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All That Glitters Isn't Gold

Critical Care in the Time of Coronavirus Disease 2019



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“All that glitters is not gold;
Often have you heard that told:
Many a man his life hath sold
But my outside to behold:
Gilded tombs do worms enfold.
Had you been as wise as bold.”

William Shakespeare, *The Merchant of Venice*¹

After cases of pneumonia of unknown origin were reported from Wuhan, China, in December 2019, a novel enveloped RNA beta-coronavirus was identified and named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).² Presently, SARS-CoV-2 has spread throughout the world, infecting > 2.4 million

people and claiming > 169,000 lives. It has created a great degree of panic and uncertainty in the global public as well as in the medical community.

Fueled by the desire to save lives, and driven in part by fear and the unfathomable numbers of critically ill patients, we are at risk of deviating from our principle of “first do no harm.” Several novel potential treatments for SARS-CoV-2 exemplify this risk. Therapies such as hydroxychloroquine, azithromycin, tocilizumab, methylprednisolone, remdesivir, convalescent plasma, tissue plasminogen activator, zinc, and vitamin C have been prescribed under the justification of compassionate use. Eager to find answers, the global collaboration of the scientific community has been swift and unprecedented.

We should exercise caution, however, that our response to this global pandemic does not come at the expense of the scientific method. The field of critical care is littered with failed therapies that seemed groundbreaking at the time but were later shown to be ineffective. We remember the promise of activated protein C for sepsis in the early 2000s,³ a drug that has now been removed from the market because of its potential serious side effects. Or the use of inhaled nitric oxide, surfactant therapy, or perfluorocarbons for ARDS, therapies that showed such promise initially but have fallen out of favor for routine usage. We have recently witnessed the rise and fall of another promising therapy, high-dose vitamins. Touted as the answer for critical illnesses, from septic shock to ARDS, high-dose vitamins were the recent darling of the critical care world. Once again, subsequent large-scale trials to date have not borne out a mortality benefit. Should we then abandon all hope? Certainly not. Instead, this is the time to lean more heavily than ever on the basic tenets of critical care.

When confronted with a novel challenge, and ARDS due to coronavirus disease 2019 (COVID-19) is surely that, intensivists can respond in two fundamentally different ways. We can choose to apply evidence-based approaches that have proved effective for critically ill patients or we can choose to adopt and create novel approaches and therapies. We have made great strides in improving the care of critically ill patients through practices such as reducing delirium, decreasing amounts of sedative medications, more rapid ventilator weaning and extubation, earlier mobilization, and increased

ABBREVIATION: COVID-19 = coronavirus disease 2019; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2

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involvement of families at the bedside. Consistent use of ICU bundles centered on these best practices has been shown to improve functional status and decrease ICU length of stay, delirium development, and mortality, outcomes of even greater importance given a global increase in the number of critically ill patients.⁴ These fundamental practices are not groundbreaking or flashy and will not play as well on social media or the local news, but they improve outcomes in critically ill patients.

Care of the critically ill patient rarely relies only on the master clinician constructing a masterpiece. Rather, these practices require intensive investment in the multi-professional team approach to providing critical care. One of the characteristics of a high-functioning team is that everyone knows what is supposed to happen, and every member knows what he or she is to do. Implementing new techniques in the midst of a pandemic deviates from established standards of care and affects the integrity of a team-based approach. If we start to bend the rules, what is the message to our colleagues and patients?

Some investigators have suggested that respiratory failure caused by SARS-CoV-2 is “atypical” (ie, relatively spared compliance, low lung recruitability) and is not true ARDS. In our experience, respiratory failure caused by SARS-CoV-2 meets the Berlin criteria for ARDS,⁵ and we advocate for adherence to evidence-based ventilation for ARDS. These therapies for ARDS are also not sexy or novel. Lung protective strategies such as minimizing repeated cyclic stretch and high tidal volume ventilation, preventing fluid overload, and prone positioning are reliable ventilatory strategies. Prone positioning in particular is a proven and cheap therapy with clear mortality benefit.⁶ Despite this mortality benefit, previous studies have shown that only 16% of ARDS patients who died had a trial of prone positioning.⁷ Whether due to lack of familiarity, lack of belief in efficacy, or the fallacy that new or more complicated options must be superior, now is not the time to forsake our established methods.

During these unprecedented times, the temptation is high to abandon routine care and basic physiology in

favor of newer or more exciting therapies. It is possible that in 1 year we will all recognize that patients with SARS-CoV-2-related respiratory failure should be treated with hydroxychloroquine, azithromycin, tocilizumab, methylprednisolone, remdesivir, convalescent plasma, tissue plasminogen activator, zinc, vitamin C, low positive end-expiratory pressure, and airway pressure release ventilation. But if that is what we know, it will be the result of well-conducted clinical trials, not the result of the private inspiration of desperate clinicians. As we rise to the challenges of pandemic medicine, high ICU capacity, and the health-care workforce being stretched extraordinarily thin, the mantra of *primum non nocere* must still reign supreme. With our eyes on the goal of liberating an increasing number of SARS-CoV-2 critical illness survivors both from our ventilators and ICUs, the stakes have never been higher for adherence to basic fundamentals of good critical care. Or perhaps, in our zeal to outsmart the ravages of this pandemic, we will veer in the wrong direction, realizing our mistake only far down the road.

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References

1. Goodreads. William Shakespeare, Quotes. <https://www.goodreads.com/quotes/379204-all-that-glisters-is-not-gold-often-have-you-heard>. Accessed June 9, 2020.
2. Guan WJ, Ni ZY, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med*. 2020;382(18):1708-1720.
3. Bernard GR, Vincent JL, Laterre PF, et al. Efficacy and safety of recombinant human activated protein C for severe sepsis. *N Engl J Med*. 2001;344(10):699-709.
4. Pun BT, Balas MC, Barnes-Daly MA, et al. Caring for critically ill patients with the ABCDEF bundle: results of the ICU Liberation Collaborative in over 15,000 adults. *Crit Care Med*. 2019;47(1):3-14.
5. Force ADT, Ranieri VM, Rubenfeld GD, et al. Acute respiratory distress syndrome: the Berlin definition. *JAMA*. 2012;307(23):2526-2533.
6. Guerin C, Reignier J, Richard JC, et al. Prone positioning in severe acute respiratory distress syndrome. *N Engl J Med*. 2013;368(23):2159-2168.
7. Bellani G, Laffey JG, Pham T, et al. Epidemiology, patterns of care, and mortality for patients with acute respiratory distress syndrome in intensive care units in 50 countries. *JAMA*. 2016;315(8):788-800.