



ON THE COVER:

Recently, spinal cord stimulation with higher frequency than in the past has been applied for treatment of chronic pain. Laboratory work in this issue shows different mechanisms and time course of effects with these higher frequencies.

- Clark: Spinal Cord Stimulation: Does Frequency Matter?, p. 243
- Shechter *et al.*: Conventional and Kilohertz-frequency Spinal Cord Stimulation Produces Intensity- and Frequency-dependent Inhibition of Mechanical Hypersensitivity in a Rat Model of Neuropathic Pain, p. 422

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Jacques Duranteau and Yannick Le Manach

■ PERIOPERATIVE MEDICINE

◆ Acute Normovolemic Hemodilution in the Pig Is Associated with Renal Tissue Edema, Impaired Renal Microvascular Oxygenation, and Functional Loss

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Franziska M. Konrad, Egbert G. Mik, Sander I. A. Bodmer, N. Bahar Ates, Henriëtte F. E. M. Willems, Karin Klingel, Hilde R. H. de Geus, Robert Jan Stolker, and Tanja Johannes

Compared to colloid (hydroxyethyl starch 6% 130/0.4), normovolemic hemodilution with crystalloid (balanced electrolyte solution) produced greater renal hypoxia indicating the diluent may be a factor when evaluating hemodilution and acute kidney injury.

◆ Refers to This Month in Anesthesiology

◆ Refers to Editorial Views

MA Meeting Article

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CME CME Article

◇ **Postoperative B-type Natriuretic Peptide for Prediction of Major Cardiac Events in Patients Undergoing Noncardiac Surgery: Systematic Review and Individual Patient Meta-analysis** 270

Reitze N. Rodseth, Bruce M. Biccard, Rong Chu, Giovana A. Lurati Buse, Lehana Thabane, Ameet Bakhai, Daniel Bolliger, Lucio Cagini, Thomas J. Cahill, Daniela Cardinale, Carol P. W. Chong, Miłostaw Cnotliwy, Salvatore Di Somma, René Fahrner, Wen K. Lim, Elisabeth Mahla, Yannick Le Manach, Ramaswamy Manikandan, Wook B. Pyun, Sriram Rajagopalan, Milan Radović, Robert C. Schutt, Daniel I. Sessler, Stuart Suttie, Thuvaraha Vanniyasingam, Marek Waliszek, and P. J. Devereaux

This individual patient level meta-analysis indicates that increased postoperative B-type natriuretic peptide predicts mortality, cardiac mortality, mortality or nonfatal myocardial infarction, and cardiac failure at 30 days and 180 days or more after noncardiac surgery.

🌐 **Increased Perioperative B-type Natriuretic Peptide Associates with Heart Failure Hospitalization or Heart Failure Death after Coronary Artery Bypass Graft Surgery** 284

Amanda A. Fox, Luigino Nascimben, Simon C. Body, Charles D. Collard, Aya A. Mitani, Kuang-Yu Liu, Jochen D. Muehlschlegel, Stanton K. Sherman, and Edward R. Marcantonio

In a secondary analysis of an observational study of 1,025 coronary artery bypass graft surgical patients, increased perioperative plasma B-type natriuretic peptide independently predicted 5-yr heart failure hospitalization and heart failure death.

Automated Alerting and Recommendations for the Management of Patients with Preexisting Hypoxia and Potential Acute Lung Injury: A Pilot Study 295

James M. Blum, Michael J. Stentz, Michael D. Maile, Elizabeth Jewell, Krishnan Raghavendran, Milo Engoren, and Jesse M. Ehrenfeld

In an open-label parallel arm study of 100 patients with acute respiratory distress syndrome receiving low tidal volume ventilation, sending the anesthesia providers an alert with a recommended tidal volume of 6 ml/kg resulted in a significant reduction in tidal volume delivered during anesthesia compared with conventional care. Complications and major morbidity did not differ between groups.

CME **Effect of Intraoperative High Inspired Oxygen Fraction on Surgical Site Infection, Postoperative Nausea and Vomiting, and Pulmonary Function: Systematic Review and Meta-analysis of Randomized Controlled Trials** 303

Frédérique Hovaguimian, Christopher Lysakowski, Nadia Elia, and Martin R. Tramèr

Intraoperative high F_{iO_2} decreases the risk of surgical site infection in surgical patients receiving prophylactic antibiotics, has a weak beneficial effect on nausea, and does not increase the risk of postoperative atelectasis.

Calabadiol: A New Agent to Reverse the Effects of Benzylisoquinoline and Steroidal Neuromuscular-blocking Agents 317

Ulrike Hoffmann, Martina Grosse-Sundrup, Katharina Eikermann-Haerter, Sebastina Zaremba, Cenk Ayata, Ben Zhang, Da Ma, Lyle Isaacs, and Matthias Eikermann

In healthy rats, calabadiol 1 produced a dose-dependent reversal of neuromuscular blockade from cisatracurium and rocuronium without affecting heart rate, blood pressure, or arterial blood gas tensions or pH.

Low-frequency Neuromuscular Depression Is a Consequence of a Reduction in Nerve Terminal Ca^{2+} Currents at Mammalian Motor Nerve Endings 326

Eugene M. Silinsky

The results demonstrate that neuromuscular depression during train-of-four monitoring is due to a decline in nerve terminal Ca^{2+} currents. More profound stimulation conditions seem to be required for depletion of acetylcholine stores.

Xenon Neurotoxicity in Rat Hippocampal Slice Cultures Is Similar to Isoflurane and Sevoflurane 335

Heather Brosnan and Philip E. Bickler


Using postnatal rat hippocampal slice cultures, the authors demonstrated that xenon used at 1 minimum alveolar concentration-equivalent concentration increased apoptosis similar to sevoflurane and isoflurane at equipotent concentrations, and that this effect was abolished by preconditioning the tissue with a subtoxic concentration of isoflurane.

Neither Xenon nor Fentanyl Induces Neuroapoptosis in the Newborn Pig Brain 345
Hemmen Sabir, Sarah Bishop, Nicki Cohen, Elke Maes, Xun Liu, John Dingley, and Marianne Thoresen

Using a model of mechanically ventilated piglets in the absence of brain injury, the authors could show that neither 24 h of 50% inhaled xenon nor fentanyl, alone or in combination, induced apoptosis in the neonatal pig brain in normothermic or hypothermic conditions. Isoflurane 2% was found to induce apoptosis in this experimental paradigm.


Developmental Effects of Neonatal Isoflurane and Sevoflurane Exposure in Rats 358
Christoph N. Seubert, Wanting Zhu, Christopher Pavlinec, Nikolaus Gravenstein, and Anatoly E. Martynyuk

At subanesthetic concentrations isoflurane and sevoflurane produce developmental effects in neonatal rats acting *via* similar mechanisms that may involve an increase in neuronal activity. At the same time, substantial differences in the effects of the two drugs suggest differences in the mechanisms mediating their actions and in their safety profile for neonatal anesthesia.



 **Interactions of Cardiopulmonary Bypass and Erythrocyte Transfusion in the Pathogenesis of Pulmonary Dysfunction in Swine** 365
Nishith N. Patel, Hua Lin, Ceri Jones, Graham Walkden, Paramita Ray, Philippa A. Sleeman, Gianni D. Angelini, and Gavin J. Murphy

Allogeneic erythrocyte transfusion of older erythrocytes causes pulmonary dysfunction that is characterized by marked neutrophil/macrophage infiltration. Moreover, transfusion interacted with cardiopulmonary bypass to increase lung injury.


■ **CRITICAL CARE MEDICINE**

 **δ Opioid Receptor Antagonist, ICI 174,864, Is Suitable for the Early Treatment of Uncontrolled Hemorrhagic Shock in Rats** 379
Liangming Liu, Kunlun Tian, Yu Zhu, Xiaoli Ding, and Tao Li

ICI 174,864 with or without low volumes of Ringer's lactate, dose-dependently increased blood pressure and prolonged short-term survival in rats subjected to uncontrolled hemorrhagic shock. Survival was markedly higher in rats treated with ICI 174,864 than those with standard fluid resuscitation once bleeding was controlled.

  **Muscle Weakness Predicts Pharyngeal Dysfunction and Symptomatic Aspiration in Long-term Ventilated Patients** 389
Hooman Mirzakhani, June-Noelle Williams, Jennifer Mello, Sharma Joseph, Matthew J. Meyer, Karen Waak, Ulrich Schmidt, Emer Kelly, and Matthias Eikermann

In 30 critically ill adult patients mechanically ventilated more than 10 days, extremity muscle weakness assessed by medical research council score was an independent predictor of swallowing dysfunction and symptomatic aspiration after extubation.

 **Higher Frequency Ventilation Attenuates Lung Injury during High-frequency Oscillatory Ventilation in Sheep Models of Acute Respiratory Distress Syndrome** 398
Songqiao Liu, Yang Yi, Maohua Wang, Qihua Chen, Yingzi Huang, Ling Liu, Jianfeng Xie, Dunyuan Zhou, and Haibo Qiu

This study suggests that high-frequency oscillatory ventilation at higher frequencies minimizes lung stress and tidal volume, resulting in less lung injury and reduced local lung inflammation.

Prolonged Administration of Pyridostigmine Impairs Neuromuscular Function with and without Down-regulation of Acetylcholine Receptors 412
Martina Richtsfeld, Shingo Yasuhara, Heidrun Fink, Manfred Blobner, and J. A. Jeevendra Martyn

Prolonged administration of pyridostigmine (25 mg·kg⁻¹·day⁻¹) leads to neuromuscular impairment, even if discontinued for 24 h. This impairment appears to be associated with, but is also independent of, acetylcholine receptor down-regulation.

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Ronen Shechter, Fei Yang, Qian Xu, Yong-Kwan Cheong, Shao-Qiu He, Andrei Sdrulla, Alene F. Carteret, Paul W. Wacnik, Xinzhong Dong, Richard A. Meyer, Srinivasa N. Raja, and Yun Guan

The effectiveness of spinal cord stimulation in the treatment of neuropathic pain depends on stimulation frequency and intensity. In a rat model of neuropathic pain, the intensity-dependent (20%, 40%, 80% of motor threshold) attenuation of pain by bipolar spinal cord stimulation at frequencies of 50 Hz, 1 kHz, and 10 kHz was studied on three consecutive days after L5 spinal nerve ligation. At a stimulation intensity that was 80% of the motor threshold, 1-kHz spinal cord stimulation reduced mechanical hypersensitivity more than 50-Hz stimulation did, with an earlier onset of analgesic effect (day 1 *vs.* day 2). The effect of 1-kHz stimulation was observed even at 40% of the motor threshold. The C-fiber component of wide dynamic range neuronal wind-up was reduced only at a 50-Hz stimulation frequency. Pain relief by kilohertz level and 50-Hz stimulation may involve different peripheral and spinal segmental mechanisms.

- Effects of General Anesthetics on Substance P Release and c-Fos Expression in the Spinal Dorsal Horn** 433

Toshifumi Takasusuki, Shigeki Yamaguchi, Shinsuke Hamaguchi, and Tony L. Yaksh

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Shruti Redhu and Bhadrinarayan Varadarajan

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Sarah F. Barnett, Ravi K. Alagar, Michael P. W. Grocott, Savvas Giannaris, John R. Dick, and Suneetha Ramani Moonesinghe

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