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PERSPECTIVE

Desperate Times Call for Temperate Measures: Practicing Infectious Diseases During a Novel Pandemic

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The coronavirus disease 2019 (COVID-19) pandemic will likely be the defining public health event of this generation. Like no other event in recent memory, it has demonstrated the resolve and commitment of so many in healthcare. Colleagues in nursing, emergency medicine, and critical care (among many others) deployed to the frontlines, and those in infection control quickly intervened to protect our staff and patients. We, as infectious disease clinicians, have been asked to play our part, as the trusted purveyors of knowledge on the evaluation and management of communicable diseases; from loved ones inquiring about antiviral prophylaxis to calls from colleagues for salvage therapies for worsening pneumonia. For a field of medicine that takes pride on its reliance on evidence and experience, these have been desperate times.

In normal times, we make every effort to respond to such requests with evidence-based decision making. In the case of COVID-19, our struggles to reply have not been for a lack of information. Between January 1 and April 12, 2020, there have been 3300 manuscripts indexed in PubMed including the terms "COVID-19" or "SARS CoV-2," and another 1552 in medRxiv or bioRxiv (with some duplications between them). However, to date, there has been scant evidence to guide evidence-based clinical decision making. Of the thousands of peer-reviewed articles indexed in PubMed, exactly 1 has reported the results of a randomized controlled trial; a single-centered study with approximately 200 COVID-19-infected individuals, investigating a drug developed for another virus, and resulting in a null finding [1]. As of this writing, there are 52 registered trials for COVID-19 in the United States, but many of these have not yet launched. This abundance of creativity based on strong foundational science has translated so far to only a handful of clinical trials that are currently enrolling, mostly at tertiary care hospitals. We need to do more and faster.

However, this phenomenon is not new to infectious disease clinicians. We are often asked to solve diagnostic and therapeutic dilemmas without the benefit of compelling clinical trial data. We take pride in our clinical acumen (and epic documentation); treating nontuberculous mycobacterial infections and fevers of unknown origin with dizzying cocktails of antebellum drugs or nothing more than the tincture of time. Experience and wisdom matter. Nonetheless, here again, we are knocked off kilter by a disease that has been in existence for less than 6 months, and with its closest equivalents being a blip in the annals of epidemic time in 2003, that only a handful of clinicians saw in person, and a contagion that only some of our grandparents were old enough to experience.

So we find ourselves without either of our 2 most reliable supports. To keep ourselves propped up, we have been desperate for information. We have scoured the literature, and the online forums, and the town halls from our own institutions and others. We have all been drinking from the COVID-19 firehose. We are soaked but still thirsty for reliable knowledge. To fill this void, we have sought information in places that, as medical academics, we have not been wont to go previously. Although we agree with ethical obligations that compel medical researchers to make their data publicly available so it can inform the epidemic response, we also remain acutely aware that there has been a corresponding pandemic of COVID-19 misinformation. Indeed, this epidemic has brought an unprecedented supply of rapidly disseminated data that are frequently not peer-reviewed, of variable quality, and, in some cases, retracted altogether. Many of the therapeutic agents proposed in this barrage are toxic, and others are being repurposed for COVID-19 on grand scales, creating shortages for patient populations who depend on them for chronic disease control. Despite all of the unknowns, one thing is clear at this time: none are proven to be beneficial for COVID-19.

This is where our test has come and our judgment will follow. Do we reach for this arsenal of unproven medications before we know how to aim? Can we resist the temptation to put our desire to offer guidance to desperate colleagues over our perspicacity about the lack of data in support of these medicines? We confess to failing this challenge more than once over the

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past few weeks. However, if we can do so, we do have a third strategy in our pockets. One well known to veteran clinicians who have been wrong before and know they will be wrong again: temperance. It is something we do as well as anyone: withdrawing antibiotics, waiting another day or week or month to decide how long their duration needs to be, or, perhaps, never starting them in the first place.

In the coming months, there will be results from well designed and peer-reviewed trials that we hope will reveal therapeutic options for the treatment and prevention of COVID-19. Even more likely, there will be at least as many that do not work. In the meantime, we will be asked countless times to help decide which ones are which, often by trusted colleagues in search of a miracle for patients in extremis. In the face of this uncertainty, we can hope that preliminary data from a preprint can provide that miracle, or we can return to first principles and ensure we are reflecting on what the data tell us when asked, simply by responding with the painfully honest truth, "I do not know. Ask me again tomorrow."

Notes

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