



ON THE COVER:

Airway management is applied daily by most anesthesiologists. This issue contains three articles, all with editorial commentary, with new knowledge on airway management. These include a description of problems with simulators for endotracheal intubation, a randomized comparison between awake fiberoptic and awake video laryngoscopy in the setting of anticipated difficult airway, and injuries associated with laryngeal mask airways and risks for their failure:

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- Fiadjo and Litman: Difficult Tracheal Intubation: Looking to the Past to Determine the Future, p. 1181
- Asai: Complications with Supraglottic Airways: Something to Worry About or Much Ado About Nothing? p. 1183
- Schebesta *et al.*: Degrees of Reality: Airway Anatomy of High-fidelity Human Patient Simulators and Airway Trainers, p. 1204
- Rosenstock *et al.*: Awake Fiberoptic or Awake Video Laryngoscopic Tracheal Intubation in Patients with Anticipated Difficult Airway Management: A Randomized Clinical Trial, p. 1210
- Ramachandran *et al.*: Predictors and Clinical Outcomes from Failed Laryngeal Mask Airway Unique™: A Study of 15,795 Patients, p. 1217

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 Refers to Editorial Views

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 CME Article

■ PERIOPERATIVE MEDICINE

- ◆◆◆ **Hospital Stay and Mortality Are Increased in Patients Having a “Triple Low” of Low Blood Pressure, Low Bispectral Index, and Low Minimum Alveolar Concentration of Volatile Anesthesia** 1195
Daniel I. Sessler, Jeffrey C. Sigl, Scott D. Kelley, Nassib G. Chamoun, Paul J. Manberg, Leif Saager, Andrea Kurz, and Scott Greenwald
- The relationship between anesthetic sensitivity and perioperative morbidity and mortality remains controversial. In this retrospective cohort analysis, perioperative data from 24,120 noncardiac surgery patients at the Cleveland Clinic were analyzed. The authors evaluated the association between cumulative minutes in the “triple low” condition, defined by mean arterial pressure (MAP) <75 mmHg, bispectral index (BIS) <45, and minimum alveolar concentration (MAC) <0.80, and excess length of stay and relative risk of 30-day mortality. The occurrence of low MAP during low MAC fraction was a strong and highly significant predictor for mortality. When combined with low BIS, mortality risk was even greater. These data warrant further studies to better understand the role of anesthetic sensitivity and perioperative morbidity and mortality.
- ◆◆ **Degrees of Reality: Airway Anatomy of High-fidelity Human Patient Simulators and Airway Trainers** 1204
Karl Schebesta, Michael Hüpfel, Bernhard Rössler, Helmut Ringl, Michael P. Müller, and Oliver Kimberger
- A radiographic evaluation of patient airway simulators discovers striking anatomical differences compared with a human patient’s airway anatomy. This finding may impact airway training and questions the common practice of using simulators for comparative airway trials.
- ◆◆◆ **Awake Fiberoptic or Awake Video Laryngoscopic Tracheal Intubation in Patients with Anticipated Difficult Airway Management: A Randomized Clinical Trial** 1210
Charlotte V. Rosenstock, Bente Thøgersen, Arash Afshari, Anne-Lise Christensen, Claus Eriksen, and Mona R. Gätke
- This multicenter study compared awake flexible fiberoptic and McGrath® (Aircraft Medical, Edinburgh, Scotland, United Kingdom) video laryngoscopic intubation in patients with anticipated difficult airway and a simplified airway risk index ≥ 4 . No difference in time to tracheal intubation was found.
- ◆◆◆ **Predictors and Clinical Outcomes from Failed Laryngeal Mask Airway Unique™: A Study of 15,795 Patients** 1217
Satya Krishna Ramachandran, Michael R. Mathis, Kevin K. Tremper, Amy M. Shanks, and Sachin Kheterpal
- Laryngeal Mask Airway Unique™ failure was seen in 1% of patients, an eighth of whom required unplanned hospital admission. Independent predictors were surgical table rotation, poor dentition, male sex, and higher body mass index.
- ◆◆ **Spontaneous Breathing during General Anesthesia Prevents the Ventral Redistribution of Ventilation as Detected by Electrical Impedance Tomography: A Randomized Trial** 1227
Oliver C. Radke, Thomas Schneider, Axel R. Heller, and Thea Koch
- During general anesthesia with a laryngeal mask airway, electrical impedance tomography detects a redistribution of ventilation toward the ventral region caused by pressure-controlled ventilation and pressure support ventilation. Spontaneous breathing (instead of positive-pressure ventilation) prevents this redistribution.

Two Etomidate Sites in $\alpha 1\beta 2\gamma 2$ γ -Aminobutyric Acid Type A Receptors Contribute Equally and Noncooperatively to Modulation of Channel Gating 1235

Grigori Guitchounts, Deirdre S. Stewart, and Stuart A. Forman

Using concatenated subunit assemblies, the authors independently introduced mutations into the two transmembrane etomidate sites formed by γ -aminobutyric acid receptor type A receptors containing 2α , 2β , and 1γ subunits. Equivalent mutations in these sites produced indistinguishable functional effects.

Adora2b Signaling on Bone Marrow Derived Cells Dampens Myocardial Ischemia-Reperfusion Injury 1245

Michael Koeppen, Patrick N. Harter, Stephanie Bonney, Megan Bonney, Susan Reithel, Cornelia Zachskorn, Michel Mittelbronn, and Tobias Eckle

Cardiac ischemia-reperfusion injury represents a major cause of tissue damage. The current study aims to understand the contribution of adenosine A2b-receptor signaling on inflammatory cells to cardiac ischemia-reperfusion injury.

In Vitro Kinetic Evaluation of the Free Radical Scavenging Ability of Propofol 1258

Weiguang Li, Yu Zhang, Yanru Liu, Feng Yue, Yiming Lu, Huanrong Qiu, Dawen Gao, Yan Gao, Yonghong Wu, Zhaoyan Wang, Rongqing Huang, and Chenggang Zhang

To evaluate the kinetics of propofol scavenging $ABTS^{+}$, the authors determined the reaction between propofol and $ABTS^{+}$. The results showed that propofol scavenges $ABTS^{+}$ with a fast and stable kinetic feature *in vitro*.

SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT

AZD-3043: A Novel, Metabolically Labile Sedative–Hypnotic Agent with Rapid and Predictable Emergence from Hypnosis 1267

Talmage D. Egan, Shinju Obara, Thomas E. Jenkins, Sarah S. Jaw-Tsai, Shanti Amagasu, Daniel R. Cook, Scott C. Steffensen, and David T. Beattie

AZD-3043 is a novel, metabolically labile ester and positive allosteric modulator of the γ -aminobutyric acid type A with a short-acting pharmacokinetic profile. SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT

■ CRITICAL CARE MEDICINE

Autologous Transplantation of Peripheral Blood-derived Circulating Endothelial Progenitor Cells Attenuates Endotoxin-induced Acute Lung Injury in Rabbits by Direct Endothelial Repair and Indirect Immunomodulation 1278

Jian-Ping Cao, Xing-Ying He, Hai-Tao Xu, Zui Zou, and Xue-Yin Shi

Autologous transplantation of circulating endothelial progenitor cells could partly restore pulmonary endothelial function and effectively attenuate endotoxin-induced acute lung injury by direct endothelial repair and indirect immunomodulation of antioxidation and antiinflammation.

Short-term, Mild Hypothermia Can Increase the Beneficial Effect of Permissive Hypotension on Uncontrolled Hemorrhagic Shock in Rats 1288

Tao Li, Xiulai Lin, Yu Zhu, Lijie Li, and Liangming Liu

Permissive hypotension in combination with mild hypothermia is beneficial to uncontrolled hemorrhagic shock before bleeding has been controlled in rats.

TT-301 Inhibits Microglial Activation and Improves Outcome after Central Nervous System Injury in Adult Mice 1299

Michael L. James, Haichen Wang, Viviana Cantillana, Beilei Lei, Dawn N. Kernagis, Hana N. Dawson, Lori D. Klamann, and Daniel T. Laskowitz

Postinjury administration of the microglial inhibitor, TT-301, improves histologic and functional outcomes in murine models of acute brain injury. These results suggest a therapeutic strategy targeting microglial activation has potential for translation into clinical trials. SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT

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■ PAIN MEDICINE

- ◆ **Effect of Perioperative Systemic α_2 Agonists on Postoperative Morphine Consumption and Pain Intensity: Systematic Review and Meta-analysis of Randomized Controlled Trials** 1312
Grégoire Blaudszun, Christopher Lysakowski, Nadia Elia, and Martin R. Tramèr

Perioperative systemic α_2 agonists have a modest beneficial effect on postoperative morphine consumption, pain intensity, and nausea. Hemodynamic adverse effects occur frequently. Recovery times are not prolonged. Data on chronic pain or hyperalgesia are lacking. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

- Modulation of Tight Junction Proteins in the Perineurium to Facilitate Peripheral Opioid Analgesia** 1323

Heike L. Rittner, Salah Amasheh, Rabih Moshourab, Dagmar Hackel, Reine-Solange Yamdeu, Shaaban A. Mousa, Michael Fromm, Christoph Stein, and Alexander Brack

Peripherally applied hydrophilic opioids can inhibit nociceptors (C-fibers) only together with hypertonic solution. Hypertonic solutions open the perineurial barrier and reduce claudin-1 *via* metalloproteinases activation. This pathway may offer new approaches for drug delivery.

- Local Anesthetic-like Inhibition of Voltage-gated Na^+ Channels by the Partial μ -opioid Receptor Agonist Buprenorphine** 1335

Andreas Leffler, Georg Frank, Katrin Kistner, Florian Niedermirtl, Wolfgang Koppert, Peter W. Reeh, and Carla Nau

Buprenorphine was identified as a potent blocker of voltage-gated Na^+ channels. Buprenorphine interacts with the intracellular local anesthetic binding site and inhibits neuronal and nonneuronal Na^+ channels more potently than other clinically applied opioids.

- Gabapentin Inhibits γ -Amino Butyric Acid Release in the Locus Coeruleus but Not in the Spinal Dorsal Horn after Peripheral Nerve Injury in Rats** 1347

Masaru Yoshizumi, Renee A. Parker, James C. Eisenach, and Ken-ichiro Hayashida

Peripheral nerve injury increases γ -amino butyric acid content in the locus coeruleus, and gabapentin decreases γ -amino butyric acid release in this structure but not in the spinal cord.

■ EDUCATION

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CLINICAL CONCEPTS AND COMMENTARY

- Patient Blood Management** 1367
Lawrence Tim Goodhough and Aryeh Shander

Patient blood management emphasizes management of anemia, optimal control of hemostasis, and optimal use of blood components with a goal of minimizing their use, in order to improve patient safety and clinical outcomes.

REVIEW ARTICLE

- High-volume Hemofiltration in the Intensive Care Unit: A Blood Purification Therapy** 1377
Thomas Rimmelé and John A. Kellum

This article analyzes data about high-volume hemofiltration with an original approach, taking into account a clear distinction between renal support for acute kidney injury and blood purification for severe inflammatory states.

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