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Chicken Soup in the Time of COVID



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The coronavirus disease 2019 (COVID-19) pandemic has led to a variety of behaviors as people try to cope with the very real personal and societal threats and the associated anxieties. Some behaviors, like toilet paper hoarding, would border on the comical if the situation were not so tragic. Others, like hand washing, social distancing, and staying at home have real impact on viral spread and are crucial. As expected, many people from ordinary citizens to biomedical researchers are seeking remedies. However, the urgency of the search for new treatments during the current crisis has a dark side. That desperate people are at risk for fraudulent exploitation is well recognized and, sadly, has been reported. Similarly, well-intentioned efforts may have

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adverse effects. In this context, chicken soup may offer some insights.

Some years ago, we conducted a limited study of a potential antiinflammatory effect of chicken soup. This was published in *Chest* and was well received.¹ Because of its resonance with common experience and belief, the study has been referenced and discussed in the lay press way beyond the scientific significance of the results. Predictably, the issue of whether chicken soup might be good for COVID-19 has come up.

Our in vitro study demonstrated a modest inhibitory effect on neutrophil migration.¹ Speculatively, this may provide a mechanism for less inflammation and fewer symptoms with "colds." Of course, an antineutrophil effect could also increase infection risk. Importantly, our study was not a clinical trial, and no conclusions could be drawn about clinical effect, either good or bad.

The distinction between supportive evidence and proof of benefit is easily lost, particularly in the face of a crisis. The vast majority of promising agents with supporting evidence fail to become medicines for a variety of reasons, including toxicity and lack of efficacy.² Although common knowledge among clinical researchers, it is often a surprise to many in the general public. As a consequence, there has been a rush to use promising agents to treat COVID-19, as there was in the Ebola crisis.³ Sadly, in the Ebola crisis, the lack of welldesigned rigorous clinical trials resulted in very little knowledge gained about which medicines are effective and which are not.³

A recent World Health Organization report listed 79 agents/combinations with potential as therapeutics for SARS-CoV-2 infection.⁴ More are likely being considered. Some experimental agents, such as remdesivir, have being requested for compassionate use,⁵ and others are being used used off label. The Food and Drug Administration (FDA) recently issued an emergency use authorization for chloroquine and hydroxychloroquine for certain patients with COVID-19.⁶ Specifically, adolescent and adult patients who are hospitalized and unable to participate in a clinical trial may qualify for the emergency use authorization. This has been interpreted by some as "Food and Drug Administration approval" for these medicines to treat

ABBREVIATIONS: COVID-19 = coronavirus disease 2019 AFFILIATIONS: From the Department of Internal Medicine (Drs Rennard and Kalil), University of Nebraska Medical Center; and the Division of Respiratory and Critical Care Physiology and Medicine (Dr Casaburi), Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center.

COVID-19, which it is not. Nevertheless, in the charged atmosphere surrounding the pandemic, there has been a run on these medicines. Despite medical society and health agency recommendations, the general public, desperate for options, continues to put tremendous pressure for access to incompletely tested and potentially unsafe therapeutics. For many of these, the data supporting their safety and efficacy are similar to or less than that for chicken soup.

Determining whether a medicine works or not is not easy. With a fatality rate of 50% for patients who are admitted to the ICU,⁷ a medicine that reduced the mortality rate to 25% would require 58 subjects to be treated with drug and 58 subjects with placebo to have an 80% chance of finding a statistically significant difference in death rates with a significance level of P < .05. For a smaller, but likely important 20% relative reduction in the mortality rate, 387 individuals would be required in each group. Alternate statistical approaches are possible, but the numbers required to have meaningful data are larger than possible at most individual centers. This means that clinical trials must be done in the context of collaborative groups. Happily, such groups have been rapidly organized.⁸ In addition, plans are in place for data pooling with open access.⁹ These efforts should help optimize learnings from the current crisis that will help going forward.

Of course, chicken soup has benefits beyond its potential medicinal value. Chicken soup, often made by a lengthy and loving process, can provide real psychosocial support. The mechanisms by which such support makes people feel better are complex and incompletely explored,¹⁰ but there is little doubt about their benefit including during humanitarian crises.¹¹ Health-care workers applauding patients who are discharged from hospital having made recovery, community members applauding health-care workers going to work, volunteers making masks, and other acts of community support are positive contributions to overall well-being and should be encouraged. Of course, these interventions should be as effective as possible, and homemade masks should be designed in accord with the best available evidence to assure their effectiveness.¹²

People will seek out these "chicken soups" because they provide social support together with the reassurance associated with doing *something*. However, it is essential

that these measures not compromise interventions with known value and not cause harm. It was easy for some, reassured by the belief that youth was protective, to forgo social distancing. Neither should homemade masks be an excuse for neglecting social distancing. Moral support to bolster the spirits of health-care workers cannot derail the calls for proper equipment and support. Nevertheless, when added to all the other efforts required to address the COVID-19 crisis, the "chicken soups" may have something to offer. "Chicken soups," if they are appropriately used, should not preclude other important actions. Most importantly, we must conduct the solid science necessary to address this crisis with a strong focus on the performance of rigorous randomized clinical trials.

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