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Michel M. R. F. Struys, Marc J. Coppens, Nikolaas De Neve, Eric P. Mortier, Anthony G. Doufas, Jan F. P. Van Bocxlaer, and Steven L. Shafer
- Propofol plasma–effect site equilibration occurs more rapidly after a bolus than after rapid infusion, based on the electroencephalogram as a drug effect measure, mostly because of misspecification of the pharmacokinetic model in the first minutes after bolus.
- ◇ **Median Frequency Revisited: An Approach to Improve a Classic Spectral Electroencephalographic Parameter for the Separation of Consciousness from Unconsciousness** 397
Denis Jordan, Gudrun Stockmanns, Eberhard F. Kochs, and Gerhard Schneider
- A more general approach to design spectral parameters leads to a new spectral parameter which separates consciousness from unconsciousness better than classic spectral parameters or Bispectral Index.

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CME CME Article

- ◇ **Apolipoprotein E $\epsilon 4$ Allele Increases the Risk of Early Postoperative Delirium in Older Patients Undergoing Noncardiac Surgery** 406

Jacqueline M. Leung, Laura P. Sands, Yun Wang, Annie Poon, Pui-yan Kwok, John P. Kane, and Clive R. Pullinger

Apolipoprotein $\epsilon 4$ carrier status was associated with an increased risk for early postoperative delirium. Genetic predisposition plays a role and may interact with anesthetic/surgical factors contributing to the development of postoperative delirium.

■ LABORATORY INVESTIGATIONS

- ◇ **A Conserved Tyrosine in the β_2 Subunit M4 Segment Is a Determinant of γ -Aminobutyric Acid Type A Receptor Sensitivity to Propofol** 412

James E. Richardson, Paul S. Garcia, Kate K. O'Toole, Jason M. C. Derry, Shannon V. Bell, and Andrew Jenkins

The aim of this study was to better understand the γ -aminobutyric acid type A receptor β_2 subunit M4 segment. Tryptophan scanning mutagenesis identified a conserved tyrosine (Y444) that selectively determines propofol.

- Mechanical Ventilation in Healthy Mice Induces Reversible Pulmonary and Systemic Cytokine Elevation with Preserved Alveolar Integrity: An *In Vivo* Model Using Clinical Relevant Ventilation Settings** 419

Michiel Vaneker, Feico J. Halbertsma, Jan van Egmond, Mihai G. Netea, Henry B. Dijkman, Dirk G. Snijdelaar, Leo A. Joosten, Johannes G. van der Hoeven, and Gert Jan Scheffer

Mechanical ventilation induces reversible cytokine increase and leukocyte influx while preserving tissue integrity. This model can be used to study the mechanisms behind ventilator-induced lung injury and the contribution of mechanical ventilation to the "multiple-hit" concept.

- Neonatal Exposure to a Combination of *N*-Methyl-D-aspartate and γ -Aminobutyric Acid Type A Receptor Anesthetic Agents Potentiates Apoptotic Neurodegeneration and Persistent Behavioral Deficits** 427

Anders Fredriksson, Emma Pontén, Torsten Gordh, and Per Eriksson

Exposure to thiopental or propofol (γ -aminobutyric acid agonist) and ketamine (*N*-methyl-D-aspartate antagonist) during a critical stage of brain development potentiated neonatal brain cell death and resulted in functional deficits in the adult mouse.

- Effects of the Antimicrobial Peptide LL-37 and Hyperthermic Preconditioning in Septic Rats** 437

Alexander Torossian, Eugeniu Gurschi, Robert Bals, Timon Vassiliou, Hinnerk F. Wulf, and Artur Bauhofer

LL-37 therapy improved outcome in septic rats. Furthermore, hyperthermic preconditioning alone was not effective, but the combination with LL-37 therapy improved survival rate and downgraded proinflammatory cytokine response after intraabdominal sepsis.

- Impact of the C2/C6 Ratio of High-molecular-weight Hydroxyethyl Starch on Pharmacokinetics and Blood Coagulation in Pigs** 442

Sebastian Schramm, Caroline Thyges, Philippe Frascarolo, Thierry Buclin, Marco Burki, Andreas Fisch, Marc-Alexander Burmeister, Lars Asmis, and Donat R. Spahn

Reducing the C2/C6 ratio in high-molecular, low-substituted hydroxyethyl starch solutions results in a slightly faster hydroxyethyl starch elimination. However, the blood coagulation compromising effect was unaffected.

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Altered Contractile Response due to Increased β_3 -Adrenoceptor Stimulation in Diabetic Cardiomyopathy: The Role of Nitric Oxide Synthase 1–derived Nitric Oxide

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Julien Amour, Xavier Loyer, Morgan Le Guen, Nejma Mabrouk, Jean-Stéphane David, Emmanuel Camors, Nunzia Carusio, Benoît Vivien, Ramaroson Andriantsitohaina, Christophe Heymes, and Bruno Riou

In the diabetic heart, β_3 adrenoceptor induces an altered positive inotropic response to β -adrenoceptor stimulation involving the nitric oxide synthase 1–derived nitric oxide production.

■ PAIN AND REGIONAL ANESTHESIA

◆ CME Continuous Preperitoneal Infusion of Ropivacaine Provides Effective Analgesia and Accelerates Recovery after Colorectal Surgery: A Randomized, Double-blind, Placebo-controlled Study

461

Marc Beaussier, Hanna El'Ayoubi, Eduardo Schiffer, Maxime Rollin, Yann Parc, Jean-Xavier Mazoit, Louisa Azizi, Pascal Gervaz, Serge Rohr, Celine Biermann, André Lienhart, and Jean-Jacques Eledjam

Continuous preperitoneal wound infiltration of 0.2% ropivacaine during 48 h after open colorectal surgery improved pain relief, reduced parenteral morphine consumption, and accelerated the postoperative rehabilitation process, as compared with parenteral morphine alone.

◆ Systemic Antiinflammatory Corticosteroid Reduces Mechanical Pain Behavior, Sympathetic Sprouting, and Elevation of Proinflammatory Cytokines in a Rat Model of Neuropathic Pain

469

Huiqing Li, Wenrui Xie, Judith A. Strong, and Jun-Ming Zhang

Systemic injections of corticosteroid (triamcinolone acetonide) mitigate proinflammatory cytokine increases, mechanical pain behaviors, and abnormal sympathetic sprouting in dorsal root ganglia after spinal nerve ligation, suggesting this nerve injury model has important inflammatory contributions.

Effects of Butorphanol on Morphine-induced Itch and Analgesia in Primates

478

Heeseung Lee, Norah N. Naughton, James H. Woods, and Mei-Chuan Ko

Systemic administration of butorphanol attenuated intrathecal morphine-induced itch/scratching responses while maintaining morphine analgesia in monkeys. Pharmacologic studies suggest that partial agonist actions at both μ - and κ -opioid receptors contribute to the antipruritic effects of butorphanol.

Effects of Topical Application of Clonidine Cream on Pain Behaviors and Spinal Fos Protein Expression in Rat Models of Neuropathic Pain, Postoperative Pain, and Inflammatory Pain

486

Chi Li, Hiroshi Sekiyama, Masakazu Hayashida, Kenji Takeda, Toshinobu Sumida, Shigehito Sawamura, Yoshitsugu Yamada, Hideko Arita, and Kazuo Hanaoka

Clonidine cream could reduce thermal hyperalgesia, mechanical allodynia, and spinal Fos-like immunoreactivity in rats with neuropathic pain, likely through peripheral mechanisms, although it had limited or no effects in those with postoperative or inflammatory pain.

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Differential Contribution of Sodium Channel Subtypes to Action Potential Generation in Unmyelinated Human C-type Nerve Fibers

495

Phillip M. Lang, Verena B. Hilmer, and Peter Grafe

Studies on isolated unmyelinated human nerve fibers indicate that tetrodotoxin-resistant sodium channels contribute to peak height of action potentials evoked by short electrical stimuli; tetrodotoxin-sensitive channels account for regulation of excitability after slow membrane depolarization.

■ **REVIEW ARTICLE**

Sedation and Anesthesia Care for Ophthalmologic Surgery during Local/Regional Anesthesia

502

Mary Ann Vann, Babatunde O. Ogunnaike, and Girish P. Joshi

This article discusses current practices and trends in anesthesia care with respect to sedation for eye surgery during local/regional anesthesia.

■ **CASE REPORT**

Histopathologic Features of Fat Embolism in Fulminant Fat Embolism Syndrome

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Fumio Arai, Takashi Kita, Takeshi Nakai, Tatsuyuki Hori, Naritoshi Maki, Masaaki Kakiuchi, and Shigeta Sasaki

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