


technology for marginalized populations in times of public health crisis.¹⁰

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WHY AM I, AS A GERIATRIC MEDICINE FELLOW WITH SYMPTOMS, UNABLE TO GET TESTED FOR COVID-19 WHILE POLITICIANS, OIL EXECUTIVES, AND NBA PLAYERS ARE?

To the Editor:

I am an integrated geriatric and palliative medicine fellow physician in the time of COVID-19. As the virus began to tear through my greater community, and as my hospital prepared for an enormous surge of patients, I spent time off work with symptoms that were consistent with a mild case

of COVID-19. After going through the proper channels, I was denied viral testing and had to sit out of clinical duties, unsure whether I had picked up a standard respiratory infection or whether this was mild COVID-19.

Around the country, physicians, nurses, and other critical providers are being denied testing for SARS-CoV-2 while stories abound of political, economic, and social elites getting tested who are equally or less symptomatic.¹⁻³ As providers in the time of COVID-19, if we ignore symptoms of a mild respiratory infection and continue to work (historically considered a point of pride in much of medical culture), we now risk becoming superspreaders of a deadly disease, putting not only our most vulnerable patients but also scores of our colleagues (and all *their* patients) in serious danger. This is particularly the case in geriatrics and palliative care, where our patients carry disproportionately high risk of morbidity and mortality from infection with SARS-CoV-2. If providers go untested, we will undoubtedly worsen this pandemic by unwittingly seeding the same communities that we care for and live in. We do not have the ability to socially distance to the same degree as the rest of society; we still go to work after all. Finally, even after sitting out from work, providers like me who go untested still do not know if we have been infected, and at least until the rollout of an accessible antibody test, we will not know if we have developed immunity. So the next time we develop concerning symptoms, we are out again, even as the healthcare system strains to the breaking point.

Given that I had relatively mild symptoms and there is a critical shortage of COVID-19 testing supplies, I do not feel I should have been tested over sicker and more vulnerable patients, especially those in need of hospitalization. In fact, my organization was following the most recent Centers for Disease Control and Prevention guidance regarding proper use of testing, and I am glad I was not shuttled past those who needed it more. But in comparison with some of those with higher socioeconomic/political capital and equal or lesser symptoms who did receive testing, I feel this reflects a deeply troubling and dangerous misallocation of resources, one firmly rooted in the profound inequality that has come to pervade our society.

It is difficult to see much silver lining to this pandemic from our current vantage point, and the totality of the fallout is far from certain. In addition to the known risks to older adults and those with chronic conditions, we are already seeing evidence that people with lower socioeconomic status are disproportionately affected by this virus^{4,5} (higher burden of chronic medical conditions leading to higher risk of morbidity and mortality; less ability overall to socially distance leading to higher risk of infection; less financial cushioning leading to worse financial distress, etc).

One fact that I hope this pandemic makes glaringly clear is that we are all in this together. SARS-CoV-2 anywhere is a threat to human health and prosperity everywhere. I hope that in the wake of this crisis we finally rebuild a fully inclusive and just healthcare system, one that ensures *all* of us, whether rich or poor, young or old, CEO or CNA, is given the right to quality, compassionate, and equitable care. This virus has exposed that we are immensely interdependent, and as the dust settles on this crisis, we will have the opportunity to rebuild our healthcare system to reflect this truth. As we can now see more clearly than ever before, the health of every individual depends collectively on the health of each and every one of us.

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GEROSCIENCE AND THE CORONAVIRUS PANDEMIC: THE WHACK-A-MOLE APPROACH IS NOT ENOUGH

To the Editor: We are in the midst of a pandemic, and it is becoming increasingly clear that health systems around the world are either not adequate or stretched to the limit. The main strain comes from severely affected patients needing intensive care, ventilators, and other medical equipment currently in short supply. Although the virus has the ability to infect people of all ages and socioeconomic status, severe symptoms and mortality occur primarily in frail older adults, and they represent most of the patients overloading the hospitals.

Because those most affected are the frail older adults, I propose to add geroscience as a new tool to our strategy against COVID-19. There is no doubt that a long-term approach to this crisis involves the rapid development of vaccines and other prophylactics. But unfortunately, this takes time, and in the meantime the frail are dying. Geroscience posits that all diseases affecting primarily older adults, even diseases as disparate as cancer and heart disease, have as a common (and major) cause the declining function and resilience that often accompanies the aging process.¹ This is true for chronic diseases, but it is also true for acute ones such as COVID-19. Weakened resilience lowers our capacity to respond to the physiologic challenge of an acute infection. Importantly, preclinical work is already showing that

interventions addressing the basic biology of aging, such as elimination of senescent cells² or inhibition of nutrient-sensing mechanisms,³ can have a positive effect on the ability of a variety of preclinical models to withstand both chronic and acute challenges. Some are already being tried in the clinic, and it is imperative that these approaches be further advanced rapidly.

For example, we should be testing the ability of senolytics (drugs that preferentially kill senescent cells) as a way to mitigate the cytokine storm that is widely believed to be at the core of why frail older adults are more susceptible to serious outcomes including death. Senescent cells accumulate in people as a consequence of age and disease, and they secrete multiple cytokines (the so-called senescent-associated secretory phenotype [SASP])⁴ that cause inflammation, activating resident macrophages and other elements of the innate immune response. As a result, when a virus or other acute insult activates this already alert innate immune system, a deadly cytokine storm might occur. Preliminary data in mice and other models indicate that killing senescent cells with these senolytic drugs alleviates the problem.² This needs to be tested immediately in animal models challenged with COVID-19, and shortly, in controlled clinical trials in patients. It is important to emphasize that senolytics do not directly target the mechanism of pathogenesis of this (or any other) virus, or even the immune system. They target the aging process itself. However, it is possible that attenuating the nonspecific cytokine storm exacerbated in frail older adults affords time for the patient to develop a better and stronger antigen-specific immune response to COVID-19 or other pathogens.

Other geroscience approaches currently under consideration include inhibition of the mechanistic target of rapamycin (mTOR) pathway of nutrient sensing.³ Inhibition of this pathway with a combination of everolimus (a derivative of rapamycin) and RTB101 (a catalytic site mTOR inhibitor), was shown to be effective in increasing antibody titers against influenza vaccination.⁵ In phase 2 trials in adults 65 years of age and older, RTB101 upregulated pan-antiviral gene expression, decreased the levels of inflammatory cytokines, and decreased the incidence and severity of laboratory-confirmed viral respiratory tract infections including coronavirus infections. Although a recent large phase 3 trial of RTB101 failed to reach its primary end point, that point was not the incidence or severity of viral respiratory tract infections. Importantly, both everolimus and RTB101 have been shown to be well tolerated in older adults at the doses and frequency used in these studies. Again, the approach here is not either to attack this specific virus or to boost the immune system by specific targeting; rather, the approach is to improve health including immune health by targeting one of the main pillars of aging biology.

Of note, this geroscience approach is not specific to COVID-19, but once tried and proven, it would be effective against any future pandemics or epidemics. As a note of caution, senolytics and other geroscience-based approaches would not limit infection rates. They would only protect the frail against the more severe consequences of the disease including death. Thus the geroscience approach needs to be viewed as an adjuvant to the current approaches, not a replacement.

COVID-19 is the largest pandemic in decades, but it is not unusual. We have been there before with severe acute respiratory syndrome (SARS), Middle East respiratory syndrome (MERS), as well as the seasonal flu. In each case, a large mobilization of research and health resources resulted in