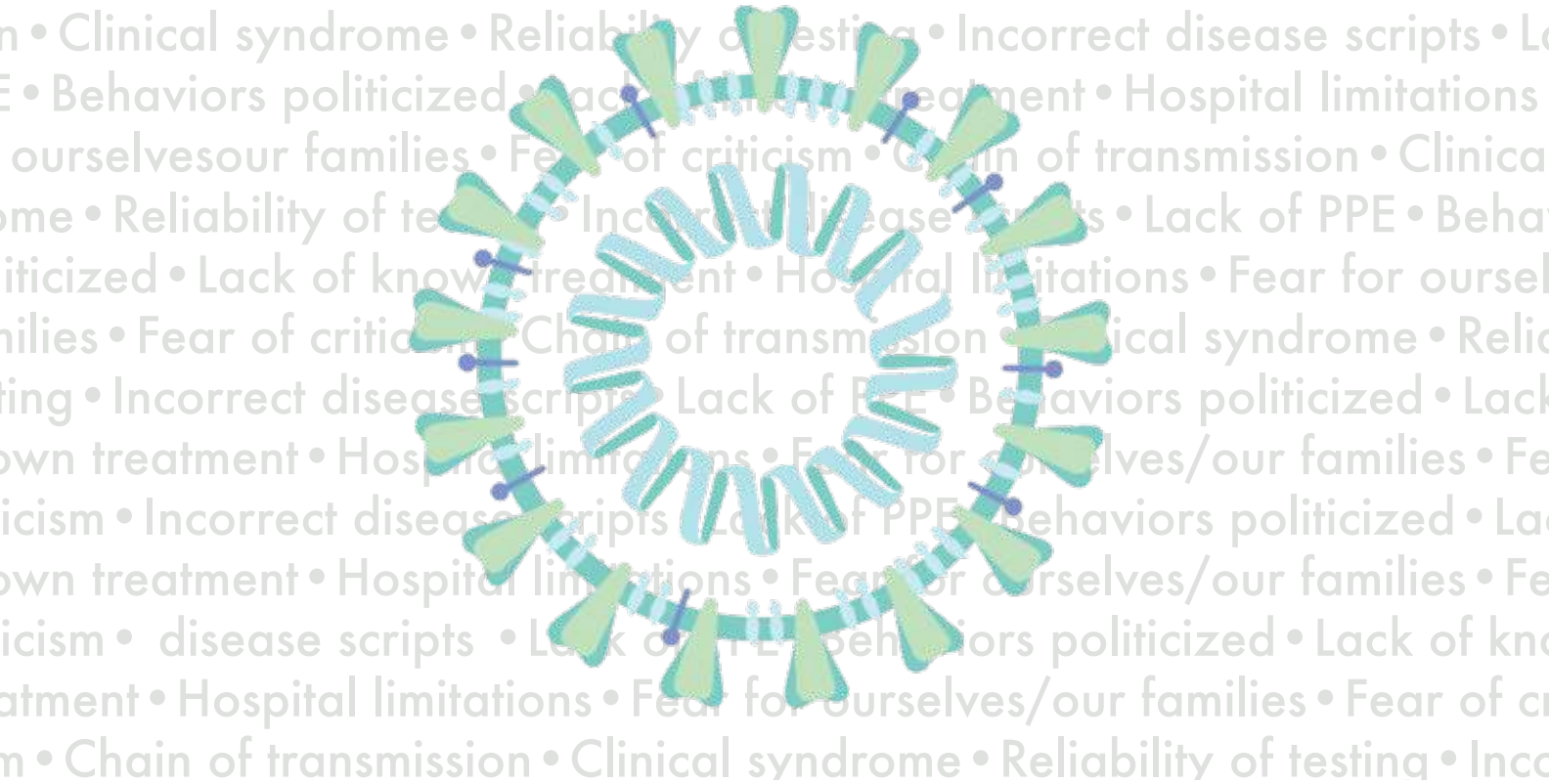

Lessons learned from COVID-19 for the puzzled clinician

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Plagues and pandemics have been part of human experience throughout recorded history. Even before the invention of the printing press, some of the most enduring literature such as *The Decameron* and *The Canterbury Tales* was inspired by the effects on society of the bubonic plague sweeping through Europe in the 14th century. Few of us practicing medicine in the 21st century have been in a rapidly developing life-threatening epidemic or pandemic. I do not think any of us imagined that we would be dodging as well as treating a serious viral infection sweeping around the globe.

The most frequent comparison of this COVID-19 pandemic is to the influenza pandemic of 1918–1919. Despite the passage of a century, we are reassessing if not reliving that experience through archival photography, museum exhibitions and regular reminders in the media. Through clever sleuthing and molecular biology breakthroughs, we now understand how the H1N1 influenza virus came to be so virulent. Developments in vaccines and antivirals give us hope that we can better understand and manage another influenza pandemic, and, by analogy, a coronavirus pandemic.

Some physicians remember the early years of the human immunodeficiency virus epidemic. We saw the first publication of what was later called AIDS in 1981, but we did not have HIV testing until 1985. We have more positive memories of the 1990s when we developed and deployed effective HIV treatment. The incredible toll of HIV in the 20th century is still being felt by the losses of so many young, creative people 30 years ago who would likely still be alive and productive but for this disease. Unfortunately, despite these gains, we are still losing people to HIV every day in the 21st century because they cannot access or adhere to treatment. However, despite the breakthroughs,

we still lack the vaccine that was promised in 1984 by President Reagan's health secretary, Margaret Heckler.

Assuming we manage to control COVID-19, there will be questions about how we used our sophisticated tools to save lives. We will evaluate errors of preparation and execution. We will review how COVID-19 changed the roles of medical professionals. Some of these changes will restructure the medical establishment permanently.

One area that may be more challenging, and thus avoided, is the impact of this pandemic on the principal tool of physicians—medical reasoning—and its apparent failure to alter the arc of COVID-19. In particular, the role of clinical judgment and decision-making will be under scrutiny.

This evolving pandemic has challenged physicians—even those with expertise in pandemic preparation and management. Infectious diseases physicians were instrumental in controlling the 2003 SARS epidemic, which was contained within months of its detection. As compared to previous pandemics and plagues, our incredible diagnostic tools and extraordinary supportive care should have made the COVID-19 virus fit right into our wheelhouse. Despite our training and experience, things still feel awkward and unbalanced more than 10 million U.S. patients later.

A perplexing element of this pandemic is the challenge of making a clinical diagnosis. With a disease that encourages maintaining distance between patient and provider, this should be the ultimate test for the master clinician. I offer 10 elements to explain the disconnect between our usual comfort in clinical decision-making and the unsettled role for clinical expertise in this pandemic.

10 disconnects

1 The first was an erroneous belief that we should find a chain of transmission for each case, as we did with SARS in 2003. The absence of sick contacts was a good surrogate for low risk of infection. As a corollary, we thought that residence in or travel to a region endemic for the disease would adjust our prior probability up, and its absence would move our prior probability down. I remember discussing travel policy and the nuances of isolating patients and staff with recent travel to Level 2 or Level 3 countries. Domestic air travel was also a risk factor because of crowds and intermingling of people at airports and on airplanes. We learned later how much worse that was on cruise ships. Recent studies have shown that the continuous wearing of face masks during flights has made air travel safer, but the cruise industry continues to be crippled by fear of infection.

2 Second, with limited clinical information, we assumed that the clinical syndrome would be reliable. It seemed unlikely that asymptomatic carriers would be the source of infection for it was plausible that coughing would be the major route of transmission. The role of environmental soiling followed by face touching could be a risk factor, but we assumed that adherence to hand hygiene would be protective.

3 Third, with limited access to testing we naively assumed that test results, once available, would be reliable and not require further validation. The analytical data showed that polymerase chain reaction tests were extremely sensitive and specific in spiked samples. We are comfortable that specificity was very high, but the high false negative rate was disappointing. This could result from specimen collection imperfections, variable levels of virus at different phases of infection, and variations in test kit, reagents, etc. We probably gave too much credence to negative test results which might have delayed treatment and resulted in further exposure.

4 Fourth, our over-reliance on tests caused us to develop incorrect disease scripts. We were unaware of the variety of presentations because we saw only the ones we tried to confirm. The debate about the presence of gastrointestinal (GI) symptoms became a debate about the infectivity of GI tract contents—a very different question. We had to trust case series to show nuances of presentation and timing of symptoms. While this was uncomfortable, it gave us an appreciation of the varied clinical manifestations, including no clinical manifestations. On April 27, when 1,000,000 Americans had been diagnosed with COVID-19, the Centers for Disease Control and Prevention (CDC) added symptoms of chills, shaking, muscle pain, headache, sore throat, and anosmia to the list of earlier symptoms of fever, cough, and shortness of breath.

5 Fifth, we were so focused on access to personal protective equipment and the implications of quarantine that we felt pressure to create a threshold of certainty about access to tests, and isolation. Had there been unlimited personal protective equipment and testing, we might have been open to conversations about managing social distance, return us to work, etc.

6 Sixth the conversation about behavior of the public in the time of a respiratory pandemic became politicized and distracting. We could not come to consensus on policies for health workers or provide counsel about the best way to implement and enforce the public social restrictions that eventually and chaotically emerged. Government took on the challenge and the message was often muddled and inconsistent. We tried to provide meaningful information

to our own institutions when we could not fully understand or implement the rapidly changing advice of respected national policy makers.

7 Seventh, the lack of known treatments to alter the course of the disease, other than supportive care, made it easy to reach for unproven treatments, including preventive regimens, with largely anecdotal support. The conflicting claims about chloroquine and hydroxychloroquine resulted in both excess cardiac toxicity for those unlikely to benefit, and a shortage of supplies for those with rheumatic diseases who needed these medications. The comparisons to the early days of the HIV pandemic are impossible to ignore. HPA-23, an experimental French treatment for HIV, generated publicity when desperate patients had to go to France to acquire it, and when Rock Hudson was reported to receive it. Despite the headlines, the drug had no benefit and was abandoned and forgotten.

8 Eighth, the limitation of inpatient beds, drugs, ventilators, and key personnel required hard choices about how to manage patients. This resulted in resource misallocation both in an excess of caution while awaiting test results, and to inadvertent staff exposures for patients with atypical presentations. This improved as test availability and understanding the limitations of testing improved. Results from chest radiographs and CT scans turned out to be more helpful than expected as radiologists became confident with the range of imaging abnormalities associated with this virus.

9 Ninth, the fear that we, our colleagues, and/or loved ones might become ill affected our reasoning. We want to be in charge and confident even when we are not. And, we want to hear everything even if the messages are contradictory, misleading, or out of date. Hence, our Bayesian instincts were muddled by a fear of uncertainty and tension between over-cautiousness leading to shortages of supplies and personnel, and insufficient concern.

10 Tenth, there was a fear that criticism could distract from the goal of team-building in adversity. This makes it hard to criticize our colleagues and our administrators. Feelings were raw and even the normal give and take often felt intense and uncaring. It could be likened to an emotional synesthesia when one ordinary, benign form of communication is perceived as another, possibly a more sinister one. This lack of candid feedback risked the propagation of errors since no one knew who had the best information.

Finding resolution

It might take years to resolve how we could have done better. The natural experiment of different regions and countries taking different approaches may be useful to study. Once the pandemic has dissipated, we will be able to reflect. Each of us must make an honest assessment of our limitations and biases. We should be candid about the imperfections of science as an early guide to policymakers during exceptional circumstances. We should also honor the critical role of science in establishing models for the assessment of diagnostic testing, epidemiology, and therapeutic intervention. The balance of humility during times of ignorance, and the willingness to stand up to do research will require threading the proverbial needle.

We teach students and residents that reading, repeated practice, and openness to feedback will make them better at the craft of medicine. They also believe that the experience of their mentors, guidelines, and critical reading are important. In this pandemic, agencies such as the Centers for Disease Control and Prevention and World Health Organization made regular changes in their recommendations based on new understanding and practical limitations, but this message was often confusing. At the bedside, even master clinicians struggled to make a confident diagnosis. How can we honor the system but do better next time?

When we look back at our response, including our missteps, we should be proud of our profession. Doctors have distinguished themselves by being willing to push through uncertainty and personal safety to provide vital services. We can take pride that we did that even as we reassess our responses to uncertainty and confusion under duress.

This is a time for transparency and candor as well as mourning. We need to honor the sacrifice of medical personnel as well as the passion and commitment under trying circumstances that have characterized the response to the COVID-19 pandemic. The most important lesson from this crisis: We must advocate for deeper resources, better preparation, and a bolstering of public health infrastructure, locally and nationally. No matter how smart and competent we get, we need a depth of expertise in epidemiology, data collection, testing, communication, and modeling when the next pandemic strikes. This may require entering into a political process that many of us have avoided to show impartiality. But the prospect of a repeated failure of preparation will be ours to own if we do not insist on being at the table, and that may be the most important lesson of all.

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