



ON THE COVER:

Emerging lines of evidence suggest that neuroinflammation in the brain with anesthesia and surgery is associated with cognitive effects during development and with postoperative cognitive dysfunction and might be targeted to prevent these events:

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- Sanders and Avidan: Postoperative Cognitive Trajectories in Adults: The Role of Inflammatory Processes, p. 484
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■ PERIOPERATIVE MEDICINE

- ◆ **Selective Anesthesia-induced Neuroinflammation in Developing Mouse Brain and Cognitive Impairment** 502
Xia Shen, Yuanlin Dong, Zhipeng Xu, Hui Wang, Changhong Miao, Sulpicio G. Soriano, Dandan Sun, Mark G. Baxter, Yiyang Zhang, and Zhongcong Xie
 Anesthesia with sevoflurane, but not desflurane, for 2 h daily for 3 days, but not 1 day, induced cognitive impairment and neuroinflammation in young but not adult mice. An enriched environment and anti-inflammatory treatment ameliorated the sevoflurane-induced cognitive impairment.
- ◆ **Sevoflurane Anesthesia in Pregnant Mice Induces Neurotoxicity in Fetal and Offspring Mice** 516
Hui Zheng, Yuanlin Dong, Zhipeng Xu, Gregory Crosby, Deborah J. Culley, Yiyang Zhang, and Zhongcong Xie
 Sevoflurane anesthesia in pregnant mice induced increases in interleukin-6 levels, reductions in synaptic marker postsynaptic density-95 and synaptophysin levels, caspase-3 activation, and learning and memory impairment in fetal and offspring mice.
- ◆ **Depletion of Bone Marrow-derived Macrophages Perturbs the Innate Immune Response to Surgery and Reduces Postoperative Memory Dysfunction** 527
Vincent Degos, Susana Vacas, Zhenying Han, Nico van Rooijen, Pierre Gressens, Hua Su, William L. Young, and Mervyn Maze
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- ◆ **Dual Effects of Isoflurane on Proliferation, Differentiation, and Survival in Human Neuroprogenitor Cells** 537
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- Bidirectional Regulation of Intravenous General Anesthetic Actions by α 3-containing γ -aminobutyric Acid_A Receptors** 562
Carolin J. Straub, Hew Mun Lau, Rosanna Parlato, Guenther Schuetz, Jean-Marc Fritschy, and Uwe Rudolph
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- Effects of Subanesthetic Dose of Nitrous Oxide on Cerebral Blood Flow and Metabolism: A Multimodal Magnetic Resonance Imaging Study in Healthy Volunteers** 577
Naranjargal Dashdorj, Kathryn Corrie, Antonio Napolitano, Esben Petersen, Ravi P. Mahajan, and Dorothee P. Auer
 In healthy volunteers, a subanesthetic dose (30%) of nitrous oxide significantly dilated cerebral blood vessels without changes in cerebral metabolism. Further studies are required to explore the potential of sub-anesthetic nitrous oxide in cerebral vasospasm.

- Drosophila* Ryanodine Receptors Mediate General Anesthesia by Halothane** 587
Shuying Gao, David J. Sandstrom, Harold E. Smith, Brigit High, Jon W. Marsh, and Howard A. Nash

The potency of halothane anesthesia paralleled gene dosage of the ryanodine receptor Ca^{2+} release channel in *Drosophila* mutants. Halothane-evoked Ca^{2+} flux in central neurons was correlated with hyperpolarization.

- Propofol Anesthesia Impairs the Maturation and Survival of Adult-born Hippocampal Neurons** 602
Marine Krzisch, Sébastien Sultan, Julie Sandell, Kornél Demeter, Laszlo Vutskits, and Nicolas Toni

Exposure of adult mice to propofol interferes with the survival and maturation of neurons generated in the adult hippocampus at specific developmental stages.

- Effect of Sedation on Pain Perception** 611
Michael A. Frölich, Kui Zhang, and Timothy J. Ness

Eighty-six healthy volunteers were assigned to receive midazolam, propofol, or dexmedetomidine for sedation while undergoing several experimental pain tasks. Midazolam increased pain, whereas propofol and dexmedetomidine reduced ischemic and cold pain modalities only.

- ◇ **Epidural versus Continuous Preperitoneal Analgesia during Fast-track Open Colorectal Surgery: A Randomized Controlled Trial** 622
Philippe Jouve, Jean-Etienne Bazin, Antoine Petit, Vincent Minville, Adeline Gerard, Emmanuel Buc, Aurelien Dupre, Fabrice Kwiatkowski, Jean-Michel Constantin, and Emmanuel Futier

Continuous wound infiltration has been proposed as an alternative to epidural analgesia after colorectal surgery. We found that, compared with continuous wound infiltration, epidural analgesia improved functional recovery and pain control and reduced hospital stay.

■ CRITICAL CARE MEDICINE

- ◇ ◆ **Association between Endothelial Dysfunction and Acute Brain Dysfunction during Critical Illness** 631
Christopher G. Hughes, Alessandro Morandi, Timothy D. Girard, Bernhard Riedel, Jennifer L. Thompson, Ayumi K. Shintani, Brenda T. Pun, E. Wesley Ely, and Pratik P. Pandharipande

Endothelial function is impaired in critically ill patients. Because endothelial dysfunction contributes to altered cerebral blood flow and blood brain barrier permeability, it could lead to acute brain dysfunction during critical illness. One hundred forty-seven medical and surgical intensive care unit patients participated in this prospective cohort study. Endothelial function was assessed at enrollment using peripheral artery tonometry to determine reactive hyperemia index. After correcting for confounding variables, lower reactive hyperemia index, which reflected worse systemic endothelial function, was independently associated with fewer delirium/coma-free days. This suggests endothelial dysfunction may play a role in the pathogenesis of acute brain dysfunction during critical illness.

- ◆ **Accuracy of Determining Hemoglobin Level Using Occlusion Spectroscopy in Patients with Severe Gastrointestinal Bleeding** 640
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In intensive care unit patients admitted for gastrointestinal hemorrhage, the determination of hemoglobin level by a noninvasive occlusion spectroscopy method lacks accuracy. Neither infusion of vasopressor agents nor site of measurement seems to influence these findings.

Effect of Hyperoxia on Resuscitation of Experimental Combined Traumatic Brain Injury and Hemorrhagic Shock in Mice 649

Brian Blasiolo, Hülya Bayır, Vincent A. Vagni, Keri Janesko-Feldman, Amin Cheikhi, Stephen R. Wisniewski, Joseph B. Long, James Atkins, Valerian Kagan, and Patrick M. Kochanek

In an experimental model of traumatic brain injury combined with hemorrhagic shock, resuscitation with supplemental oxygen reduced resuscitation fluid requirements and attenuated neuronal death despite modest increases in oxidative stress and proinflammatory aspects of neuroinflammation.

■ PAIN MEDICINE

◇ Role of Meningeal Mast Cells in Intrathecal Morphine-evoked Granuloma Formation 664

Tony L. Yaksh, Jeffery W. Allen, Samantha L. Veasart, Kjersti A. Horais, Shelle A. Malkmus, Miriam Scadeng, Joanne J. Steinauer, and Steve S. Rossi

Intrathecal morphine infusion leads to a meningeally derived granuloma. The present work in the dog points to a close correlation between the origin of these intrathecal granulomas and the degranulation of meningeal mast cells.

Critical Role of Protease-activated Receptor 2 Activation by Mast Cell Trypsin in the Development of Postoperative Pain 679

Sara M. Oliveira, Cássia R. Silva, and Juliano Ferreira

Some surgeries cause mast cell degranulation. In a mice model, trypsin or protease-activated receptor 2 inhibition reduced postoperative nociception in a manner consistent with mast cell degranulation and trypsin release.

σ₁ Receptors Are Involved in the Visceral Pain Induced by Intracolonic Administration of Capsaicin in Mice 691

Rafael González-Cano, Manuel Merlos, José M. Baeyens, and Cruz M. Cendán

Pharmacologic blockade or genetic inactivation of σ₁ receptors inhibits pain-related behaviors and mechanical referred hyperalgesia in a pure visceral pain model in mice.

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ORIGINAL INVESTIGATIONS IN EDUCATION

🌐 Efficacy of an Online Education Program for Ultrasound Diagnosis of Pneumothorax 715

Sundar Krishnan, Taften Kuhl, Waseemuddin Ahmed, Kei Togashi, and Kenichi Ueda

Ultrasound has been shown to be a reliable tool for ruling out pneumothorax. After viewing a 5-min online training video, physicians were able to reliably rule out pneumothorax on an optimal ultrasound image.

CLINICAL CONCEPTS AND COMMENTARY

- CE** **Perioperative Therapeutic Plasmapheresis** 722
Sloan C. Youngblood, Yi Deng, Alice Chen, and Charles D. Collard

Perioperative indications for therapeutic plasmapheresis have expanded significantly. The physiologic effects of plasmapheresis are reviewed, including a discussion of potential complications. Specific perioperative considerations, including calcium hemostasis, coagulopathy, and pharmacokinetic effects, are emphasized.

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Christian M. Schulz, Mica R. Endsley, Eberhard F. Kochs, Adrian W. Gelb, and Klaus J. Wagner

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