1 October 2020

BRIEF19

A daily review of covid-19 research and policy.

RESEARCH BRIEFING

The body's reaction to covid-19 may be, in parts, counterproductive.

SARS-CoV-2 causes illness directly by infecting cells and indirectly by provoking an infected person's body to retaliate in a self-destructive manner. In particular, SARS-CoV-2 is thought to increase the risk of blood clots in the lungs, which can itself be life-threatening, as such clots block the flow of blood in the lungs and therefore prevent the delivery of oxygen into the bloodstream and to the rest of the body. This combination of direct and indirect harm is not unique to SARS-CoV-2, or even the coronavirus family. Infections can cause prolonged pain (herpes viruses), bone marrow failure (parvoviruses) and are linked to cervical cancer (human papillomaviruses) and lymphoma (Epstein-Barr viruses). In addition, many different viral and bacterial infections are linked to myocarditis, a life-threatening infection of the heart, while others can cause the thyroid to go through dangerous periods of overactivity or underactivity.

A recent study in *The Lancet* aimed to better understand the biology behind this increased risk by performing detailed autopsies on 21 patients, aged 41-78, who died of complications from covid-19. The authors found overabundant inflammatory cells through the body including in the brain and blood. One type of inflammatory cell, the neutrophil, can jumpstart clotting if they are present in large numbers. The authors did not find high levels of circulating virus nor any evidence of the virus sheltering in various organs or in the inflammatory cells themselves. Even as levels of SARS-CoV-2 decreased in patients, they became gravely ill, which led the study's authors to hypothesize that the body's exuberant inflammatory response may be behind some of covid-19's mortality. This is similar to how we now think of sepsis; that condition is triggered by infections but is driven by the body's counterproductive and ultimately harmful response to them.

There are notable limitations to the *Lancet* study, however. First, it only involved 21 fatal cases, a relatively small number. Second, information gleaned from autopsies can be tricky, as tissue degradation between death and the time of autopsy may inadvertently *decrease* estimates of the viral load. Additionally, there was no comparison group to determine whether the burden of clots observed is greater when compared to death by other causes including serious viral infections other than SARS-CoV-2; it is important to realize that clots also form naturally in deceased bodies as stationary blood pools and hardens. Despite these limitations, this study is an important reminder of our incomplete understanding of SARS-CoV-2 infection and our body's responses. Until that knowledge is more complete, our most effective tool against covid-19 remains public health measures that limit our exposure, though hopefully a vaccine will be our next line of defense.

—Michael Chary, MD PhD

POLICY BRIEFING

Life science companies commit to the worldwide distribution of covid-19 diagnostics, therapeutics and vaccines.

For-profit pharmaceutical companies including AstraZeneca, Baye, Eli Lilly, Gilead, Johnson & Johnson, Pfizer, and Merck & Co. have partnered with the Bill & Melinda Gates Foundation to initiate "the most expansive and ambitious pandemic R&D response effort in history, with the promise of a range of interventions that can help end the pandemic." This commitment will involve developing clinical trials to represent racial, ethnic and socioeconomic demographics across the globe and a promise to develop scalable technologies that can be implemented in low-income settings. The hope is that these efforts will address disparities that have been reported in other clinical trials related to covid-19.

The signed letter outlines a focus on timeliness, affordability, equitable technology distribution, and R&D transparency for eventual recipients around the globe. The document closes by calling on governments to develop evolving guidance on how innovations are to be implemented in each distribution setting, while, "enhanc[ing] country readiness and in-country delivery systems."

It remains to be seen whether calling on countries to prepare for incoming aid is enough to ensure effective implementation of technologies meant to end the covid-19 pandemic, or whether the planned $38 billion in funding will materialize from wealthier entities such as Britain, the European Union, and the United States

—Aida Haddad, M.Div.