Hi, this is Evan Kharasch, Editor-in-Chief of Anesthesiology, and you're listening to the Anesthesiology Editor-in-Chief podcast. I'll be giving you some highlights from the November 2020 issue, which have been selected by the journal editors.

I'll begin this month with the simple measurement of blood pressure, which has been assessed for decades using the familiar blood pressure cuff. This first investigation was a clinical study examining the effectiveness of a new, high-fidelity upper-arm blood pressure cuff, that incorporates a hydraulic sensor pad. Dr. Josef Briegel of University Hospital, Ludwig-Maximilians-Universität Munich, and colleagues there and elsewhere in Germany conducted the study. They assessed the new cuff's accuracy and precision of noninvasive blood pressure measurements. They compared these results with invasive measurements using a femoral artery catheter. The study population consisted of 110 patients having major noncardiac surgery. The authors selected 5 measurements per patient for comparison. These included the minimum, maximum, and intermediate values to cover the measured arterial pressure range. The average bias of mean arterial blood pressure measurements was 0 mmHg and the precision was 3 mmHg. The investigators concluded that the new high-fidelity upper arm cuff method met the current international standards in terms of accuracy and precision. It was also very accurate at tracking changes in blood pressure and reliably detected severe hypotension during noncardiac surgery.

Our next clinical study touches on the controversial question of whether anesthesia and surgery are associated with pediatric developmental abnormalities in patients. The study examined whether childhood exposure to general anesthesia and surgery before age 4 was associated with later adverse neurodevelopmental outcomes, at ages 7 to 16. Dr. Graham Walkden and colleagues at the University of Bristol conducted the study. They studied a population-based, representative United Kingdom birth cohort of 13,400 children. Children were grouped based on whether they had undergone single, multiple, or no exposures to general anesthesia and surgery by age 4. In this cohort there were 1,110 children who had a single exposure to anesthesia and surgery, and 212 who were multiply exposed to general anesthesia and surgery. The authors used a variety of methods to evaluate children's outcomes at ages 7 to 16. These included many domains, including motor, cognitive, linguistic, and behavioral development. The investigation found no overall evidence for statistically or clinically significant long-term neurotoxic effects of anesthesia and surgery. There was some evidence of impairments in a few specific neurodevelopmental subdomains, however. These included motor function, manual dexterity, and social communication. The authors concluded that early childhood general anesthesia and surgery were not associated with a global picture of neurodegenerative effects, and this provided reassurance about lack of neurotoxic potential of general anesthesia and surgery.

Next, we have a clinical study that explores whether the dissociative and analgesic properties of ketamine are independent of each other. Jacob Gitlin and colleagues at Massachusetts General Hospital conducted the study. The authors conducted a single-site, open-label study of ketamine at 2mg/kg in 15 healthy subjects. They assessed pain and dissociative symptoms. One hour later they gave the subjects 2 mg of midazolam to attenuate ketamine associated dissociation. The authors used Patient-Reported Outcomes Measurement Information System questionnaires to assess the intensity and quality of pain, caused by a pre-calibrated pneumatic cuff. They also used the Clinician Administered Dissociative States Scale to assess dissociation. This scale measures perceptual, behavioral, and attentional alterations during dissociative experiences. The authors found that ketamine produced both analgesia and dissociation. They also found that midazolam attenuated ketamine-induced dissociation in all subjects. The effect of ketamine in reducing pain intensity scores was not exclusively caused by dissociation. The authors concluded that ketamine-induced analgesia had no strong inherent relationship with ketamine-induced dissociation beyond both being independently modulated by ketamine. They suggest that ketamine or its metabolites modulate distinct neural circuits to produce dissociation and analgesia.

Our next clinical study is a subanalysis of the Protective Ventilation in Cardiac Surgery (PROVECS) randomized controlled trial. The main PROVECS trial found that an open-lung ventilation strategy did not improve postoperative respiratory outcomes after on-pump cardiac surgery. This study was a prespecified subanalysis, to assess the regional distribution of ventilation and plasma biomarkers of lung epithelial and endothelial injury produced by that the open lung strategy. Dr. David Lagier of Massachusetts General Hospital and colleagues there and at Aix Marseille University, Marseille, France, conducted the study. The authors assessed the regional distribution of ventilation and plasma biomarkers of lung epithelial and endothelial injury in the open-lung ventilation strategy. This strategy included a moderate PEEP (8 cmH2O), recruitment maneuvers, and mechanical ventilation. The control group received low PEEP (2 cmH2O) and no recruitment maneuvers. The authors tested their open-lung ventilation hypothesis in 86 patients undergoing elective on-pump cardiac surgery. Before median sternotomy, open-lung ventilation produced larger dorsal tidal ventilation than that achieved with a low-PEEP strategy. However that benefit to regional ventilation distribution did not persist, even to the end of surgery or beyond to two days later. Open-lung ventilation was also associated with higher intraoperative pulmonary venous plasma sRAGE concentrations, a biomarker of lung epithelial and endothelial injury. This raised concerns about epithelial lung injury induced by the intervention. However the open lung strategy had no effect on plasma angiopoietin-2 concentrations, which implies a lower likelihood of endothelial lung injury. The authors concluded that open-lung ventilation had very brief benefits, but may have risk for lung epithelial injury consistent with lung overdistension.

Our next study examined fundamental receptor properties of volatile anesthetics, using a drug interactions approach. Dr. Jaideep Pandit and colleagues at the University of Oxford conducted the study. They used a rat model to examine whether the volatile anesthetics halothane and isoflurane act additively on carotid body potassium TASK channels. The investigators tested the hypothesis that the less efficacious anesthetic might antagonize the more efficacious anesthetic, as predicted by classical drug-receptor theory. They used isolated neonatal rat glomus cells to study halothane and isoflurane effects on hypoxia-evoked rise in intracellular calcium. They also used patch clamping to study TASK single-channel activity in native glomus cells and a cell line that transiently expressed TASK-1. In vitro, both halothane and isoflurane depressed hypoxia-evoked rise in intracellular calcium in rat carotid body cells. Both anesthetics also activated TASK potassium channels. At equivalent concentrations, halothane exhibited stronger effects on hypoxic responses and TASK channel activation than isoflurane. However, coapplications of these two drugs resulted in lesser effects than halothane alone. These observations suggest that isoflurane and halothane act as competitive agonists on TASK channels where the weaker agonist (isoflurane) antagonizes the effects of the stronger agonist (halothane).

Next, we have a study that used a sheep model to increase our mechanistic understanding of pulmonary atelectasis. Dr. Congli Zeng at Massachusetts General Hospital and colleagues there and elsewhere conducted the study. They tested the hypothesis that atelectasis produces local transcriptomic changes related to immunity. They also tested the hypothesis that atelectasis affects alveolar–capillary barrier function, potentially causing lung injury, and this effect is further exacerbated by systemic inflammation. The authors created a sheep model of one-lung collapse and mechanical ventilation with global and regional physiological properties comparable to those of humans. Of 12 sheep, half received systemic lipopolysaccharide infusion to cause systemic inflammation and half did not. The investigators used a variety of imaging techniques to guide tissue sampling for next-generation sequencing and transcriptome analysis. They found that atelectasis alone dysregulated the local pulmonary transcriptome. Genes for immune response and alveolar–capillary barrier function were downregulated. With added systemic inflammation, the local immune response genes were enhanced, but barrier function genes remained downregulated. The authors concluded that atelectasis dysregulates the local pulmonary transcriptome, with downregulated immune response and alveolar-capillary barrier function genes. Systemic lipopolysaccharide upregulated immune response genes, but not those of local barrier function. They also concluded that interferon-stimulated genes and Yes-associated protein may have important regulatory roles. And, these genes may point to novel candidate targets for therapy of atelectasis-associated injury.

Our Clinical Focus Review article this month discusses anesthesiologists' recently expanded roles in in cardiothoracic critical care. Drs. Kenneth Shelton and Jeanine Wiener-Kronish of Massachusetts General Hospital wrote this article. They emphasize that anesthesiologists involved in cardiothoracic critical care have embraced new roles as experts in the management of cardiogenic shock and extracorporeal membrane oxygenation. The authors review how Mass General is handling cardiothoracic critical care. They cite their institution as an example of a successful multidisciplinary team that has been established in an institution with strong departmental interests. They also discuss the evolution of treatments for heart failure and shock and a brief history of extracorporeal membrane oxygenation. The current role of anesthesiology critical care specialists in both venovenous and venoarterial extracorporeal membrane oxygenation are then considered. This review emphasizes how the investigation of both cardiac and lung function in these critically ill patients is now essential. The authors next evaluate the early data regarding both venovenous and venoarterial extracorporeal membrane oxygenation in COVID-19 patients. The review concludes with speculation regarding possible future roles of cardiothoracic critical care anesthesiologists. One possibility is as remote monitors to selectively triage patients that may benefit from mechanical assist devices. These subspecialists may also function as part of hospital echocardiography teams.

November's Review article examines two innovative regional analgesic modalities, cryoneurolysis and percutaneous peripheral nerve stimulation. Dr. Brian Ilfeld and Dr. John Finneran, both of the University of California San Diego and the Outcomes Research Consortium in Cleveland, Ohio, wrote this review. Both innovative regional modalities are cleared by the U.S. Food and Drug Administration. Both modalities also have the potential to provide postoperative analgesia without many of the limitations of opioids and local anesthetic-based techniques. Cryoneurolysis uses exceptionally low temperature to reversibly ablate a peripheral nerve, resulting in temporary analgesia. Its extended duration of action is measured in weeks to months after a single application. Percutaneous peripheral nerve stimulation involves inserting an insulated lead through a needle to lie adjacent to a peripheral nerve. Analgesia is produced by introducing electrical current with an external pulse generator. Uniquely, this regional analgesic does not induce sensory, motor, or proprioception deficits and is cleared for up to 60 days of use. Cryoneurolysis can be applied to multiple target nerves and may provide more focused analgesia at a lower cost without the risk of lead dislodgement or retained lead fragments. However, validation efforts for both modalities have been limited. Randomized, controlled trials are required to define both the benefits and risks of cryoneurolysis and percutaneous peripheral nerve stimulation.

More noteworthy articles await readers in the November issue of Anesthesiology. I'll be back in just a few short weeks with an inside look at our December issue. As always, I hope that this podcast and our journal help you deepen your knowledge and strengthen your clinical practice.