





ON THE COVER:

Some evidence suggests that children have a lower incidence of perioperative respiratory adverse events when intravenous propofol is used compared with inhalational sevoflurane for the anesthesia induction. In this issue of *ANESTHESIOLOGY*, Ramgolam *et al.* report the results of a randomized controlled trial of inhalation *versus* intravenous induction in 300 high-risk children. In an accompanying Editorial View, Davidson places the new research findings in the context of the management of anesthesia for children in everyday practice. Illustration by Annemarie Johnson, Vivo Visuals.

- Ramgolam *et al.*: Inhalational *versus* Intravenous Induction of Anesthesia in Children with a High Risk of Perioperative Respiratory Adverse Events: A Randomized Controlled Trial, p. 1065
- Davidson: Induction of Anesthesia for Children: Should We Recommend the Needle or the Mask? p. 1051

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CLINICAL SCIENCE


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◆◆ Inhalational *versus* Intravenous Induction of Anesthesia in Children with a High Risk of Perioperative Respiratory Adverse Events: A Randomized Controlled Trial **1065**
A. Ramgolam, G. L. Hall, G. Zhang, M. Hegarty, and B. S. von Ungern-Sternberg

In a randomized trial it was found that, in at risk children, intravenous induction reduces the risk of perioperative respiratory adverse events compared to inhalational induction.

◆ Refers to This Month in Anesthesiology	CME CME Article
◆ Refers to Editorial Views	 This article has a Video Abstract
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 See Supplemental Digital Content	 This article has a Visual Abstract


- ◆ ◆ **Can Mathematical Modeling Explain the Measured Magnitude of the Second Gas Effect?** 1075
B. Korman, R. K. Dash, and P. J. Peyton
 Modeling of ventilation-perfusion inhomogeneity confirmed that the second gas effect is greater in blood than it is in expired gas, and its magnitude increases in blood but decreases in expired gas as the degree of ventilation-perfusion mismatch increases. Minimum alveolar concentration calculations based on end-tidal anesthetic concentration measurements may well underestimate the depth of anesthesia when nitrous oxide is supplemented with a volatile agent.
- ◆ ◆ **Etiology of Acute Coronary Syndrome after Noncardiac Surgery** 1084
M. A. Helwani, A. Amin, P. Lavigne, S. Rao, S. Oesterreich, E. Samaha, J. C. Brown, and P. Nagele
 The dominant mechanism of perioperative acute coronary syndrome in this cohort was demand ischemia. A subset of patients had no evidence of obstructive coronary artery disease, but findings were consistent with stress-induced cardiomyopathy. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*
- ◆ **Does Equi-Minimum Alveolar Concentration Value Ensure Equivalent Analgesic or Hypnotic Potency? A Comparison between Desflurane and Sevoflurane** 1092
K.-H. Ryu, K. Song, T.-Y. Lim, W.-J. Choi, Y.-H. Kim, and H.-S. Kim
 In patients anesthetized with 1.0 minimum alveolar concentration of either desflurane or sevoflurane, analgesic and hypnotic potency, as measured by surgical pleth index and bispectral index, were greater with desflurane than with sevoflurane. The results suggest that volatile agent equivalence of effect at the spinal cord is not equivalent to the effect at the brain, when evaluated by analgesia and hypnosis.
- ◆ **Amisulpride Prevents Postoperative Nausea and Vomiting in Patients at High Risk: A Randomized, Double-blind, Placebo-controlled Trial** 1099
P. Kranke, S. D. Bergese, H. S. Minkowitz, T. I. Melson, D. G. Leiman, K. A. Candiotti, N. Liu, L. Eberhart, A. S. Habib, J. Wallenborn, A. L. Kovac, P. Diemunsch, G. Fox, and T. J. Gan
 In a double-blind, randomized, placebo-controlled trial, the hypothesis that amisulpride, a potent dopamine D₂ and D₃ receptor antagonist, is superior to placebo in the prevention of postoperative nausea and vomiting when used with another antiemetic (primarily ondansetron or dexamethasone) was tested in 1,147 patients with three or four risk factors for postoperative nausea and vomiting. Complete response, defined as no emesis or rescue medication use in the 24-h postoperative period, occurred in 57.7% of the amisulpride group and 46.6% of the control group.
- ◆ **Pharmacokinetic/Pharmacodynamic Model of CW002, an Investigational Intermediate Neuromuscular Blocking Agent, in Healthy Volunteers** 1107
J. D. Kaulen, J. S. Owen, K. L. R. Brouwer, P. M. Heerdt, C. A. Lien, J. J. Savarese, and V. D. Schmith
 The pharmacokinetic properties of CW002 in humans are very similar to those of other neuromuscular blocking agents with intermediate durations of action. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*
- ◆ **Positive End-expiratory Pressure Alone Minimizes Atelectasis Formation in Nonabdominal Surgery: A Randomized Controlled Trial** 1117
E. Östberg, A. Thorisson, M. Enlund, H. Zetterström, G. Hedenstierna, and L. Edmark
 Patients were randomly assigned to 7 to 9 cm H₂O or zero end-expiratory pressure. Atelectasis was assessed by computed tomography at the end of nonabdominal surgery while patients remained anesthetized. Positive end-expiratory pressure, without recruitment maneuvers, largely prevented atelectasis and maintained normal oxygenation.
- ◆ **Hyperinsulinemic Normoglycemia during Cardiac Surgery Reduces a Composite of 30-day Mortality and Serious In-hospital Complications: A Randomized Clinical Trial** 1125
A. E. Duncan, D. I. Sessler, H. Sato, T. Sato, K. Nakazawa, G. Carvalho, R. Hatzakorzian, T. Codere-Maruyama, A. Abd-Elseyed, S. Bose, T. Said, M. Mendoza-Cuartas, H. Chowdary, E. J. Mascha, D. Yang, A. M. Gillinov, and T. Schricker
 Intraoperative hyperinsulinemic normoglycemia reduced mortality and morbidity after cardiac surgery. Providing exogenous glucose while targeting normoglycemia may be preferable to simply normalizing glucose concentrations.

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- ◆  **Association of Polypharmacy with Survival, Complications, and Healthcare Resource Use after Elective Noncardiac Surgery: A Population-based Cohort Study** 1140
D. I. McIsaac, C. A. Wong, G. L. Bryson, and C. van Walraven

Polypharmacy is associated with increased postoperative adverse events. The association is tenuous, may be limited to specific patient groups or medication types, and may be a marker for disease burden. Further study is necessary before any clinical practice changes can be considered. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

BASIC SCIENCE

- ◆  **Sodium Channel Nav1.3 Is Expressed by Polymorphonuclear Neutrophils during Mouse Heart and Kidney Ischemia *In Vivo* and Regulates Adhesion, Transmigration, and Chemotaxis of Human and Mouse Neutrophils *In Vitro*** 1151
M. Poffers, N. Böhne, C. Herzog, A. Thorenz, R. Chen, F. Güler, A. Hage, A. Leffler, and F. Echtermeyer

Nav1.3 is expressed in neutrophils and exerts functional roles including attachment, transmigration, and chemotaxis. Such findings may represent antiinflammatory target molecules for local anesthetics. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

- Ketamine Action in the *In Vitro* Cortical Slice Is Mitigated by Potassium Channel Blockade** 1167
L. J. Voss, S. Karalus, V. Englund, and J. W. Sleight


In addition to the previously demonstrated inhibition of hyperpolarization-activated cyclic nucleotide-gated channels, ketamine has a facilitatory action at two-pore potassium channels. The available data suggest that ketamine produces anesthesia by multiple mechanisms that include *N*-methyl-D-aspartate receptor antagonism, hyperpolarization-activated cyclic nucleotide-gated channel antagonism, and facilitation of two-pore potassium channels.

- In Vitro* Negative Inotropic Effect of Low Concentrations of Bupivacaine Relates to Diminished Ca²⁺ Sensitivity but Not to Ca²⁺ Handling or β -Adrenoceptor Signaling** 1175
F. Flenner, N. Arlt, M. Nasib, S. Schobesberger, T. Koch, U. Ravens, F. Friedrich, V. Nikolaev, T. Christ, and S. N. Stehr

This study demonstrates the negative inotropic effect of bupivacaine may be caused mainly by a reduction in myofilament sensitivity to Ca²⁺.



■ CRITICAL CARE MEDICINE

CLINICAL SCIENCE

-  **Effects of Prone Positioning on Transpulmonary Pressures and End-expiratory Volumes in Patients without Lung Disease** 1187
A. Kumaresan, R. Gerber, A. Mueller, S. H. Loring, and D. Talmor

In healthy patients during general anesthesia, switching from the supine to the prone position was associated with an increase in end-expiratory transpulmonary (distending) pressure and lung volume, which may account for its benefit in acute respiratory distress syndrome. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

BASIC SCIENCE

- ◆ ◆  **Biologic Impact of Mechanical Power at High and Low Tidal Volumes in Experimental Mild Acute Respiratory Distress Syndrome** 1193
 *R. S. Santos, L. d. A. Maia, M. V. Oliveira, C. L. Santos, L. Moraes, E. F. Pinto, C. d. S. Samary, J. A. Machado, A. C. Carvalho, M. V. d. S. Fernandes, V. Martins, V. L. Capelozzi, M. M. Morales, T. Koch, M. Gama de Abreu, P. Pelosi, P. L. Silva, and P. R. M. Rocco*

In an *in vivo* study of experimental acute respiratory distress syndrome, different combinations of tidal volume and respiratory rate were used to demonstrate that mechanical power and tidal volume can independently contribute to ventilator-induced lung injury. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

PAIN MEDICINE

BASIC SCIENCE

- Endothelin Signaling Contributes to Modulation of Nociception in Early-stage Tongue Cancer in Rats** 1207
A. Furukawa, M. Shinoda, A. Kubo, K. Honda, R. Akasaka, Y. Yonehara, and K. Iwata

Using a model of squamous cell carcinoma of the tongue, levels of endothelin-1 and β -endorphin were found to be increased at an early stage. The enhanced expression of β -endorphin in early-stage tongue cancers may conceal their presence.

- Peripherally Acting μ -Opioid Receptor Agonists Attenuate Ongoing Pain-associated Behavior and Spontaneous Neuronal Activity after Nerve Injury in Rats** 1220
V. Tiwari, M. Anderson, F. Yang, V. Tiwari, Q. Zheng, S.-Q. He, T. Zhang, B. Shu, X. Chen, S. A. Grenald, K. E. Stephens, Z. Chen, X. Dong, S. N. Raja, and Y. Guan

The selective and peripherally-restricted μ -opioid receptor dermorphin [D-Arg2, Lys4] (1–4) amide reduces evidence of an ongoing aversive state and increases wheel running in rodent models of neuropathic pain. Repeated administration of dermorphin [D-Arg2, Lys4] (1–4) amide leads to analgesic tolerance and opioid-induced hyperalgesia, similar to nonperipherally-restricted opioids.

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K. T. Martucci and S. C. Mackey

Neuroimaging has advanced our understanding of chronic pain and has collectively provided a framework for patient–clinician conversation regarding the complex, biopsychosocial aspect of chronic pain and the importance of multimodal therapy for its alleviation.

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