



ON THE COVER:

Of three classes of anesthetics, most EEG-based monitors fail to recognize the anesthetized state produced by ketamine. In this issue, Mashour and colleagues use high-resolution EEG and connectivity analysis to support a common EEG feature of anesthesia, including that produced by ketamine.

- Sleight: The Study of Consciousness Comes of Age, p. 1245
- Lee *et al.*: Disruption of Frontal–Parietal Communication by Ketamine, Propofol, and Sevoflurane, p. 1264

THIS MONTH IN ANESTHESIOLOGY

3A

EDITORIAL VIEWS

The Study of Consciousness Comes of Age

Jamie W. Sleight

1245

MA Clinical Prediction of Postoperative Respiratory Failure

Amy Young and Satya Krishna Ramachandran

1247

MA A Novel Approach to Preoperative Blood Orders

Alparslan Turan, Jonathan H. Waters, and Daniel I. Sessler

1250

Multivariable Risk Prediction Models: It's All about the Performance

Gary Collins and Yannick Le Manach

1252

Protect the Lungs during Abdominal Surgery: It May Change the Postoperative Outcome

Marcos F. Vidal Melo and Matthias Eikermann

1254

Nitrous Oxide Genotoxicity

Kirk Hogan

1258

Primum Non Nocere or How to Resolve Drug-induced Respiratory Depression

Albert Dahan, Margot Roozkrans, Rutger van der Schrier, Terry Smith, and Leon Aarts

1261

PERIOPERATIVE MEDICINE

Disruption of Frontal–Parietal Communication by Ketamine, Propofol, and Sevoflurane

UnCheol Lee, SeungWoo Ku, GyuJeong Noh, SeungHye Baek, ByungMoon Choi, and George A. Mashour

1264

This study demonstrates in human surgical patients that both GABAergic and non-GABAergic anesthetics disrupt frontal–parietal communication, despite distinct neurophysiologic profiles. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

◇ Refers to This Month in Anesthesiology

◆ Refers to Editorial Views

MA Meeting Article

🌐 See Supplemental Digital Content

CME CME Article

-  **◆ Development and Validation of a Score for Prediction of Postoperative Respiratory Complications** 1276
Britta Brueckmann, Jose L. Villa-Urbe, Brian T. Bateman, Martina Grosse-Sundrup, Dean R. Hess, Christopher L. Schlett, and Matthias Eikermann
 The authors developed a score for the prediction of postoperative respiratory complications based on five preoperative patients' characteristics. It can be used preoperatively by anesthesiologists to identify patients at increased risk for severe postoperative respiratory complications.
-     **◆ Optimizing Preoperative Blood Ordering with Data Acquired from an Anesthesia Information Management System** 1286
Steven M. Frank, James A. Rothschild, Courtney G. Masear, Richard J. Rivers, William T. Merritt, Will J. Savage, and Paul M. Ness
 The recommended maximum surgical blood order schedule (MSBOS) for common surgical procedures that was published over 30 yr ago may be obsolete because many new procedures have been introduced while others have been improved upon. Data on 53,526 surgical patients having 1,632 types of surgical procedures were acquired from an anesthesia information management system (AIMS). The type and crossmatch-to-transfusion ratios of all surgical services except cardiac and vascular/transplant greatly exceeded the proposed optimal ratio of 2. An updated, institution-specific MSBOS for each surgical specialty was created from a novel blood order algorithm and the AIMS data. Implementing the algorithm and an institution-specific MSBOS could improve operating room efficiency, enhance patient safety, and reduce costs. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*
- ◆ Impact of Present-on-admission Indicators on Risk-adjusted Hospital Mortality Measurement** 1298
Jarrod E. Dalton, Laurent G. Glance, Edward J. Mascha, John Ehrlinger, Nassib Chamoun, and Daniel I. Sessler
 The authors estimate a baseline risk index for in-hospital mortality using present-on-admission indicators and show that hospital performance measures appear to be dependent on whether or not the underlying model includes hospital-acquired conditions.
- ◆ Protective Mechanical Ventilation during General Anesthesia for Open Abdominal Surgery Improves Postoperative Pulmonary Function** 1307
Paolo Severgnini, Gabriele Selmo, Christian Lanza, Alessandro Chiesa, Alice Frigerio, Alessandro Bacuzzi, Gianlorenzo Dionigi, Raffaele Novario, Cesare Gregoretti, Marcelo Gama de Abreu, Marcus J. Schultz, Samir Jaber, Emmanuel Futier, Maurizio Chiaranda, and Paolo Pelosi
 A protective mechanical ventilation strategy during open abdominal surgery may influence postoperative modified Clinical Pulmonary Infection Score, arterial blood gases, and pulmonary functional tests.
- ◆ Leukocyte DNA Damage and Wound Infection after Nitrous Oxide Administration: A Randomized Controlled Trial** 1322
Yan Chen, Xiaodong Liu, Christopher H. K. Cheng, Tony Gin, Kate Leslie, Paul Myles, and Matthew T. V. Chan
 Nitrous oxide administration induces leukocyte DNA damage in patients undergoing major colorectal surgery. DNA damage was associated with postoperative wound infection.
-  **◆ Development and Psychometric Evaluation of a Postoperative Quality of Recovery Score: The QoR-15** 1332
Peter A. Stark, Paul S. Myles, and Justin A. Burke
 This study consisted of the development and psychometric evaluation of a short-form 15-item patient-rated postoperative quality of recovery score, the QoR-15. The QoR-15 is a valid, reliable, responsive, and clinically acceptable measure of postoperative quality of recovery. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

- Using the Entropy of Tracheal Sounds to Detect Apnea during Sedation in Healthy Nonobese Volunteers** 1341
Lu Yu, Chien-Kun Ting, Bryce E. Hill, Joseph A. Orr, Lara M. Brewer, Ken B. Johnson, Talmage D. Egan, and Dwayne R. Westenskow
 The entropy of the acoustic signal from a microphone placed over the trachea can detect apnea in sedated volunteers with satisfactory sensitivity and specificity, and provide an early warning of the onset of apnea.
- Validity of the Lipid Sink as a Mechanism for the Reversal of Local Anesthetic Systemic Toxicity: A Physiologically Based Pharmacokinetic Model Study** 1350
Ilin Kuo and Belinda S. Akpa
 The sink mechanism results in a redistribution of anesthetic from tissues to the blood stream. However, the extent to which this occurs and the associated timescale may not be adequate to explain the dramatic recoveries observed clinically.
- Bone Fracture Exacerbates Murine Ischemic Cerebral Injury** 1362
Vincent Degos, Mervyn Maze, Susana Vacas, Jan Hirsch, Yi Guo, Fanxia Shen, Kristine Jun, Nico van Rooijen, Pierre Gressens, William L. Young, and Hua Su
 Stroke is a risk factor for fracture and 1–1.5% of stroke patients suffer a fracture within 24 h of a stroke. The authors showed that fracture enhances stroke injury *via* HMGB1 release and macrophage/microglia brain infiltration.
- Atorvastatin-induced Cardioprotection of Human Myocardium Is Mediated by the Inhibition of Mitochondrial Permeability Transition Pore Opening *via* Tumor Necrosis Factor- α and Janus Kinase/Signal Transducers and Activators of Transcription Pathway** 1373
Sandrine Lemoine, Lan Zhu, Damien Legallois, Massimo Massetti, Alain Manrique, and Jean-Luc Hanouz
 Atorvastatin-induced cardioprotection of human myocardium involves activation of tumor necrosis factor- α , Janus kinase-2, and signal transducers and activators of transcription-3, and inhibition of the mitochondrial Permeability Transition Pore opening in early reoxygenation.
- Xenon and Isoflurane Reduce Left Ventricular Remodeling after Myocardial Infarction in the Rat** 1385
Anna B. Roehl, Sandra Funcke, Michael M. Becker, Andreas Goetzenich, Christian Bleilevens, Rolf Rossaint, Paul Steendijk, and Marc Hein
 Compared to isoflurane and s-ketamine, xenon limited progressive adverse cardiac remodeling and contractile dysfunction 28 days after perioperative myocardial infarction.
- Modeling the Influence of the A118G Polymorphism in the *OPRM1* Gene and of Noxious Stimulation on the Synergistic Relation between Propofol and Remifentanil: Sedation and Analgesia in Endoscopic Procedures** 1395
Xavier Borrat, Iñaki F. Trocóniz, José F. Valencia, Silvia Rivadulla, Oriol Sendino, Josep Llach, Jenifer Muñoz, Sergi Castellví-Bel, Mathieu Jospin, Erik W. Jensen, Antoni Castells, and Pedro L. Gambús
 Remifentanil has no effect on its synergistic relation with propofol with respect to the bispectral index in patients with the A118G genetic polymorphism. Noxious stimulation increases requirements of remifentanil by 4%.
- Propofol and Thiopental Suppress Amyloid Fibril Formation and GM1 Ganglioside Expression through the γ -Aminobutyric Acid A Receptor** 1408
Naoki Yamamoto, Hajime Arima, Takeshi Sugiura, Hiroyuki Hirate, Hideo Taniura, Kenji Suzuki, and Kazuya Sobue
 The effects of GM1 ganglioside on amyloid β -protein fibrillogenesis have not been reported. The results of the current study suggested that propofol and thiopental have direct and indirect inhibitory effects on amyloid β -protein fibrillogenesis.

CONTENTS

- The Benzodiazepine Diazepam Potentiates Responses of $\alpha 1\beta 2\gamma 2L$ γ -Aminobutyric Acid Type A Receptors Activated by either γ -Aminobutyric Acid or Allosteric Agonists** 1417
Ping Li, Megan M. Eaton, Joe Henry Steinbach, and Gustav Akk

Benzodiazepines act in the nervous system by potentiating the function of the γ -aminobutyric acid type A receptor. The authors present novel data that demonstrate that the benzodiazepine diazepam acts by increasing the channel gating efficacy.

■ CRITICAL CARE MEDICINE

- ◇ **Hypoxia-inducible Factor and Target Gene Expression Are Decreased in Patients with Sepsis: Prospective Observational Clinical and Cellular Studies** 1426
Simon T. Schäfer, Stilla Frede, Sandra Winning, Alexandra Bick, Paktis Roshangar, Joachim Fandrey, Jürgen Peters, and Michael Adamzik

In sepsis, oxygen utilization can be impaired. Hypoxia-inducible factor-1 α , the key player in adaptation to inflammation/hypoxia, was suppressed both in leukocytes from septic patients and in endotoxin-tolerant monocytic cells. This might contribute to disturbed adaptation to tissue hypoxia in sepsis.

■ PAIN MEDICINE

- ◆ **Coadministration of the AMPAKINE CX717 with Propofol Reduces Respiratory Depression and Fatal Apneas** 1437
Jun Ren, Floriane Lenal, Michael Yang, Xiuqing Ding, and John J. Greer

Propofol can induce respiratory depression including lethal apnea. Coadministration of AMPAKINE CX717 with propofol markedly reduced propofol-induced respiratory depression and thus increases the safety margin against profound apnea and death.

■ EDUCATION

CASE SCENARIO

- Hemodynamic Management of Postoperative Acute Kidney Injury** 1446
Matthieu Legrand and Didier Payen

IMAGES IN ANESTHESIOLOGY

- Symmetric Peripheral Gangrene** 1455
Shigeru Akamatsu, Akiko Kojima, Aki Tanaka, Keishu Hayashi, and Tomoki Hashimoto

- Infographics in Anesthesiology: A Volatile Tale of Two Institutions** 1456
Jonathan P. Wanderer, Jesse M. Ehrenfeld, Warren S. Sandberg, and James P. Rathmell

ANESTHESIA LITERATURE REVIEW

1457

CLINICAL CONCEPTS AND COMMENTARY

- Positive Inotropic Agents in Myocardial Ischemia–Reperfusion Injury: A Benefit/Risk Analysis** 1460
Jean-Luc Fellahi, Marc-Olivier Fischer, Georges Daccache, Jean-Louis Gerard, and Jean-Luc Hanouz

Positive inotropic agents should be used judiciously when managing surgical patients with acute myocardial ischemia–reperfusion injury, as use of these inotropes is not without potential adverse effects.

REVIEW ARTICLE

- CME Managing New Oral Anticoagulants in the Perioperative and Intensive Care Unit Setting** 1466
Jerrold H. Levy, David Faraoni, Jenna L. Spring, James D. Douketis, and Charles M. Samama

CONTENTS

MIND TO MIND

- Count Backwards from 10** 1475
Richard L. Saupé
- Endurance** 1477
Mark J. Lenart

■ CORRESPONDENCE

- Role of the Photoplethysmographic Waveform in the Care of High-risk Surgical Patients** 1479
Kirk H. Shelley, Aymen A. Alian, and Adam J. Shelley

In Reply
Maxime Cannesson and Yannick Le Manach

In Reply
Baptiste Hengy, Mathieu Gazon, Jean-Paul Viale, and Frederic Aubrun

-
- Closing the Loop on Relaxant Reversal** 1482
Lawrence J. Caruso and David A. Paulus

In Reply
Stephan R. Thilen, Bradley E. Hansen, Miriam M. Treggiari, and Sanjay M. Bhananker

-
- Is 64 the New 57? Probably Not!** 1483
Richard A. Steinbrook and Marcia L. Weinstein

In Reply
Judi A. Turner and Daniel J. Cole

In Reply
Fredrick K. Orkin, Gaetano J. Forte, Sandra L. McGinnis, Mary Dale Peterson, Joseph M. Garfield, Jonathan D. Katz, Stephen H. Jackson, Norman A. Cohen, Robert S. Holzman, Donald E. Martin, Armin Schubert, and Arnold J. Berry

■ ANESTHESIOLOGY REFLECTIONS FROM THE WOOD LIBRARY-MUSEUM

- Paul Meyer Wood Learns the Drill** 1260
George S. Bause

From Fish Poison to Merck Picrotoxin 1263
George S. Bause

From Giessen to Munich to the Readers of ANESTHESIOLOGY: Justus von Liebig 1340
George S. Bause

■ REVIEWS OF EDUCATIONAL MATERIAL

1486

■ ACKNOWLEDGMENT

1488

■ CAREERS & EVENTS

23A

INSTRUCTIONS FOR AUTHORS

The most recently updated version of the Instructions for Authors is available at www.anesthesiology.org. Please refer to the Instructions for the preparation of any material for submission to ANESTHESIOLOGY.

Manuscripts submitted for consideration for publication must be submitted in electronic format. The preferred method is via the Journal's Web site (<http://www.anesthesiology.org>). Detailed directions for submissions and the most recent version of the Instructions for Authors can be found on the Web site (<http://www.anesthesiology.org>). Books and educational materials should be sent to Michael J. Avram, Ph.D., Department of Anesthesiology, Northwestern University Feinberg School of Medicine, Ward Memorial Building, Room 13-199, 303 East Chicago Avenue, Chicago, IL 60611-3008. Requests for permission to duplicate materials published in ANESTHESIOLOGY should be submitted in electronic format, to the Permissions Department (journalpermissions@lww.com). Advertising and related correspondence should be addressed to Advertising Manager, ANESTHESIOLOGY, Lippincott Williams & Wilkins, Two Commerce Square, 2001 Market Street, Philadelphia, Pennsylvania 19103 (Web site: <http://www.lww.com/advertisingratecards/>). Publication of an advertisement in ANESTHESIOLOGY does not constitute endorsement by the Society or Lippincott Williams & Wilkins, Inc. of the product or service described therein or of any representations made by the advertiser with respect to the product or service.

ANESTHESIOLOGY (ISSN 0003-3022) is published monthly by Lippincott Williams & Wilkins, 16522 Hunters Green Parkway, Hagerstown, MD 21740-2116. Business office: Two Commerce Square, 2001 Market Street, Philadelphia, PA 19103. Periodicals postage paid at Hagerstown, MD, and at additional mailing offices. Copyright © 2013, the American Society of Anesthesiologists, Inc.

Annual Subscription Rates: *United States*—\$719 Individual, \$1309 Institution, \$289 In-training. *Rest of World*—\$759 Individual, \$1454 Institution, \$289 In-training. Single copy rate \$126. Subscriptions outside of North America must add \$52 for airfreight delivery. Add state sales tax, where applicable. The GST tax of 7% must be added to all orders shipped to Canada (Lippincott Williams & Wilkins' GST Identification #895524239, Publications Mail Agreement #1119672). Indicate in-training status and name of institution. Institution rates apply to libraries, hospitals, corporations, and partnerships of three or more individuals. Subscription prices outside the United States must be prepaid. Prices subject to change without notice. Subscriptions will begin with currently available issue unless otherwise requested. Visit us online at www.lww.com.

Individual and in-training subscription rates include print and access to the online version. Online-only subscriptions for individuals (\$245) and persons in training (\$245) are available to nonmembers and may be ordered by downloading a copy of the Online Subscription FAXback Form from the Web site, completing the information requested, and faxing the completed form to 301-223-2400/44 (0) 20 7981 0535. Institutional rates are for print only; online subscriptions are available via Ovid. Institutions can choose to purchase a print and online subscription together for a discounted rate. Institutions that wish to purchase a print subscription, please contact Lippincott Williams & Wilkins, 16522 Hunters Green Parkway, Hagerstown, MD 21740-2116; phone: 1-800-638-3030 (outside the United States 301-223-2300/44 (0) 20 7981 0525); fax: 301-223-2400/44 (0) 20 7981 0535. Institutions that wish to purchase an online subscription or online with print, please contact the Ovid Regional Sales Office near you or visit www.ovid.com/site/index.jsp and select Contact and Locations.

Address for non-member subscription information, orders, or change of address: Lippincott Williams & Wilkins, 16522 Hunters Green Parkway, Hagerstown, MD 21740-2116; phone: 1-800-638-3030 (outside the United States 301-223-2300/44 (0) 20 7981 0525); fax: 301-223-2400/44 (0) 20 7981 0535; email: customerservice@lww.com. In Japan, contact LWW Japan Ltd., 3-23-14 Hongo, Bunkyo-ku, Tokyo 113, Japan; phone: 81-3-5689-5400; fax: 81-3-5689-5402; email: bclaim@lww.co.jp. In Bangladesh, India, Nepal, Pakistan, and Sri Lanka, contact Globe Publications Pvt. Ltd., B-13 3rd Floor, A Block, Shopping Complex, Naraina, Vihar, Ring Road, New Delhi 110028, India; phone: 91-11-25770411; fax: 91-11-25778876; email: info@globepub.com.

Address for member subscription information, orders, or change of address: Members of the American Society of Anesthesiologists receive the print and online journal with their membership. To become a member or provide a change of address, please contact the American Society of Anesthesiologists, 520 N. Northwest Highway, Park Ridge, IL 60068-2573; phone: 847-825-5586; fax: 847-825-1692; email: membership@ASAhq.org. For all other membership inquiries, contact Lippincott Williams & Wilkins Customer Service Department, P.O. Box 1580, Hagerstown, MD 21741-1580; phone: 1-800-638-3030 (outside the United States 301-223-2300/44 (0) 20 7981 0525); fax: 301-223-2400/44 (0) 20 7981 0535; email: memberservice@lww.com.

Postmaster: Send address changes to ANESTHESIOLOGY, P.O. BOX 1550, Hagerstown, MD 21740.

Advertising: Please contact Michelle Smith, Senior Account Manager, Advertising, Lippincott Williams & Wilkins, 333 Seventh Avenue, 19th Floor, New York, NY 10001; tel: (646) 674-6537, fax: (646) 607-5479, e-mail: Michelle.Smith@wolterskluwer.com. For classified advertising: Keida Spurlock, Recruitment Advertising Representative, Lippincott Williams & Wilkins, Two Commerce Square, 2001 Market Street, Philadelphia, PA 19103; tel: (215) 521-8501, fax: (215) 689-2453. e-mail: Keida.Spurlock@wolterskluwer.com.