in the world, issued Expressions of Concern yesterday regarding two studies published therein. The *NEJM* study assessed the safety of a class of blood pressure medicines known as ACEs and ARBs in patients with covid-19. The study in *The Lancet* purports to describe >96,000 patients all over the world, some of whom took HCQ after becoming infected with SARS-CoV-2. In both cases, the company (Surgisphere) that provided large quantities of "Big Data" to the investigators has come under intense scrutiny. Many observers feel that full retractions are all but inevitable, but no formal announcements have been made.

POLICY BRIEFING

Democrats seek information about contracts for vaccine development. The Trump administration has selected five companies whose coronavirus vaccine projects it considers the most promising and plans to invest in, senior officials told the *New York Times* on Wednesday. Meanwhile, however, House Democrats say they want more information about the contracts the Department of Health and Human Services has entered into with these and other drug companies working on coronavirus vaccines or therapeutics. The CARES Act allocated $3.5 billion for developing and procuring vaccines and therapeutics, and HHS has entered into contracts with more than a dozen private companies. In a letter sent on Tuesday to HHS Secretary Alex Azar, Rep. James Clyburn (D-SC), the chairman of the House Select Committee on the Coronavirus Crisis, and Carolyn Maloney (D-NY), the chairwoman of the House Oversight and Reform Committee, said they were particularly concerned about whether the companies were required to make the drugs they developed affordable and whether the government would keep any intellectual property rights in the drugs whose development it funded. *Various.*

–Jordan M. Warchol, MD, MPH

Snags in the Senate for small business relief. Despite passing the often fractured House by a 417-1 margin, a bill to give small businesses more latitude in how they spend funds from the Paycheck Protection Program (PPP) is now being held up in the Senate. The bill, which has the backing of both Senate Majority Leader Mitch McConnell (R-KY) and Senate Minority Leader Chuck Schumer (D-NY), has not yet been able to get the support of all Senators which is needed to pass legislation by a process known as Unanimous Consent. Passing the bill through this process allows it to move forward without the periods of debate that would otherwise be required, freeing up more time on the Senate floor to address other matters. Concerns about the PPP have been raised on both sides of the aisle as large companies have received millions of dollars through the program while many small businesses have reported difficulty accessing funds that could keep them afloat. *Politico* *–Jordan M. Warchol, MD, MPH*

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