Hi, this is Evan Kharasch, Editor-in-Chief of Anesthesiology, with some highlights from the March 2021 issue, as selected by the journal editors.

Let's begin this month with a clinical study on the important issue of postoperative pain. A team of investigators evaluated patterns in acute postoperative pain in a mixed surgical patient cohort. Dr. Terrie Vasilopoulos and colleagues at the University of Florida conducted the study. Their hypothesis was that there would be heterogeneity in the patterns of postoperative pain. Using the Brief Pain Inventory, the authors measured pain daily on postoperative days 1 through 7 among 360 patients. They then used group-based trajectory modeling to estimate trajectories and patterns of postoperative pain. They identified five distinct postoperative pain trajectories. These five trajectories were low pain, moderate-to-low pain, moderate-to-high pain, high pain, and decreasing pain. Nearly half of the patients were in the moderate-to-high pain group, with an average pain score of 6 out of 10. One quarter of the patients were in the moderate-low group. The rest of the patients were in either the high, low or decreasing pain groups. In general, nearly two-thirds of patients had high or moderate-high pain over the first 7 days following surgery. Multivariable analysis showed that younger age, female sex and greater anxiety made it more likely that patients would be in the high-pain group. Postoperative pain trajectories were not associated with preoperative or intraoperative opioid use. The pain trajectory group was, however, associated with postoperative opioid use. Patients in the high- pain group required four times more opioids than the low pain group. The investigators concluded that postoperative pain trajectories were predominantly defined by patient factors and not surgical factors.

Our next clinical study explored the effects of severe COVID-19 on patients' hemostatic balance. Dr. Christoph Heinz and colleagues at University Hospital Frankfurt, Goethe University, Frankfurt, Germany, conducted the study. They assessed the details of clot formation and lysis in 27 critically ill COVID-19 patients using point-of-care-diagnostics. They performed aggregometric and viscoelastometric measures in the ICU to assess the patient population's comprehensive hemostatic profile. Then they compared the data to healthy controls. The study did not find a greater platelet aggregability based on impedance aggregometric tests. But thromboelastometry in COVID-19 patients revealed greater maximum clot firmness and longer lysis time in extrinsic activation and activation of fibrinolysis. This was generally described as greater fibrinolysis resistance. The authors concluded that these findings may contribute to our understanding of the hypercoagulable state of critically ill patients with COVID-19.

Next, we have a clinical study that addresses the question of how best to appropriately transfuse red blood cells to patients. It examined the role that central venous oxygen saturation measurements can play in deciding whether to transfuse patients after cardiac surgery. Dr. Norddine Zeroual and colleagues at Montpellier University, Montpellier, France, conducted the study. They designed a randomized trial to test whether transfusion decisions guided by central venous oxygen saturation could reduce transfusion incidence in the ICU after cardiac surgery. Adult patients were screened before cardiac surgery. Patients were randomized to either the control group or the central venous oxygen saturation measurement group. The patient then entered the study if they developed anemia, defined as a hemoglobin <9 g/dL, and without active bleeding, during their postoperative ICU stay. Control patients were transfused at each anemia episode based only on hemoglobin concentration. Patients in the active intervention group were transfused only if their central venous oxygen saturation was ≤ 65%. All 50 control patients were transfused in the ICU. In the group whose transfusion was guided by central venous oxygen saturation, only about two-thirds of patients were transfused. Control patients received a total of 94 red blood cell units, while the intervention group received only 65 red blood cell units. The investigators concluded that a more restrictive transfusion strategy, guided by central venous oxygen saturation measurement, may allow for significant reduction in the incidence of transfusion.

Our next clinical study compared postoperative cognitive outcomes associated with two commonly used anesthetics. Dr. Yujuan Li of Sun Yat-sen University, Guangzhou, China, and colleagues elsewhere conducted the study. They tested the hypothesis that patients with laparoscopic abdominal surgery under propofol-based anesthesia are less likely to have delayed neurocognitive recoveries than patients under sevoflurane-based anesthesia. The authors also sought blood biomarkers that could predict delayed neurocognitive recovery. They conducted a randomized, double blind, parallel-group, controlled study at four hospitals in China. Eligible patients were older adults whose laparoscopic abdominal surgery was expected to last longer than 2 hours. These patients were randomized to receive either a propofol-based or sevoflurane-based regimen. The primary outcome was the incidence of delayed neurocognitive recovery, 5 - 7 days after surgery. Approximately 21% of patients in the sevoflurane group, and 17% of patients in the propofol group had delayed neurocognitive recovery. This was not a significant difference. The authors concluded that the choice of propofol or sevoflurane did not appear to affect the incidence of delayed neurocognitive recovery 5 - 7 days after laparoscopic abdominal surgery.

Next, we have a clinical feasibility study that evaluated whether on-demand washing of allogeneic red blood cells may help mitigate adverse transfusion reactions. Dr. Ian Welsby of Duke University and colleagues there and elsewhere conducted the study. They tested the hypothesis that on-demand, bedside washing of allogeneic red cell units could successfully remove soluble factors such as cell-derived microvesicles, soluble CD40 ligand, chemokine ligand 5 and neutral lipids, all of which were previously associated with transfusion reactions. They also wanted to test the feasibility of using a cell saver during cardiac surgery. The authors collected laboratory data from the first 75 washed units given to a subset of patients in an intervention arm of a clinical trial. Paired pre- and post-wash samples from the blood unit bags were centrifuged, supernatant aspirated and frozen, and then batch-tested for soluble factors. The authors found that cell-derived microvesicles, soluble CD40 ligand, and chemokine ligand 5 concentrations all decreased significantly after washing. Cell free hemoglobin concentrations increased 3-fold after washing but neutral lipids were unchanged. The authors concluded that bedside red blood cell washing in the operating room was clinically feasible. Washing significantly reduced concentrations of soluble factors thought to be associated with transfusion-related adverse reactions. Cell free hemoglobin concentrations were increased, but hemolysis remained within an acceptable degree, <0.8%.

Our next article reports a laboratory study which used a mouse model to explore the role of positive regulatory domain I–binding factor 1 (PRDM1) in the regulation of nociception after peripheral nerve injury. Dr. Cunjin Wang of Fudan University, Shanghai, and colleagues there and elsewhere in China conducted the study. They tested the hypothesis that PRDM1 in the dorsal root ganglion may contribute to the regulation of nociception caused by chronic nerve constriction injury, injection of complete Freund's adjuvant, or injection of capsaicin. They also tested a hypothesis that this mechanism may involve Kv4.3 potassium channels. After causing the various injuries, the authors evaluated the responses of mice to mechanical stimulation, thermal stimulation, and analyzed their gait. The authors evaluated the role of PRDM1 by knocking down PRDM1. They found that peripheral nerve injury increased PRDM1 expression in the dorsal root ganglion. This increased expression reduced the activity of the Kv4.3 promoter and repressed the expression of Kv4.3 channels. The authors concluded that PRDM1 contributes to nociception caused by peripheral nerve injury, and, by repressing Kv4.3 channel expression in injured dorsal root ganglion neurons.

Next, we have a Clinical Focus Review article that discusses perioperative platelet therapy. Dr. Aaron Stansbury Hess of the University of Wisconsin and colleagues there and at the University of Washington authored this report. They examined multiple aspects of perioperative platelet therapy, including guidelines, physiologic evidence, and the results of randomized clinical trials. The authors emphasize that most perioperative practices are not supported by high-quality evidence, leaving much to each anesthesiologist's clinical judgment. The authors suggest that platelet therapy is best guided by predefined protocols incorporating laboratory testing. They posit that most patients will tolerate various surgical procedures without severe complications at lower platelet counts than many society guidelines suggest. They emphasize the urgent need for high-quality clinical trials to investigate platelet storage technologies, platelet function testing, perioperative

transfusion strategies, and alternatives to platelets. They conclude that the anesthesiologist must weigh limited evidence alongside patient, operator, and institutional factors as they decide when to transfuse.

I'll close this month with a Narrative Review article that examines perioperative stroke. Drs. Phillip Vlisides and Laurel Moore of the University of Michigan authored this review. They discuss etiology, common risk factors, and potential risk reduction strategies relating to perioperative stroke. Strategies for reducing the risk of perioperative stroke include delaying elective surgery after recent stroke and medication optimization. The review also addresses screening methods to detect postoperative cerebral ischemia. Additionally, anesthesiologists should consider how multidisciplinary collaborations, including endovascular interventions, could be used to improve patient outcomes. Further investigation is required to determine the role of intraoperative physiologic management and stroke risk. In addition, novel strategies are required to improve stroke detection postoperatively. Anesthesiologists can play an important role in leading the required scientific and clinical efforts to advance perioperative stroke understanding and improve clinical management.

As always, thank you for interest in and support of our journal. I hope that you will use the information published in Anesthesiology to guide and improve your clinical practice. I look forward to keeping you informed as Anesthesiology continues to publish important research and trusted evidence each month.