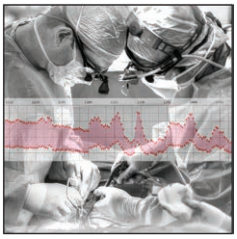
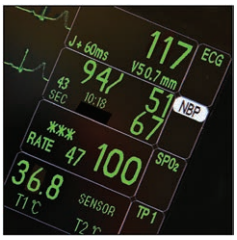
THIS MONTH IN
ANESTHESIOLOGY



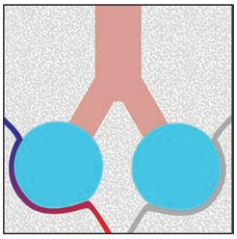
510 Postoperative Hypotension after Noncardiac Surgery and the Association with Myocardial Injury

Intraoperative hypotension has been suggested to be a major contributor to postoperative myocardial injury. Recent studies have confirmed postoperative hypotension to be associated with myocardial injury and infarction. The hypothesis that both the degree of postoperative hypotension severity and longer durations would be associated with myocardial injury (a peak high-sensitivity troponin T measurement ≥ 50 ng/l) was tested in an observational cohort study of 1,710 patients 60 yr old and older undergoing intermediate- to high-risk noncardiac surgery. Postoperative duration under a mean arterial pressure (MAP) threshold of 75 mmHg was associated with increased risk of myocardial injury after adjusting for potential confounders and remained statistically significant after intraoperative hypotension was added to the model; adjusted odds ratio (95% CI) of 2.68 (1.46 to 5.07) for the fourth quartile of postoperative minutes (more than 635 min) with a MAP of less than 75 mmHg (n = 361). Intraoperative hypotension as cumulative duration under the predefined MAP threshold of 65 mmHg was not associated with myocardial injury. *See the accompanying Editorial on* **page 489.** *(Summary: M. J. Avram. Photo: J. P. Rathmell. Photo Illustration: S. M. Jarret.)*



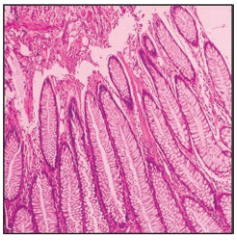
523 Preoperative Fluid Fasting Times and Postinduction Low Blood Pressure in Children: A Retrospective Analysis

The hypothesis that prolonged clear fluid fasting time before elective anesthesia would be associated with low blood pressure was tested in a retrospective cohort study of 15,543 anesthetized children. The two postanesthesia induction epochs studied were: epoch 1, from induction of anesthesia to completion of anesthesia preparation; and epoch 2, after the end of anesthesia preparation to completion of surgical preparation. In epoch 1, 697 (5.2%) of 13,497 patients had at least one episode of low systolic blood pressure (SBP; more than 2 standard deviations below the mean). During epoch 2, 889 (6.9%) of 12,917 patients had low SBP measurements. There was a significant association between longer fasting duration and increased odds of low SBP compared with the group that fasted less than 4 h in epoch 2 after controlling for multiple confounders in groups fasting 4 to 8 h and more than 12 h but not in the group fasting 8 to 12 h. The adjusted associations between fasting and low SBP in epoch 1 were not significant. *See the accompanying Editorial on* **page 493.** *(Summary: M. J. Avram. Image: J. P. Rathmell.)*



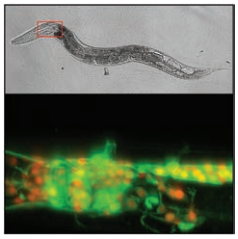
534 End-tidal to Arterial Gradients and Alveolar Deadspace for Anesthetic Agents

General anesthesia increases the inhomogeneity (scatter) of the distribution of ventilation-perfusion ratios in the lung, widening alveolar to arterial partial pressure gradients for respired gases. This inhomogeneity is reflected in increased alveolar deadspace fraction in the traditional three-compartment model of ventilation-perfusion scatter. The alveolar to arterial partial pressure difference for isoflurane is inconsistent with that measured simultaneously using end-tidal and arterial carbon dioxide partial pressures. Alveolar deadspace fractions calculated for volatile anesthetic agents (mean ± SD, 0.47 ± 0.08 for halothane; 0.55 ± 0.09 for isoflurane; 0.61 ± 0.10 for sevoflurane; and 0.65 ± 0.07 for desflurane) are much larger than that calculated simultaneously for carbon dioxide (mean ± SD, 0.23 ± 0.07), and its magnitude increases as blood solubility decreases. Although ideal alveolar and pulmonary end-capillary partial pressures for any gas are theoretically identical, there was a significant difference between the calculated values for all agents combined. Physiologically realistic multicompartment modeling of ventilation-perfusion scatter explains the relative differences between inhalational agents in alveolar to arterial partial pressure gradients and alveolar deadspace. *(Summary: M. J. Avram. Image: J. P. Rathmell.)*



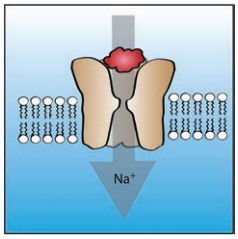
548 Anesthesia and Circulating Tumor Cells in Primary Breast Cancer Patients: A Randomized Controlled Trial

Anesthesia may contribute to the distant spread of cancer during surgical treatment. The presence of circulating tumor cells may be independently associated with both a higher risk of disease recurrence and reduced survival in both nonmetastatic and metastatic breast cancer. The hypothesis that postoperative circulating tumor cell counts would be higher in primary breast cancer patients receiving sevoflurane anesthesia than in those receiving intravenous anesthesia with propofol was tested in a randomized controlled trial of 210 patients. The type of anesthesia did not affect circulating tumor cell counts over time (median circulating tumor cell count/7.5 ml blood [interquartile range]: propofol 1 [0 to 4] at 0 h, 1 [0 to 2] at 48 h, and 0 [0 to 1] at 72 h; sevoflurane 1 [0 to 4] at 0 h, 0 [0 to 2] at 48 h, and 1 [0 to 2] at 72 h). The primary analysis used a mixed Poisson model with random intercept per patient, the results of which are presented as rate ratios. The sevoflurane *versus* propofol rate ratio was 1.27 (95% CI, 0.95 to 1.71). *(Summary: M. J. Avram. Image: Adobe Stock.)*



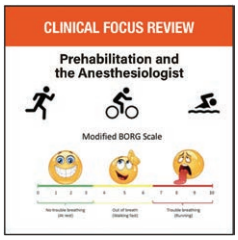
569 Isoflurane Exposure in Juvenile *Caenorhabditis elegans* Causes Persistent Changes in Neuron Dynamics

Larvae of the nematode *Caenorhabditis elegans* exposed to volatile anesthetics have deficits as adults in their ability to perform chemotaxis, a complex behavior relying on chemosensation and modulation of behavioral crawling states. The postanesthetic effects within the neurocircuitry underlying *C. elegans* locomotion were studied using functional imaging. Fifteen hours after timed egg laying, half of the newly hatched L1-stage larvae were exposed to an atmosphere of 8% isoflurane in room air for 3 h while the other half were maintained under room air only. Locomotion was assessed in early and late adulthood. Exposure to isoflurane at a critical developmental stage resulted in a defect in the spontaneous reversal rate in the adult animal due to a pathological alteration in the transition dynamics of a key command interneuron controlling the animal's forward and reverse crawling states. These effects were broadly observed throughout the command interneuron circuitry centrally involved in the behavioral crawling states and were modulated by a loss of FoxO transcription factor daf-16 or mechanistic Target of Rapamycin (mTOR) activity. *See the accompanying Editorial on* **page 495.** *(Summary: M. J. Avram. Image: C. Connor, Brigham and Women's Hospital/Harvard Medical School.)*



611 Computer-aided Discovery of a New Nav1.7 Inhibitor for Treatment of Pain and Itch

Voltage-gated sodium channels are a family of nine transmembrane ion channel proteins (Nav1.1 to Nav1.9), with Nav1.7 expressed almost exclusively in the peripheral nervous system. Its enrichment in dorsal root ganglion neurons corresponds to its critical role in pain and itch signaling. The analgesic effect of nonselective Nav inhibitors is accompanied by serious side effects caused by interaction with other sodium channel subtypes. A search of a database containing 1.5 million compounds identified 20,000 structurally similar to known inhibitors of Nav1.7, which were subjected to docking simulations to predict the predominant binding mode(s) with the target protein. Molecular dynamic simulations were performed on the 25 compounds with the highest affinity scores. Nine of these then underwent *in vitro* and *in vivo* activity assessment. The best performing molecule, DA-0218, inhibits sodium currents in a Nav1.7-expressing cell line at IC_{50} of 0.74 μM. Systemic, intrathecal, and intraplantar administration of DA-0218 reduced formalin-induced inflammatory pain and DA-0218 was effective in reducing paclitaxel-induced neuropathic pain and lymphoma-induced chronic itch in mouse models. *See the accompanying Editorial on* **page 497.** *(Summary: M. J. Avram. Image: J. P. Rathmell.)*



645 Prehabilitation for the Anesthesiologist (Clinical Focus Review)

Functional capacity, the ability to perform activities of daily living, is determined by the integrity of the pulmonary, cardiovascular, and musculoskeletal systems. Low preoperative functional capacity has been associated with a higher rate of surgical complications, longer postoperative hospital stay, and greater chance of dying within 30 days after surgery. Prehabilitation is a program of enhancing an individual's functional capacity to enable them to better withstand a stressful event. The preoperative period may be an opportune time to evaluate and stratify surgical risk and intervene on those modifiable risk factors that influence postoperative outcome by preparing patients for surgery with prehabilitation. As a perioperative physician, the anesthesiologist has the opportunity to assume a leadership role in the multidisciplinary team that collaborates in screening patients, evaluating their needs, and planning patient-centric interventions. After providing an overview of prehabilitation, this Clinical Focus Review presents important considerations when implementing a prehabilitation program, including its duration, patient adherence, and the challenge of the frail older patient. *(Summary: M. J. Avram. Image: From original article.)*

653 Autopilots in the Operating Room: Safe Use of Automated Medical Technology (Review Article)

Advanced medical technology that includes automation can make clinical care more efficient and improve patient safety because machines can accomplish many tasks more efficiently than humans. Although automated systems can be powerful tools that clinicians can use to prevent human error and improve patient care, the introduction of automated medical technology into clinical practice introduces the potential for errors that can be caused by the device, the clinician, or the human-machine interface. This article reviews how automated medical technology affects the practice of anesthesia. It also describes how other industries have dealt with the unintended consequences of imperfect automation, including under- or over-reliance, degradation of manual skills, loss of trust in the automation, and management of system failures. It recommends that all clinicians receive generalized training in how to manage automation and that, before using medical devices in patient care, trainees and experienced physicians alike receive instruction on how each device can fail and how to manage these malfunctions. *(Summary: M. J. Avram. Image: A. Johnson, Vivo Visuals.)*

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