



Hi, this is Evan Kharasch, Editor-in-Chief of ANESTHESIOLOGY, with some highlights from the June 2020 issue, as selected by the journal editors.

We are proud to note that this issue includes a Special Section on COVID-19. It represents our specialty's best efforts to rapidly learn all we can about the new virus and disease, while providing the best possible clinical care under very trying circumstances. These articles were all published online, ahead of print, and free for all to read, in March 2020, as a service to patients and practitioners.

We begin this month with a special review of the clinical implications of COVID-19 for perioperative and critical care physicians, as they were understood in early March. A team of authors led by Dr. John Greenland and colleagues at San Francisco Veterans Administration Health Care System and the University of California-San Francisco wrote this review. They summarize COVID-19 pathogenesis, presentation, diagnosis, and potential therapeutics. The authors draw on literature from other viral epidemics and treatment of acute respiratory distress syndrome. They also summarize recent publications on COVID-19, as well as guidelines from major health organizations. Greenland and colleagues find reason for optimism about future virus control. A number of antiviral drugs have shown promise in vitro. Even a partially effective antiviral could allow the immune system to respond enough to prevent lethal disease. There is even potential that antivirals could be used in chemoprophylaxis. The authors note that, although patients with HIV quickly developed resistance to antivirals, coronavirus studies suggest this might be less of a problem. As COVID-19 evolves, physicians will likely have a variety of therapeutic and vaccination options to minimize morbidity and mortality. Until then, anesthesiologists will be called upon to provide supportive care while minimizing the risk of viral transmission to themselves and others.

Next, we have another COVID-19 Special Section article. The Joint Task Force of the Chinese Society of Anesthesiology and the Chinese Association of Anesthesiologists have issued recommendations for the perioperative management of patients infected with coronavirus and having COVID-19. Dr. Xiangdong Chen of Union Hospital of Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China, was the lead author. This document was created based on World Health Organization and National Health Commission guidelines for the prevention and treatment of COVID-19. The task force also considered clinical experiences from frontline care providers and performed a comprehensive literature review on the perioperative management of infectious patients. This first edition is not intended to replace any existing guidelines on anesthesia care and infectious disease control. The recommendations were mainly based on the experience of anesthesiologists who provided care in China. Therefore, adoption of these recommendations outside of China must be done with caution. Each country's environment, culture, healthcare system, and patient needs should be considered. The task force will continuously update their recommendations as new information becomes available. Our next clinical study focuses on the World Health Organization Disability Assessment Schedule version 2.0. This assessment tool is finding widespread adoption as a patient-centered outcome measure in clinical studies. Dr. Mark Shulman and colleagues at Monash University, Melbourne, Australia, conducted the study. They attempted to determine the minimal clinically important difference or patient-acceptable symptom state scores for postoperative patients. The authors analyzed prospectively collected data from three studies that measured disability 3 and 6 months after surgery. These studies included data from 4,300 patients. Shulman and colleagues found that a change in the assessment score of 5% after surgery is clinically significant. They concluded that patients with a scaled disability score less than 16% after surgery can be considered as disability-free. Conversely, patients with a score of 35% or more can be considered as having at least moderate clinically significant disability.

Our next clinical study evaluated the incidence of persistent postoperative opioid use. Dr. Naheed Jivraj of the University of Toronto and colleagues there and elsewhere conducted the study. They began with a literature search to identify observational studies that evaluated persistent opioid use among

opioid-naïve surgical patients. They found 29 distinct definitions of persistent opioid use in 39 different studies. Next, the authors performed a population-based cohort study of opioid-naïve adults undergoing one of 18 common surgical procedures during a 4-year period. The cohort consisted of 162,000 opioid-naïve surgical patients in Ontario, Canada. The primary outcome was the incidence of persistent opioid use. Applying the 29 different definitions yielded an incidence rate for persistent opioid use in the first postoperative year ranging from 0.01% to 14.7%. The median was 0.7%. The authors concluded that the incidence of persistent opioid use reported after surgery varies more than 100-fold depending on the definition used. Definitions varied markedly in their sensitivity for identifying adverse opioid-related events. However, all definitions showed low sensitivity overall across measures.

Our next study compared the use of neostigmine vs. sugammadex for neuromuscular blockade reversal. Sugammadex provides more rapid and effective restoration of neuromuscular tone without systemic anticholinergic activity. However, neostigmine currently remains the mainstay of practice. Dr. Sachin Kheterpal of the University of Michigan, and colleagues there and elsewhere, conducted the study, which is known as the STRONGER trial. The authors hypothesized that the choice of neuromuscular blockade reversal may be associated with a lower incidence of major pulmonary complications. Twelve U.S. hospitals participated in this multicenter observational matched-cohort study of surgical cases during a four-year period. Investigators included adults undergoing elective inpatient noncardiac surgical procedures who received a nondepolarizing neuromuscular blockade agent and reversal. The composite primary outcome was major postoperative pulmonary complications like pneumonia, respiratory failure, and pneumothorax. Out of 45,000 patients studied, 4.1% were diagnosed with the composite primary outcome. In the sugammadex group, 3.5% of patients developed pulmonary complications, compared with 4.8% of patients who received neostigmine. Kheterpal and colleagues concluded that the use of sugammadex was associated with a 30% reduced risk of pulmonary complications compared to neostigmine. This included a 47% reduced risk of pneumonia and a 55% reduced risk of respiratory failure.

Our next study examined functional magnetic resonance imaging-derived global brain signals as a candidate marker for a conscious state in both rats and humans. Sean Tanabe of the University of Michigan and colleagues there and in Canada and China conducted the study. They hypothesized that unconsciousness would be accompanied by a loss of global temporal coordination. They also expected to see specific patterns of decoupling between local regions and global activity differentiating among various unconscious states. The authors studied functional magnetic resonance imaging global signals in physiologic, pharmacologic, and pathologic states of unconsciousness. Subjects studied included humans in natural sleep, with propofol anesthesia, and with neuropathology. The authors also studied a cohort of rats with propofol anesthesia. Tanabe and colleagues quantified global signal amplitude and the correlation between global signal and signals of local voxels. Each distinct state of unconsciousness, including sleep, general anesthesia, and unresponsive wakefulness syndrome, showed state-specific alterations in global signal topography. Tanabe and colleagues concluded that the global temporal coordination of various modules across the brain may distinguish the coarse-grained state of consciousness versus unconsciousness. Additionally, the relationship between the global and local signals may define the particular qualities of a particular unconscious state.

Our next study used a mouse model to examine chemotherapy-induced neuropathic pain in the extremities. Dr. Raquel Tonello and colleagues at the University of Cincinnati conducted the study. They tested the hypothesis that the same local sympathetic blockade used to treat pain conditions can also treat chemotherapy-induced neuropathic pain. Tonello and colleagues performed local surgical sympathectomy in mice that received intraperitoneal injections of paclitaxel. The authors then assessed mechanical and cold allodynia and neuroimmune and electrophysiologic responses. They found that local microsympathectomy produced a fast recovery from mechanical allodynia in male mice. It also prevented the development of cold allodynia in both male and female mice. Additionally, transforming growth factor- $\beta$  was enhanced in mice after sympathectomy and was capable of reducing paclitaxel-induced mechanical sensitization. Tonello and colleagues concluded that local sympathetic nerves control the progression of immune responses in dorsal root ganglia and pain-like behaviors in mice

after paclitaxel. These findings raise the possibility that clinical strategies already in use for local sympathetic blockade may also offer an effective treatment for chemotherapy-induced neuropathic pain.

Finally, we close this month with a Clinical Focus Review article that examines neuromuscular blockade applicability in early acute respiratory distress syndrome. Dr. William Hurford of the University of Cincinnati authored this review. He recounts the findings of two key clinical trials: the Papazian et al. trial from 2010 and the 2019 Reevaluation of Systemic Early Neuromuscular Blockade Study. He then applies their findings to the current management of early ARDS. First, patients successfully managed with low plateau or transpulmonary pressures should not routinely receive continuous neuromuscular blockade. Second, patients with persistently increased airway pressures or with evident adverse

patient-ventilator interactions should receive a trial period of ventilator adjustments and/or changes in sedation level. Neuromuscular blockade may be considered in patients who require deep sedation to reduce vigorous spontaneous respiratory efforts, reduce asynchrony, or permit adjunctive therapies. Third, partial neuromuscular blockade and higher levels of PEEP may be useful to decrease the magnitude of spontaneous efforts. Both neuromuscular block and deep sedation should be tapered as soon as clinically feasible. Lastly, cisatracurium remains a reasonable choice if neuromuscular blockade is needed because it is free of active metabolites and significant side effects.

Thanks for joining me for this brief exploration of the exciting work being done in our specialty. I'll be back in a few weeks with highlights from the July issue of *ANESTHESIOLOGY*.