AHA UPDATE

COVID-19 at 1 Year American Heart Association Presidents Reflect on the Pandemic

s we write these words, the United States is climbing the steep grade of the third wave of the coronavirus pandemic, and a bleak winter with tens, if not hundreds, of thousands of deaths awaits us. As you read these words, it has been a year since coronavirus disease 2019 (COVID-19) first reached US shores. Within that year, remarkably, vaccines have been rolled out, and the beginning of the end of the pandemic is in sight. Over the past months, we have learned a tremendous amount, which we distill into 3 main lessons. First, Mother Nature, in the form of COVID-19, has presented a breadth of medical mysteries, perhaps foreshadowing future challenges that we can only imagine. Second, the scientific enterprise, including projects supported by the American Heart Association (AHA), is alive and more robust than ever. And third, despite the strength of the response of the research community, translation of the knowledge gained into effective treatment and public health requires more than scientific evidence; the mitigation of mortality from COVID-19 and the ultimate end of the pandemic require education, trust, and political leadership. We need better coordination between clinical medicine and public health.

Back in February 2020, as reports of the illness caused by severe acute respiratory distress syndrome coronavirus 2 (SARS-CoV-2) began to filter to the United States, cardiovascular clinicians and scientists learned that the virus caused not only respiratory illness but also, in some cases, a diffuse syndrome that affects the heart, nervous system, gastrointestinal tract, kidneys, and other organs throughout the body.¹ Probably attributable in part to the presence of its receptor, angiotensin-converting enzyme 2, on the surface of cells that participate in vascular function, SARS-CoV-2 was discovered to induce endothelial activation, leading to the release of inflammatory and prothrombotic factors, including von Willebrand factor, promoting microvascular and macrovascular thrombosis and diffuse tissue injury.² In other words, in some respects, COVID-19 is inherently a vascular disorder. COVID-19 was also discovered to induce severe inflammation and immune activation through the release of cytokines and other inflammatory mediators. A multi-inflammatory syndrome of childhood was reported in a small number of children, and a presumably related syndrome was also noted in adults. In addition to respiratory failure, patients presented with myocardial infarction, heart failure, myocarditis, strokes, kidney failure, diarrhea, and other manifestations of a systemic illness.¹ As with syphilis in the 19th century, COVID-19 appears to be a "great imitator" because it mimics so many other conditions. Similar to pandemic influenza in the past century, COVID-19 may also lead to lingering aftereffects, the so-called long-haul COVID syndrome, which remains poorly understood. All these mysteries of the virus, however, were not entirely without precedent. SARS-CoV-2 is only one of a family of coronaviruses, including Middle East Respiratory Syndrome (MERS) virus found in camels, that causes seasonal outbreaks of even more Mitchell S.V. Elkind[®], MD, MS Robert A. Harrington, MD Donald M. Lloyd-Jones[®], MD

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severe disease and continues to infect individuals in Saudi Arabia.³ SSARS-CoV-2 was more contagious than MERS, perhaps because of the latter's greater fatality and the fact that it does not spread in asymptomatic individuals. Should the future evolve a virus that marries the transmissibility of SARS-CoV-2 with the severity of MERS or SARS-CoV-1, the death and destruction could outstrip even what we have experienced during the past 12 months.

Despite the horrors of the virus, the clinical and scientific community rose to the challenge. The genetic sequence of the virus was made widely available within days of the discovery of the virus, allowing experts to begin work on developing and testing of vaccines. Epidemiologists, informaticians, and geospatial scientists began to study and model the disease and to demonstrate the benefits of social distancing and masking. Clinical trialists began to test interventions within weeks of cases climbing, leading to evidence that some treatments, such as dexamethasone and remdesivir, could improve outcomes, if not cure the disease, and that other treatments, such as hydroxychloroquine, would not.⁴ We also learned that angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers did not increase risk of infection or contribute to worse outcomes in patients taking these important medications. Virologists, immunologists, and scientists across a multitude of other fields changed the course of their own work and reorganized their laboratories and their staff to study SARS-CoV-2 and its associated manifestations. Projects that in usual times would have taken years to get off the ground were started and-in many cases-were completed within months.⁵ Studies of interactions between the virus and platelets, the discovery of specific proteins in different parts of the body that interact with those in the virus, and epidemiological analyses showing the increased effect of the virus on Black and other historically marginalized populations were all conducted with AHA funding and oversight. Some of these projects were presented at the AHA's own Scientific Sessions in November 2020. Nearly everyone became engaged in the search for a solution, for a way to mitigate the damage, and for understanding. Journals across multiple specialties devoted pages to the virus, reflecting the ways in which the virus affected nearly the entire field of medicine, and online webinars on various topics related to the virus were made available. Most of us became experts in at least some aspect of COVID-19 this year, even as we watched, heartbroken, as it took the health and sometimes the lives of many of our colleagues and friends.

All this heroic effort, however, was not universally embraced in the public sphere. Cynicism, misinformation, belligerence, and sheer incompetence often stood on the other side of the door of the laboratory or clinic. Some were perhaps skeptical toward expertise, guided by a strange and mistaken notion that public health

experts, scientists, and clinicians had some motive other than saving lives in the midst of a crisis. For others, perhaps, the primary value was not human life, but a twisted view of economics, or a notion that their freedom must be unconstrained, even by a threat to public health, an idea never enshrined in law. For many, simple ignorance, exacerbated by disinformation and amplified by social media, may have been enough to blunt awareness. The pandemic has thus brought to light many weaknesses in our health care infrastructure: for example, longstanding disparities in health care access and quality have been rightly condemned as leading to the increased mortality from COVID-19 borne by historically marginalized communities in the United States.⁶ Another weakness is the low level of scientific and statistical literacy among the general public, including those with college-level educations. Placing the burden of the pandemic response exclusively on clinicians and scientists, as though they could miraculously manage this disease without the help of political leadership or the majority of the public, was a critical mistake in the United States. The AHA has contributed to educating the public about the threats of the virus, seeking emergency care when needed, and the benefits of mask wearing and vaccination; but our efforts, as important as they were, could not alone mitigate the effects of the pandemic. In a medical crisis of this magnitude, everyone, led by the federal government, needs to learn, understand, and act within the bounds of scientific evidence.

Moving forward, not just over the next few months, but even after the promised benefits of vaccines reach fruition and we begin to remove our masks, hug one another, and gather in groups, will require a dramatic change in how science, and civics, as well, is taught and communicated. Mother Nature will throw even more dangerous darts in the future, and we can anticipate that future scientists will discover new defenses. The AHA will continue to do its part through the support of science, clinical and public education, and advocacy for improved public health and health care infrastructure. But there are no guarantees; without education, trust, and leadership, science alone cannot help. Mother Nature does not suffer fools.

ARTICLE INFORMATION

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