

## ◆ THIS MONTH IN ANESTHESIOLOGY

9A

## ◆ EDITORIAL VIEWS

- Anesthesia: How to Organize and Train Our Teachers** 773  
Manuel Pardo, Jr.
- Improving on Reality: Can Simulation Facilitate Practice Change?** 775  
Randolph H. Steadman
- Opioid Medication Management: Clinician Beware!** 777  
Robert N. Jamison and J. David Clark

## ■ SPECIAL ARTICLES

- We Need Leaders: The 48th Annual Rovenstine Lecture** 779  
Peter J. Pronovost  
*Far too many people are harmed rather than helped from healthcare. In this article, the author provides insights regarding how we can change this.*
- After You, Please: The Second Annual John W. Severinghaus Lecture on Translational Science** 786  
Edmond I Eger II  
*Most of what I have accomplished in my scientific life has resulted from others, particularly John W. Severinghaus, M.D., pointing the way.*
- Improving Perioperative Outcomes: My Journey into Risk, Patient Preferences, Guidelines, and Performance Measures: Ninth Honorary FAER Research Lecture** 794  
Lee A. Fleisher  
*Although the application of evidence and guidelines can lead to improved outcomes, an understanding of baseline risk assessment and patient preferences must be incorporated into generalizing the recommendation.*
- Sapere Aude! The 2009 Excellence in Research Lecture** 802  
William L. Young  
*We need to think of ourselves out of intellectual handcuffs, beyond the confines of our clinical horizons in terms of academic inquiry. Investigative independence can coexist with intellectual interdependence.*
- **Practice Guidelines for Chronic Pain Management: An Updated Report by the American Society of Anesthesiologists Task Force on Chronic Pain Management and the American Society of Regional Anesthesia and Pain Medicine** 810  
*The American Society of Anesthesiologists Task Force on Chronic Pain Management presents updated Practice Guidelines for chronic pain management. The Guidelines provide recommendations intended to optimize pain control, recognizing that a pain-free state may not be attainable; enhance functional abilities, physical and psychological well-being; enhance the quality of life for patients; and minimize adverse outcomes.*  
SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT

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◆ Refers to This Month in Anesthesiology  
◆ Refers to Editorial Views

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CME CME Article

- 
**Isoflurane-induced Neuroapoptosis in the Neonatal Rhesus Macaque Brain** 834  
 Ansgar M. Brambrink, Alex S. Evers, Michael S. Avidan, Nuri B. Farber, Derek J. Smith, Xuezhao Zhang, Gregory A. Dissen, Catherine E. Creeley, and John W. Olney  
*Six-day-old rhesus macaques were exposed for 5 h to isoflurane anesthesia or to room air. Histologic evaluation revealed a 13-fold increase in neuroapoptosis affecting all divisions of the cerebral cortex in the isoflurane-exposed brains. SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*
- Comparison of the Utility of Preoperative *versus* Postoperative B-type Natriuretic Peptide for Predicting Hospital Length of Stay and Mortality after Primary Coronary Artery Bypass Grafting** 842  
 Amanda A. Fox, Jochen D. Muehlschlegel, Simon C. Body, Stanton K. Shernan, Kuang-Yu Liu, Tjorvi E. Perry, Sary F. Aranki, E. Francis Cook, Edward R. Marcantonio, and Charles D. Collard  
*Preoperative B-type natriuretic peptide may be better than peak postoperative B-type natriuretic peptide (measured on postoperative days 1–5) for predicting hospital length of stay and longer term all-cause mortality after primary coronary artery bypass graft surgery.*
- Cognitive Function after Major Noncardiac Surgery, Apolipoprotein E4 Genotype, and Biomarkers of Brain Injury** 852  
 David L. McDonagh, Joseph P. Mathew, William D. White, Barbara Phillips-Bute, Daniel T. Laskowitz, Mihai V. Podgoreanu, and Mark F. Newman, for the Neurologic Outcome Research Group  
*Postoperative cognitive decline does not correlate with apolipoprotein E4 genotype or plasma biomarkers of brain injury and inflammation.*
- 
**Role of Intraoperative and Postoperative Blood Glucose Concentrations in Predicting Outcomes after Cardiac Surgery** 860  
 Andra E. Duncan, Alaa Abd-Elseyed, Ankit Maheshwari, Meng Xu, Edward Soltesz, and Colleen G. Koch  
*This observational study examined the role of intraoperative and postoperative blood glucose concentrations, glycemic variability, episodes of hypoglycemia, and diabetic status as predictors of postoperative morbidity and mortality after cardiac surgery. SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*
- 
**Noxious Stimulation Response Index: A Novel Anesthetic State Index Based on Hypnotic–Opioid Interaction** 872  
 Martin Luginbühl, Peter M. Schumacher, Pascal Vuilleumier, Hugo Vereecke, Björn Heyse, Thomas W. Bouillon, and Michel M. R. F. Struys  
*The noxious stimulation response index better predicts response to noxious stimulation than estimated propofol or remifentanyl concentrations, bispectral index, or acoustic evoked potential index. SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*
- Limb Remote Ischemic Preconditioning Protects the Spinal Cord from Ischemia–Reperfusion Injury: A Newly Identified Nonneuronal but Reactive Oxygen Species–dependent Pathway** 881  
 Hai-Long Dong, Yi Zhang, Bin-Xiao Su, Zheng-Hua Zhu, Qiu-Han Gu, Han-Fei Sang, and Lize Xiong  
*Our study proved that increased antioxidant enzyme activity initiated by oxidative stress plays an important role in the formation of the ischemic tolerance against spinal cord ischemia by remote ischemic preconditioning.*
- Gantacurium and CW002 Do Not Potentiate Muscarinic Receptor-mediated Airway Smooth Muscle Constriction in Guinea Pigs** 892  
 Hiroshi Sunaga, Yi Zhang, John J. Savarese, and Charles W. Emala  
*The novel bisquaternary nondepolarizing muscle relaxants gantacurium or CW002 do not mimic rapacuronium's potentiation of muscarinic receptor-mediated constriction of guinea pig airways in vivo.*

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**Cysteine Reversal of the Novel Neuromuscular Blocking Drug CW002 in Dogs: Pharmacodynamics, Acute Cardiovascular Effects, and Preliminary Toxicology** 900

Hiroshi Sunaga, Jaideep K. Malhotra, Edward Yoon, John J. Savarese, and Paul M. Heerdt  
*L-cysteine reversal is fully effective even at only 1 min after administration of nine times ED<sub>95</sub> of CW002 in dogs, with minimal hemodynamic effect and no apparent organ toxicity.*

◆ **Pharmacodynamics and Cardiopulmonary Side Effects of CW002, a Cysteine-reversible Neuromuscular Blocking Drug in Dogs** 910

Paul M. Heerdt, Jaideep K. Malhotra, Brian Y. Pan, Hiroshi Sunaga, and John J. Savarese  
*CW002 is a potent, cysteine-reversible neuromuscular blocking drug with minimal cardiopulmonary effects when administered at doses less than or equal to 25 × ED<sub>95</sub> to beagles.*

■ **CRITICAL CARE MEDICINE**

CME ◆ **Temporal Trends in the Epidemiology of Severe Postoperative Sepsis after Elective Surgery: A Large, Nationwide Sample** 917

Brian T. Bateman, Ulrich Schmidt, Mitchell F. Berman, and Edward A. Bittner  
*This study analyzed the epidemiology of postoperative sepsis using the Nationwide Inpatient Sample. Data from adults with a length of stay greater than 3 days for the 20 most common elective operative procedures were evaluated for the years 1997–2006. Criteria for postoperative sepsis and severe sepsis, sepsis with organ dysfunction, were defined. Data for temporal trends were analyzed. In more than 2 million admissions, the rate of severe sepsis rose from 0.3% in 1997 to 0.9% in 2006. The in-hospital mortality rate for patients with severe postoperative sepsis declined from 44.4% in 1997 to 34.0% in 2006. Despite the marked increase in the rate of severe postoperative sepsis, there was a concomitant decrease in the in-hospital mortality rate. SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

**Plasma Proteome to Look for Diagnostic Biomarkers of Early Bacterial Sepsis after Liver Transplantation: A Preliminary Study** 926

Catherine Paugam-Burtz, Miguel Albuquerque, Gabriel Baron, Frederic Bert, Hélène Voitot, Didier Delefosse, Federica Dondero, Daniele Sommacale, Claire Francoz, Nadine Hanna, Jacques Belghiti, Philippe Ravaut, Pierre Bedossa, Jean Mantz, and Valérie Paradis  
*Plasma proteomic profiling identified five peaks as good candidates to serve as biomarkers of early postoperative sepsis after liver transplantation.*

**Renal Effects of Saline-based 10% Pentastarch versus 6% Tetrastarch Infusion in Ovine Endotoxemic Shock** 936

Christian Ertmer, Gabriele Köhler, Sebastian Rehberg, Andrea Morelli, Matthias Lange, Björn Ellger, Bernardo Bollen Pinto, Eva Rübig, Michael Erren, Lars G. Fischer, Hugo Van Aken, and Martin Westphal  
*This study found kidney dysfunction and tubular injury associated with saline-based 10% pentastarch infusion in ovine endotoxemic shock. These alterations were significantly more pronounced when compared with both saline-based 6% tetrastarch and balanced crystalloid infusion.*

■ **PAIN MEDICINE**

◆◆ **Malpractice Claims Associated with Medication Management for Chronic Pain** 948

Dermot R. Fitzgibbon, James P. Rathmell, Edward Michna, Linda S. Stephens, Karen L. Posner, and Karen B. Domino  
*Medication management for chronic pain is associated with increasing liability. Death was the outcome in more than half of the claims. Patient's noncooperation with care and inappropriate medication management by physicians were factors in many claims.*

**Predictive Risk Factors for Persistent Postherniotomy Pain** 957

Eske K. Aasvang, Eliza Gmaehle, Jeanette B. Hansen, Bjorn Gmaehle, Julie L. Forman, Jochen Schwarz, Reinhard Bittner, and Henrik Kehlet  
*A prospective consecutive cohort study was conducted in 464 patients. Significant risk factors for persistent postherniotomy pain were preoperative pain-related functional impairment, heat stimulation pain, pain on day 30 postoperatively, and signs of nerve damage.*

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## ■ EDUCATION

### CASE SCENARIO

#### **Perioperative Airway Management of a Patient with Tracheal Stenosis** 970

Shiroh Isono, Yuji Kitamura, Takashi Asai, and Tim M. Cook

### IMAGES IN ANESTHESIOLOGY

#### **Internal Jugular Valve and Central Catheter Placement** 979

Kyota Fukazawa, Luz Aguina, and Ernesto A. Pretto, Jr.

### ANESTHESIA LITERATURE REVIEW

980

### ORIGINAL INVESTIGATIONS IN ANESTHESIOLOGY

#### ◆ **Simulation-based Training Improves Physicians' Performance in Patient Care in High-stakes Clinical Setting of Cardiac Surgery** 985

Heinz R. Bruppacher, Syed K. Alam, Vicki R. LeBlanc, David Latter, Viren N. Naik, Georges L. Savoldelli, C. David Mazer, Matt M. Kurrek, and Hwan S. Joo

*In this blinded, randomized controlled trial, we demonstrated that simulation-based training improves patient care during weaning from cardiopulmonary bypass compared with interactive seminars. Skills acquired during the training were translated into real life performance.*

### ORIGINAL INVESTIGATIONS IN EDUCATION

#### **Anesthesiology Residents' Performance of Pediatric Resuscitation during a Simulated Hyperkalemic Cardiac Arrest** 993

Kimberly J. Howard-Quijano, Marjorie A. Stiegler, Yue Ming Huang, Cecilia Canales, and Randolph H. Steadman

*Simulation was used to assess the pediatric resuscitation skills of anesthesiology residents who had completed their required pediatric experience. Knowledge gaps were identified.*

### CLINICAL CONCEPTS AND COMMENTARY

#### **Biomarkers of Acute Kidney Injury: An Evolving Domain** 998

David R. Mollroy, Gebhard Wagener, and H. Thomas Lee

*There is an urgent need for new biomarkers of acute kidney injury to facilitate early diagnosis, making early targeted intervention a possibility. Several candidate biomarkers are under investigation and their current state is reviewed here.*

#### **From Creatine Kinase-MB to Troponin: The Adoption of a New Standard** 1005

Sylvia Archan and Lee A. Fleisher

*Cardiac biomarkers evolved from creatine kinase to the more sensitive troponin. To understand how best to interpret elevations in cardiac biomarkers, it is important to understand their prognostic ability both perioperatively and long term.*

#### **Residual Paralysis after Emergence from Anesthesia** 1013

Benoît Plaud, Bertrand Debaene, François Donati, and Jean Marty

*Residual paralysis after emergence from anesthesia directly and markedly worsens patient outcome.*

## ■ REVIEW ARTICLES

#### **Statistical Evaluation of a Biomarker** 1023

Patrick Ray, Yannick Le Manach, Bruno Riou, and Tim T. Houle

*Biomarker studies are often presented with poor biostatistics and methodologic flaws that precludes them from providing a reliable and reproducible scientific message. Recommendations are offered to improve the statistical evaluation and reporting of biomarker studies.*

#### **Simulation-based Assessment in Anesthesiology: Requirements for Practical Implementation** 1041

John R. Boulet and David J. Murray

*The use of simulations in anesthesiology is growing. For practical implementation in assessment programs, both formative and summative, evaluators must pay special attention to defining the relevant skills, scenario development, and score validation.*

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## ■ CORRESPONDENCE

### **Rapid Eye Movement Sleep and General Anesthesia** 1053

George A. Mashour

#### **In Reply**

James Sleigh and Kate Leslie

### **Early Labor Neuraxial Analgesia: Effects on the Progress and Outcome of Labor** 1053

Cynthia A. Wong, Barbara M. Scavone, John T. Sullivan, and Robert J. McCarthy

#### **In Reply**

FuZhou Wang, XiaoFeng Shen, XiRong Guo, YuZhu Peng, XiaoQi Gu, and ShiQin Xu

### **Sensory Nerve Damage after the Use of the *LMA Supreme*<sup>TM</sup>** 1055

Michele Carron, Ulderico Freo, and Carlo Ori

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Michel M. R. F. Struys, Jörg Fechner, Jürgen Schüttler, and Helmut Schwilden

## ■ RETRACTION

### **Fospropofol Assay Issues and Impact on Pharmacokinetic and Pharmacodynamic Evaluation: Retraction** 1058

### **Pharmacokinetics and Clinical Pharmacodynamics of the New Propofol Prodrug GPI 15715 in Volunteers: Retraction** 1058

### **Comparative Pharmacokinetics and Pharmacodynamics of the New Propofol Prodrug GPI 15715 and Propofol Emulsion: Retraction** 1058

### **AQUAVAN Injection, a Water-soluble Prodrug of Propofol, as a Bolus Injection: A Phase I Dose-escalation Comparison with DIPRIVAN (Part 1): Pharmacokinetics: Retraction** 1058

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George S. Bause

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### **Corning's "Ice-Water Cap" for Congestive Headaches** 935

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