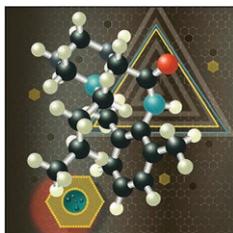


# THIS MONTH IN ANESTHESIOLOGY



## 147 Perineural Liposomal Bupivacaine Is Not Superior to Nonliposomal Bupivacaine for Peripheral Nerve Block Analgesia: A Systematic Review and Meta-analysis

The effectiveness of perineural liposomal bupivacaine in improving peripheral nerve block analgesia across various surgical procedures compared to that of nonliposomal local anesthetics was evaluated in this systematic review and meta-analysis of nine randomized controlled trials involving 619 patients. The primary outcome was the difference in weighted mean area under the curve of the pooled 24- to 72-h rest pain scores, evaluated on a 0- to 10-cm scale, between patients receiving perineural analgesia including liposomal bupivacaine and those receiving nonliposomal local anesthetics. Across 24 to 72 h, the mean difference (95%

CI) in area under the curve of rest pain was found to be 1.0 (0.5 to 1.6) cm · h in favor of liposomal bupivacaine but this difference failed to meet the threshold for clinical significance (2.0 cm · h). Excluding an industry-sponsored trial rendered the difference between the groups nonsignificant (0.7 [-0.1 to 1.5] cm · h). See the accompanying Editorial on [page 139](#). (Summary: M. J. Avram. Image: A. Johnson, Vivo Visuals.)



## 165 Exposure–Response Relationship of Tranexamic Acid in Cardiac Surgery: A Model-based Meta-analysis

Tranexamic acid is an antifibrinolytic agent that reduces postoperative blood loss and rates of erythrocyte transfusion and reoperation in cardiopulmonary bypass surgery. There also appears to be a dose-response relationship between tranexamic acid and the risk of postoperative seizure. The present study quantified the effect of tranexamic acid exposure on postoperative bleeding events and seizure using model-based meta-analysis, an extension of traditional meta-analysis that includes parametric models to describe the effect of dose. A total of 82 clinical trials (49,817 patients) were selected, including 64 randomized controlled trials (12,378 patients) for the effectiveness analysis and 18 observational studies (37,439 patients) for the analysis of seizure. This analysis found

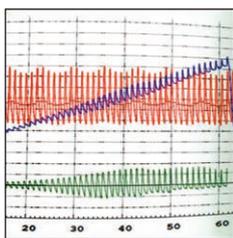
that low-dose tranexamic acid (total dose approximately 20 mg/kg) was sufficient to reduce postoperative blood loss and erythrocyte transfusion in cardiopulmonary bypass surgery. Although higher tranexamic acid doses were found to achieve a marginal gain in effectiveness, they increased the risk of postoperative seizure, particularly in procedures involving a high risk of bleeding. See the accompanying Editorial on [page 143](#). (Summary: M. J. Avram. Image: J. P. Rathmell.)



## 189 Intraoperative Oxygen Concentration and Neurocognition after Cardiac Surgery: A Randomized Clinical Trial

Excessive oxygen use leading to hyperoxia may be injurious, especially in the context of ischemia-reperfusion injury. Although cardiac surgery with cardiopulmonary bypass is associated with exposure to ischemia-reperfusion, patients undergoing such surgery are often treated with higher oxygen concentrations to protect against myocardial and cerebral hypoxia. The hypothesis that titration of intraoperative oxygenation to achieve normoxia reduces postoperative cognitive dysfunction on the second postoperative day compared to standard practice hyperoxia was tested in a randomized doubled blind trial of 100 patients 65 yr or older having coronary artery bypass graft surgery requiring cardiopulmonary bypass. Normoxic patients received a minimum fraction of inspired oxygen

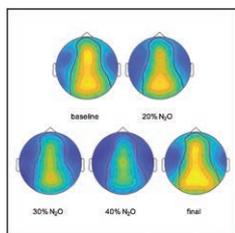
of 0.35 to maintain an arterial partial pressure of oxygen above 70 mmHg before and after cardiopulmonary bypass and between 100 and 150 mmHg during it. Hyperoxic patients received a fraction of inspired oxygen of 1.0 throughout surgery. The median (interquartile range) Telephonic Montreal Cognitive Assessment score of the hyperoxia and normoxia groups on postoperative day 2 were not different (18 [16 to 20] vs. 18 [14 to 20]). (Summary: M. J. Avram. Image: J. P. Rathmell.)



## 179 Intraoperative Blood Pressure Monitoring in Obese Patients: Arterial Catheter, Finger Cuff, and Oscillometry

Perioperative blood pressure monitoring in obese patients can be a challenge because of the limitations of both continuous intraarterial and intermittent noninvasive oscillometric blood pressure monitoring in these patients. The hypothesis that the agreement between continuous noninvasive finger cuff blood pressure measurements and continuous intraarterial measurements is better than that between oscillometric blood pressure measurements at the upper arm, forearm, and lower leg and intraarterial measurements was tested in a prospective method comparison study in 90 patients with a body mass index of 40 kg/m<sup>2</sup> or more having bariatric surgery. The absolute and trending agreement of finger cuff blood pressure measurements with intraarterial blood

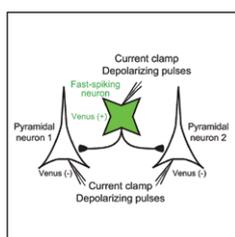
pressure measurements were only moderate but for mean arterial pressure and diastolic blood pressure they were better than between oscillometric (at each of the three measurement sites) and intraarterial blood pressure measurements. The absolute and trending agreement of forearm oscillometric measurements with intraarterial blood pressure measurements was better than the agreement of upper arm oscillometric measurements with intraarterial blood pressure measurements. (Summary: M. J. Avram. Image: A. Johnson, Vivo Visuals.)



## 202 An Electroencephalogram Metric of Temporal Complexity Tracks Psychometric Impairment Caused by Low-dose Nitrous Oxide

Nitrous oxide, an *N*-methyl-d-aspartate receptor antagonist, has analgesic and hypnotic properties as well as strong dissociative effects. It can be used to understand mechanisms of progressive cognitive impairment by non- $\gamma$ -aminobutyric acid (GABA) drug sedation. The temporal complexity of the electroencephalogram (EEG), the evolution in time of EEG motifs, indicates the dynamics of cortical transitions between metastable states and has been shown to correlate with cognitive task performance. The hypothesis that nitrous oxide would reduce temporal complexity was tested in a multidose, single-blind, crossover trial of twelve participants breathing nitrous oxide (end-tidal concentration of 20%, 30%, or 40%, in a random order), while a 32-channel EEG and psychometric function were recorded. At

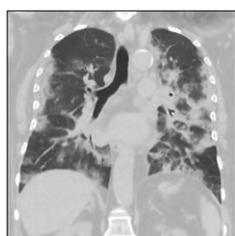
baseline, regional temporal complexity was greater in the midline than in channels overlying lateral temporal brain regions, while it did not change in the lateral temporal region. A quantitative EEG default-mode-network complexity metric based on temporal complexity was sensitive to psychometric impairment caused by low-dose nitrous oxide. (Summary: M. J. Avram. Image: From original article.)



## 219 Fast-spiking Interneurons Contribute to Propofol-induced Facilitation of Firing Synchrony in Pyramidal Neurons of the Rat Insular Cortex

Propofol primarily potentiates  $\gamma$ -aminobutyric acid-mediated (GABAergic) inhibitory synaptic transmission in the cerebral cortex. The propofol-induced alpha rhythm in an electroencephalogram is correlated with propofol-induced loss of consciousness. Fast-spiking GABAergic neurons are the principal inhibitory neurons in the cerebral cortex. The hypothesis that propofol-induced facilitation of unitary inhibitory postsynaptic currents results in firing synchrony among postsynaptic pyramidal neurons that receive inhibitory input from the same presynaptic fast-spiking neuron was tested using whole-cell patch-clamp recordings simultaneously from one fast-spiking neuron and two or three pyramidal neurons in rat insular cortical slice preparations.

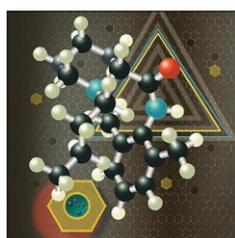
Propofol facilitated spike synchrony among pyramidal neurons by enhancing inhibitory input from fast-spiking neurons. Bath application of 1 and 10  $\mu$ M propofol promoted postsynaptic pyramidal neuron firing synchrony when a presynaptic fast-spiking neuron was activated with 100- and 100/150-ms interburst intervals (in the alpha range), respectively. Propofol failed to synchronize pyramidal neuron firing when the presynaptic fast-spiking neuron was activated with 1050-, 250-, or 75-ms interburst intervals. (Summary: M. J. Avram. Image: From original article.)



## 262 “Silent” Presentation of Hypoxemia and Cardiorespiratory Compensation in COVID-19 (Clinical Focus Review)

A lack of dyspnea in response to hypoxemia (silent hypoxia) is commonly observed. COVID-19 is bringing large numbers of severely hypoxemic patients to medical care and highlighting the phenomenon of silent hypoxia. COVID-19 patients may not present with marked dyspnea because their main gas exchange abnormality involves intrapulmonary shunt and even mild hyperventilation is capable of significantly reducing arterial carbon dioxide and decreasing respiratory drive mediated by both the carotid and central chemoreceptors. Hypoxemia is well tolerated when compensated by cardiovascular responses normally involving increased cardiac output, mediated predominately by tachycardia, with only moderate augmentation of blood pressure.

Deterioration in oxygen saturation and cardiovascular compensation can occur rapidly in hypoxemic patients, particularly in patients with profound shunt physiology. Deterioration in oxygenation is caused most often by a combination of factors, including increasing shunt, reduced cardiac output, decreased ventilation, and gas exchange on the steep portion of the oxyhemoglobin dissociation curve. (Summary: M. J. Avram. Image: J. P. Rathmell.)



## 283 Clinical Effectiveness of Liposomal Bupivacaine Administered by Infiltration or Peripheral Nerve Block to Treat Postoperative Pain: A Narrative Review (Review Article)

Bupivacaine hydrochloride is the longest acting local anesthetic approved by the U.S. Food and Drug Administration. Sustained local anesthetic release that may extend the analgesic duration can be achieved by encasing the local anesthetic within various carriers. Liposomal bupivacaine is a sustained release bupivacaine preparation that has been approved for clinical use by the U.S. Food and Drug Administration. The present article provides a comprehensive summary of the 76 published randomized controlled trials involving the clinical use of liposomal bupivacaine when administered to control acute postsurgical pain. The overwhelming

majority of the randomized controlled trials comparing liposomal bupivacaine with unencapsulated bupivacaine or ropivacaine failed to demonstrate the superiority of liposomal bupivacaine even though the dose of liposomal bupivacaine was almost always maximized, while that of the comparator was rarely optimized. Even when compared to a placebo, infiltration with liposomal bupivacaine provided greater analgesia in only a minority of randomized controlled trials. The review concludes by identifying knowledge gaps for future research. (Summary: M. J. Avram. Image: A. Johnson, Vivo Visuals.)