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

I'll begin this month with a clinical study that examined the feasibility and safety of cold-stored platelets compared with platelets that are stored at room temperature. Dr. Geir Strandenes of Haukeland University Hospital, Bergen, Norway, and colleagues there and elsewhere in Norway and the United States conducted the study. They performed a single-center, two-stage pilot study on adult patients undergoing elective or semi-urgent complex cardiothoracic surgery. In stage I of the study, 50 patients were randomized to receive either platelets stored at room temperature or platelets stored up to 7 days in the cold. Stage II was similar except that the storage time for the cold-stored platelets was extended to 8 to 14 days. The primary outcome for both parts was clinical effect measured by chest drain output. In Stage I, there was no significant difference between groups in chest drain output. The median chest drain output was 720 ml in the standard treatment group of room temperature platelets and 645 ml in patients who received cold-stored platelets. The median difference between the arms was 75 ml, which was not statistically significant. In stage II, the 15 patients with extended cold-stored platelets had a median chest drain output of 690 ml. Here the median difference was 30 ml, which was also not statistically different. Clinical factors like total blood use, adverse events and length of ICU stay were comparable among all groups. The authors concluded that this pilot trial supports the feasibility of using platelets cold-stored for up to 14 days. Their results also provide guidance for future trials in high-risk cardiothoracic bleeding patients.

Next we have another clinical study, this one examining a hypotension prediction algorithm and its use in maintaining intraoperative blood pressure. Dr. Kamal Maheshwari of the Cleveland Clinic and colleagues there and at Fairview Hospital, Cleveland, Ohio, conducted the study. The Hypotension Prediction Index algorithm uses arterial waveform features to predict hypotension. The authors tested the hypothesis that using guidance from the hypotension prediction index reduces the duration and severity of hypotension during noncardiac surgery. The study defined hypotension as mean arterial pressure less than 65 mmHg for at least 1 minute. They randomized adults having moderate- or high-risk noncardiac surgery to receive hemodynamic management either with or without guidance from the index. Clinicians caring for patients assigned to the guidance group were alerted when the index exceeded 85 on a 0 to 100 scale. A treatment algorithm then suggested giving vasopressor, fluids or inotrope, or observation. Clinicians assigned to the control group did not have access to the prediction index. The primary outcome was the amount of hypotension, defined as time-weighted average mean arterial pressure less than 65 mmHg. Among 214 enrolled patients approximately half were in the index guidance group. The median time weighted average of mean arterial pressure less than <65 mmHg was not at all different in the index-guided patients versus the unguided patients. Index guidance also did not reduce amount of hypotension below 60 or 55 mmHg. Maheshwari et al. concluded that index guidance did not reduce the amount of intraoperative hypotension. However half of the alerts were not followed by treatment. This may have been due to short warning time, complex treatment algorithm, or clinicians ignoring the alert, however the answer is not known.

Our next clinical study attempted to correlate postoperative delirium with a preoperative assessment of patient frailty and cognitive impairment. Dr. Maria Susano of Brigham and Women's Hospital and colleagues there and elsewhere in Boston conducted the study. They tested the hypothesis that even brief preoperative screening for frailty or cognitive impairment can identify patients at risk for postoperative delirium. The authors gave frailty and cognitive screening tests to 229 older adults before elective spine surgery. They used the five-item FRAIL scale and the Mini-Cog and Animal Verbal Fluency tests. They also gathered perioperative variables and postoperative outcomes, including the primary outcome of delirium. Susano et al. found that frailty was a strong independent predictor of postoperative delirium in a multivariable model. Naming fewer animals on the verbal fluency test was also associated with increased odds of postoperative delirium, as was more invasive surgery. Susano et al. concluded that brief preoperative screening for frailty and cognitive impairment in older elective spine surgery patients successfully identified those at high risk for developing postoperative delirium.

Next we turn to a meta-analysis that examined several models of ketamine pharmacokinetics in different populations. Dr. Jasper Kamp of Leiden University Medical Center, The Netherlands, and colleagues there and at the University of Colorado conducted the study. First, they conducted a meta-analysis of 18 studies that used different methods of ketamine administration and blood sampling. Simulations showed that models based on venous sampling showed substantially higher context sensitive half-times than those based on arterial sampling. Next, the authors constructed a new pharmacokinetic population model derived from a subset of raw data from 14 studies. They then compared this new model to the meta-analytical analysis of the prior models. They found few differences in output of new and the meta-analytical approach. Kamp et al. concluded that the meta-analytical approach gives a clinically applicable approximation of ketamine population parameter estimates. Further, this approach may be used when no raw datasets are available.

Our next clinical study evaluated the effects of oral dexmedetomidine. Dexmedetomidine is currently only commercially available for intravenous use. Dr. Shubham Chamadia and colleagues at Massachusetts General Hospital conducted the study. They tested the hypothesis that oral dexmedetomidine would increase the duration of non-rapid eye movement stage 2 sleep during polysomnography. This was a single-site, placebo-controlled, randomized, crossover, double-blind, phase II study. Fifteen healthy volunteers received 700 mcg oral dexmedetomidine, or placebo. The primary outcome was polysomnography sleep quality. The subjects completed a motor sequence task and psychomotor vigilance task each evening and then again in the morning. They also completed sleep questionnaires. Polysomnography showed that the duration of nonrapid eye movement stage 2 sleep (non-REM sleep) was 63 minutes greater in the subjects who received dexmedetomidine, averaging 325 versus 256 minutes. REM sleep averaged 16 min in subjects who received dexmedetomidine, and 23 mins in the placebo group. Total sleep time was not different, averaging 544 versus 523 minutes in subjects who received dexmedetomidine versus placebo. Overnight motor sequence task performance improved in the morning after placebo sleep but not after oral dexmedetomidine-induced sleep, but there was no significant difference between groups. Chamadia et al. concluded that nighttime administration of oral dexmedetomidine was associated with increased non-REM sleep and decreased REM sleep. In addition, oral dexmedetomidine may possibly impair sleep-dependent motor memory consolidation.

Our next study used a laboratory rat model to examine the role of upregulation of the acid-sensing ion channel (ASIC3) in postoperative nociception. Dr. Hao Li of West China Second University Hospital, Chengdu, China, and colleagues elsewhere in China, conducted the study. The authors tested the hypothesis that upregulation of ASIC3 in injured tissues is induced by nerve growth factor through the phosphoinositide 3–kinase/protein kinase B signaling pathway. They tested their hypothesis using a rat plantar incisional pain model and sham-incised rats. Li et al. found that ASIC3 concentration was increased in incised skin and muscle. Both male and female animals showed less wound-area sensitization when ASIC3 channels were pharmacologically blocked or when they were knocked down using small interfering RNA. There was bidirectional transport of ASIC3 between incised tissue and the dorsal root ganglia after sciatic nerve ligation. Li et al. concluded that anti–nerve growth factor treatment blocked the upregulation of acid-sensing ion channel 3 expression after incision and reduced the pain-related behaviors.

Next, we have a Clinical Focus Review article that discusses platelet function testing in patients on antiplatelet therapy before cardiac surgery. Dr. Elisabeth Mahla of Medical University of Graz, Austria, and colleagues there and at Sinai Hospital of Baltimore, Maryland authored this review. Dual antiplatelet treatment is the first line treatment of acute coronary syndromes. Although current guidelines only issue class IIa or IIb recommendations for preoperative platelet function assays, there is growing evidence of an association between platelet inhibition and increased bleeding after coronary artery surgery. Preoperative platelet function testing may identify

patients at risk for increased surgery-related bleeding. Testing may also guide the timing of elective surgery after discontinuing antiplatelet therapy. The authors note that testing may trigger targeted postpump hemostatic therapy in conjunction with viscoelastic assays. Currently no universal cutoff point of platelet function associated with bleeding has been well defined in surgical patients. Even the optimal assay for such a cutoff point remains elusive. In addition to platelet inhibition, multiple confounders affect the severity of surgery-related bleeding. Thus, we need larger prospective studies using consensus-based bleeding endpoints to establish the utility of platelet function testing in these surgical patients. Such studies can also establish a potential therapeutic window for on-treatment platelet reactivity. Knowing an individualized preoperative waiting time and targeted intraoperative blood management concept could improve patient outcomes while shortening hospital stays and reducing costs.

Finally, we close this month with a Review Article that considers the perioperative management of aneurysmal subarachnoid hemorrhage. Dr. Deepak Sharma of the University of Washington in Seattle wrote this review. He notes that aneurysmal subarachnoid hemorrhage is an acute neurologic emergency that requires immediate stabilization. Prompt definitive treatment of the aneurysm is needed to prevent rebleeding. Treatment can consist of craniotomy and clipping or endovascular intervention with coils and/or stents. Extracranial manifestations of aneurysmal subarachnoid hemorrhage include cardiac dysfunction and neurogenic pulmonary edema. Additional manifestations include fluid and electrolyte imbalances and hyperglycemia. Data do not exist on how anesthesia affects long-term neurologic outcomes of aneurysmal subarachnoid hemorrhage. Perioperative management should therefore focus on optimizing systemic physiology and facilitating timely definitive treatment. Selecting an anesthetic technique should be based on patient characteristics, hemorrhage severity, and the planned intervention. Anesthesiologists should be familiar with evoked potential monitoring and electroencephalographic burst suppression. Knowledge of temporary clipping, managing external ventricular drains, adenosine-induced cardiac standstill, and rapid ventricular pacing are also needed to effectively care for these patients.

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