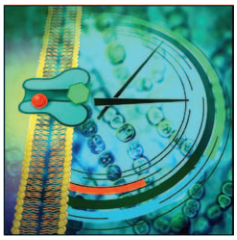
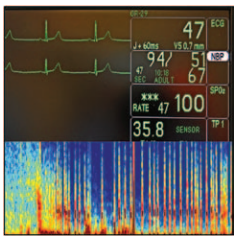
THIS MONTH IN

ANESTHESIOLOGY



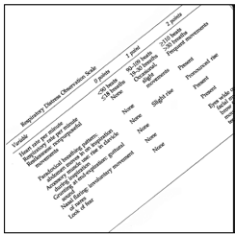
873 A Phase 1, Dose-escalation, Double-blind, Block-randomized Controlled Trial of Safety and Efficacy of Neosaxitoxin Alone and in Combination with 0.2% Bupivacaine, with and without Epinephrine, for Cutaneous Anesthesia

Neosaxitoxin is a site 1 sodium channel blocker that binds to the outer pore of voltage-gated sodium channels, a completely different site than traditional local anesthetics. The local anesthetic effect of neosaxitoxin is potentiated and prolonged when it is administered with bupivacaine or vasoconstrictors. The safety and cutaneous anesthetic efficacy of neosaxitoxin alone and in combination with 0.2% bupivacaine, with and without epinephrine, were determined in 84 male volunteers. Neuromuscular, respiratory, and cardiovascular effects of neosaxitoxin were mild and dose-dependent. Perioral numbness and tingling increased with neosaxitoxin dose for neosaxitoxin–saline and neosaxitoxin–bupivacaine. Addition of epinephrine reduced symptom frequency and severity. Median time to near-complete recovery for bupivacaine was 10 h whereas that for 10 μg neosaxitoxin–bupivacaine–epinephrine was 50 h. *See the accompanying Editorial View on* **page 741**. *(Summary: M.J. Avram. Illustration: A. Johnson, Vivo Visuals; background photomicrograph of cyanobacteria, ©Science Photo Library.)*



775 Concurrence of Intraoperative Hypotension, Low Minimum Alveolar Concentration, and Low Bispectral Index Is Associated with Postoperative Death

The intraoperative concurrence of mean arterial pressure less than 75 mmHg, bispectral index less than 45, and minimum alveolar concentration less than 0.8 (the "triple low" state) for more than 15 min has been associated with an increased risk of postoperative mortality. This retrospective study evaluated the relationship between the triple low state and 30- and 90-day postoperative mortality using data from 13,198 patients from three clinical trials. Mortality at 30 and at 90 days increased in patients who experienced more than 15 min of triple low (1.9% and 3.7%, respectively) compared with those who did not (0.4% and 1.1%, respectively). When 2,497 controls were matched to 3,950 cases with triple low according to their likelihood of experiencing a triple low state, it remained an independent predictor of postoperative mortality. *(Summary: M.J. Avram. Image: J.P. Rathmell.)*



830 Diagnostic Accuracy of Respiratory Distress Observation Scales as Surrogates of Dyspnea Self-report in Intensive Care Unit Patients

Because dyspnea involves sensory identification of afferent signals by the brain and their cognitive and affective processing, its characterization depends on self-report. The relationship of an eight-component respiratory distress observation scale (RDOS), which has been validated as a surrogate for self-reported dyspnea in palliative care, to a dyspnea visual analog scale was evaluated in intensive care unit patients. An adapted intensive care RDOS (IC-RDOS) was derived in a cohort of 120 communicating intensive care unit patients and validated in a separate cohort of 100 patients. A five-item (heart rate, neck muscle use during inspiration, abdominal paradox, facial expression of fear, and supplemental oxygen) IC-RDOS was better correlated with a dyspnea visual analog scale (r=0.61) than was RDOS (r=0.43) in the derivation cohort. Similar results were found in the validation cohort. *(Summary: M.J. Avram. Image: From the article in this issue of* ANESTHESIOLOGY.*)*

929 Risk and Outcomes of Substance Use Disorder in Anesthesiology Residents: A Matched Cohort Analysis (Original Investigations in Education)

Available risk factors and outcomes for substance use disorders (SUD) were evaluated in physicians enrolled from 1975 to 2009 in Accreditation Council for Graduate Medical Education–approved anesthesiology residencies. The 384 individuals with evidence of SUD were each matched to two controls. Cases were more likely to have received their medical education in the United States. In-Training Examination scores of cases and controls did not differ in the clinical base year. Program size was not consistently associated with incidence rates. Cases were less likely to complete residency training and to achieve primary board certification. Cases were also more likely to have actions unrelated to SUD against their medical licenses. Fifty-four of the cases (14.1%) and 10 of the controls (1.3%) were deceased as of December 31, 2013. *(Summary: M.J. Avram. Image: J.P. Rathmell.)*

851 Novel 10-kHz High-frequency Therapy (HF10 Therapy) Is Superior to Traditional Low-frequency Spinal Cord Stimulation for the Treatment of Chronic Back and Leg Pain: The SENZA-RCT Randomized Controlled Trial

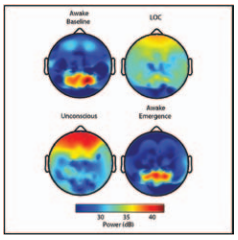
Traditional spinal cord stimulation devices for treatment of chronic intractable trunk and limb pain typically deliver pulse frequencies in the range of 40 to 60 Hz to produce paresthesias overlapping the pain distribution. HF10 therapy involves application of short-duration, high-frequency (10 kHz), low-amplitude pulses to the spinal epidural space without producing paresthesia. One hundred seventy-one patients with chronic, intractable pain of the trunk or limbs were randomly assigned to receive spinal cord stimulation with the HF10 therapy system or a traditional system. Back and leg pain responder (at least 50% reduction in pain without stimulation-related neurological deficit) rates were not less with HF10 than traditional therapy according to the planned, noninferiority analysis, and were numerically and statistically significantly greater in those receiving HF10 therapy. *(Summary: M.J. Avram. Image: J.P. Rathmell.)*

838 Up-regulation of Cathepsin G in the Development of Chronic Postsurgical Pain: An Experimental and Clinical Genetic Study

Central sensitization, which occurs when nociceptive neurons in the spinal dorsal horns become sensitized by peripheral tissue inflammation, may be important in the development of chronic pain. Proteases modulate peripheral and central inflammation by regulating chemotaxis of immune cells and production of cytokines and chemokines. Using a genome-wide screening approach, cathepsin G was identified as an up-regulated protease in the dorsal horns of rats with persistent hyperalgesia after intraplantar injection of complete Freund's adjuvant. Inhibition of cathepsin G attenuated chronic inflammation-associated hyperalgesia, and this was accompanied with a decrease in neutrophilic infiltration and a lower level of interleukin 1β in the spinal dorsal horn. Variations in the cathepsin G gene were associated with reduced risks of chronic postsurgical pain in 1,152 patients. *See the accompanying Editorial View on* **page 745**. *(Summary: M.J. Avram. Image: ©Thinkstock.)*

861 Psychiatric Comorbidity Is Associated Prospectively with Diminished Opioid Analgesia and Increased Opioid Misuse in Patients with Chronic Low Back Pain

High levels of negative affect (NA) are the most frequent presenting symptoms of a comorbid major depression or anxiety disorder, which afflict 30 to 50% of patients with chronic low back pain. Percent improvement in average daily pain was determined in a prospective cohort study of oral opioid therapy in 55 chronic low back pain patients with low, moderate, and high levels of NA. The high-NA group was titrated to a higher average daily dose of morphine equivalents (94.7 mg) than the low group (75.6 mg). During the continuation phase, the high group had 20.6% average improvement in pain while that of the low group was 38.6%. The rate of opioid misuse was 39.1% in the high-NA group and 8.3% in the low-NA group. *(Summary: M.J. Avram. Image: ©Thinkstock.)*



937 Clinical Electroencephalography for Anesthesiologists, Part I: Background and Basic Signatures (Review Article)

The behavioral effects of anesthetics are due to neural oscillations produced by their actions in specific neural circuits, which disrupt normal brain communication. Different anesthetics act at different molecular targets and neural circuits to produce distinct brain states that are readily visible in the electroencephalogram. The basic neurophysiology of the electroencephalogram is reviewed. The electroencephalographic signatures of propofol, dexmedetomidine, ketamine, sevoflurane, isoflurane, desflurane, and nitrous oxide are then reviewed and related to their molecular targets and the neural circuits in the brain at which these drugs act. A new approach to brain monitoring of patients receiving general anesthesia or sedation is proposed that defines the anesthetic state using drug-specific electroencephalogram signatures. *(Summary: M.J. Avram. Image: From the article in this issue of* Anesthesiology, *adapted from Proc Natl Acad Sci USA.)*