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**Liposomal Bupivacaine: Effective, Cost-effective, or (Just) Costly?**  
*M. E. McCann* ..... 139

**Optimal Tranexamic Acid Dosing Regimen in Cardiac Surgery: What Are the Missing Pieces?**  
*D. Faraoni, J. H. Levy* ..... 143

**Perioperative Medicine**

**CLINICAL SCIENCE**

**CME** ◆ ◆ **Perineural Liposomal Bupivacaine Is Not Superior to Nonliposomal Bupivacaine for Peripheral Nerve Block Analgesia: A Systematic Review and Meta-analysis**  
*N. Hussain, R. Brull, B. Sheehy, M. K. Essandoh, D. L. Stahl, T. E. Weaver, F. W. Abdallah* ..... 147


Nine trials were included in a meta-analysis examining the difference in 24- to 72-h rest pain severity scores for liposomal and nonliposomal bupivacaine. The area under the curve pain scores for the 24- to 72-h period were statistically but probably not clinically significant. Secondary outcome analysis likewise failed to uncover benefits for liposomal bupivacaine regarding analgesic consumption, length of stay, and functional recovery.

◆ ◆ **Exposure–Response Relationship of Tranexamic Acid in Cardiac Surgery: A Model-based Meta-analysis**  
*P. J. Zufferey, J. Lanoiselée, B. Graouch, B. Vieille, X. Delavenne, E. Ollier* ..... 165

This model-based meta-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. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

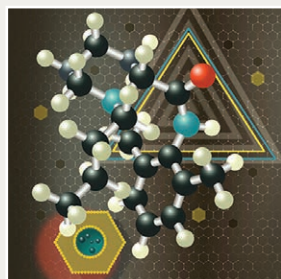
◆ ◆ **Intraoperative Blood Pressure Monitoring in Obese Patients: Arterial Catheter, Finger Cuff, and Oscillometry**  
*R. Schumann, A. S. Meidert, I. Bonney, C. Koutentis, W. Wesselink, K. Kouz, B. Saugel* ..... 179

In a study of 90 obese patients having bariatric surgery, the agreement between finger cuff and intraarterial measurements was better than the agreement between oscillometric and intraarterial measurements for mean arterial and diastolic blood pressure, but not systolic blood pressure. Forearm oscillometry demonstrated better measurement performance than upper arm or lower leg oscillometry. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

◆ Refers to This Month in ANESTHESIOLOGY  
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**ON THE COVER:** Liposomal bupivacaine is purported to extend analgesia associated with wound infiltration and peripheral nerve blocks. However, evidence of the clinical effectiveness of liposomal bupivacaine is mixed. In this issue of ANESTHESIOLOGY, Hussain *et al.* present a meta-analysis to evaluate the effectiveness of perineural liposomal bupivacaine in improving peripheral nerve block analgesia as compared to nonliposomal local anesthetics. In the same issue, Ilfeld *et al.* provide a comprehensive summary of all currently published randomized controlled trials involving the clinical administration of liposomal bupivacaine to control postoperative pain. In an accompanying editorial, McCann reviews the history of clinical trial data and approval of liposomal bupivacaine by the U. S. Food and Drug Administration. Cover Illustration: A. Johnson, Vivo Visuals.

- Hussain *et al.*: Perineural Liposomal Bupivacaine Is Not Superior to Nonliposomal Bupivacaine for Peripheral Nerve Block Analgesia: A Systematic Review and Meta-analysis, p. 147
- Ilfeld *et al.*: Clinical Effectiveness of Liposomal Bupivacaine Administered by Infiltration or Peripheral Nerve Block to Treat Postoperative Pain: A Narrative Review, p. 283
- McCann: Liposomal Bupivacaine: Effective, Cost-effective, or (Just) Costly? p. 139



-   **Intraoperative Oxygen Concentration and Neurocognition after Cardiac Surgery: A Randomized Clinical Trial**  
 *S. Shaefi, P. Shankar, A. L. Mueller, B. P. O’Gara, K. Spear, K. R. Khabbaz, A. Bagchi, L. M. Chu, V. Banner-Goodspeed, D. E. Leaf, D. S. Talmor, E. R. Marcantonio, B. Subramaniam* .....189

A total of 100 cardiac surgical patients were randomly assigned to 35 or 100% inspired oxygen before and after cardiopulmonary bypass. Neurocognitive function 2 days, 1 month, 3 months, and 6 months after surgery was similar in each group. Supplemental intraoperative oxygen does not worsen postoperative neurocognitive function. Inspired oxygen fraction should be chosen on the basis of other considerations. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*


-   **An Electroencephalogram Metric of Temporal Complexity Tracks Psychometric Impairment Caused by Low-dose Nitrous Oxide**  
*X. C. E. Vrijdag, H. van Waart, S. J. Mitchell, J. W. Sleigh* .....202

A quantitative electroencephalogram analysis can identify associations between treatment with low-dose nitrous oxide and performance on psychometric tests. Temporal complexity decreases in the medial cortical regions during nitrous oxide administration and is correlated with psychometric performance. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

## BASIC SCIENCE

-   **Fast-spiking Interneurons Contribute to Propofol-induced Facilitation of Firing Synchrony in Pyramidal Neurons of the Rat Insular Cortex**  
*Y. Koyanagi, Y. Oi, M. Kobayashi* .....219


Multiple whole cell patch clamp recordings in rat cortical slices reveal that propofol facilitates firing synchrony among pyramidal neurons. Propofol-induced activation of presynaptic fast-spiking interneurons was necessary to achieve firing synchrony of postsynaptic pyramidal neurons. These observations suggest that propofol facilitates pyramidal neuron firing synchrony in the cerebral cortex by enhancing inhibitory inputs from fast-spiking interneurons.

-  **Molecular Modification of Transient Receptor Potential Canonical 6 Channels Modulates Calcium Dyshomeostasis in a Mouse Model Relevant to Malignant Hyperthermia**  
*J. R. Lopez, A. Uryash, J. Adams, P. M. Hopkins, P. D. Allen* .....234

Muscle-specific overexpression of the nonconducting transient receptor potential canonical 6 channel both reduced intracellular  $Ca^{2+}$  concentration in RYR1-p.R163C mice at rest and reduced the absolute maximum levels of intracellular  $Ca^{2+}$  concentration reached during exposure to halothane. Despite this, its overexpression did not restore intracellular  $Ca^{2+}$  concentration to wild-type levels, and although its overexpression increased the length of survival after halothane exposure, it was unable to rescue the lethal phenotype. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

## Education

### IMAGES IN ANESTHESIOLOGY


-  **Using Left Ventricular Assist Device Doppler Assessment to Understand Pump–Patient Interactions during a Venous Arterial–Extracorporeal Membrane Oxygenation Weaning Trial**  
*S. P. De Ridder, S. Jacobs, D. F. Dauwe* .....248

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### CLINICAL FOCUS REVIEW

- Perioperative Blood Pressure Management**  
*B. Saugel, D. I. Sessler* .....250

Intraoperative hypotension is common during noncardiac surgery and associated with myocardial injury, acute kidney injury, and death. Postoperative hypotension is also common and associated with myocardial injury and death, and largely missed by conventional monitoring.



-  **“Silent” Presentation of Hypoxemia and Cardiorespiratory Compensation in COVID-19**  
*P. E. Bickler, J. R. Feiner, M. S. Lipnick, W. McKleroy* .....262

Severe hypoxemia presents variably, and sometimes silently, without subjective complaints of dyspnea. The adequacy of cardiovascular compensation for oxygen delivery to tissues should be a focus in all hypoxemic patients.

- Acute Respiratory Distress Syndrome: Contemporary Management and Novel Approaches during COVID-19**  
*G. W. Williams, N. K. Berg, A. Reskallah, X. Yuan, H. K. Eltzschig* .....270

Acute respiratory distress syndrome remains a condition that carries a high mortality. Evidence-based clinical management and emerging concepts for new therapies for COVID-19 are reviewed.

### REVIEW ARTICLE

-   **Clinical Effectiveness of Liposomal Bupivacaine Administered by Infiltration or Peripheral Nerve Block to Treat Postoperative Pain: A Narrative Review**  
*B. M. Ilfeld, J. C. Eisenach, R. A. Gabriel* .....283

This review summarizes the evidence from randomized, controlled trials for the use of liposomal bupivacaine in providing postoperative analgesia. The preponderance of evidence fails to support the routine use of liposomal bupivacaine over standard local anesthetics.

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### A “Soothing” Syrup? How “Father” Wiley Saved Infants from “Mother” Winslow’s Morphine Elixir

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