



ON THE COVER:

The American College of Surgeons and the American Geriatrics Society have suggested that preoperative cognitive screening should be performed in older surgical patients. In this issue of *ANESTHESIOLOGY*, Culley *et al.* cognitively screened 211 patients aged 65 yr old or older without a diagnosis of dementia who were scheduled for an elective hip or knee replacement. Many older elective orthopedic surgical patients were found to have probable cognitive impairment preoperatively. This impairment was associated with development of delirium postoperatively, a longer hospital stay, and lower likelihood of going home upon hospital discharge.

- Culley *et al.*: Poor Performance on a Preoperative Cognitive Screening Test Predicts Postoperative Complications in Older Orthopedic Surgical Patients, p. 765

◆ THIS MONTH IN ANESTHESIOLOGY	1A
■ SCIENCE, MEDICINE, AND THE ANESTHESIOLOGIST	15A
■ INFOGRAPHICS IN ANESTHESIOLOGY	19A
◆ EDITORIAL VIEWS	
Errors and Integrity in Seeking and Reporting Apparent Research Misconduct <i>E. D. Kharasch and T. T. Houle</i>	733
Promoting Safety, Quality, and Value through Patient Blood Management <i>J. H. Waters</i>	738
MAC Meeting MIGET: Leaps of Faith <i>J. F. A. Hendrickx, P. J. Peyton, and A. M. De Wolf</i>	741
Precision Correction of Coagulopathy or Prothrombin Complex Concentrates? Reversal Options for Dabigatran following Trauma <i>M. D. Neal and J. H. Levy</i>	744
■ SPECIAL ARTICLE	
Earliest English Definitions of <i>Anaesthesia</i> and <i>Anaesthesia</i> <i>R. P. Haridas</i>	747
The earliest identified English definition of <i>anaesthesia</i> is in a medical dictionary published in 1684.	

◆ Refers to This Month in Anesthesiology

◆ Refers to Editorial Views

 This article has an Audio Podcast


 See Supplemental Digital Content

 CME Article



 This article has a Video Abstract

■ PERIOPERATIVE MEDICINE

CLINICAL SCIENCE

- ◆ ◆  **Implementing a Health System–wide Patient Blood Management Program with a Clinical Community Approach** 754
S. M. Frank, R. N. Thakkar, S. J. Podlasek, K. H. Ken Lee, T. L. Wintermeyer, W. W. Yang, J. Liu, L. C. Rotello, T. A. Fleury, P. A. Wachter, L. E. Ishii, R. Demski, P. J. Pronovost, and P. M. Ness
- Methods are described for implementing a patient blood management program across a multiinstitutional healthcare system as a quality improvement and patient safety effort. Promoting best practices for patient blood management across a health system can reduce unnecessary transfusions, overall blood utilization, and costs, with a 400% return on financial investment. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*
-  ◆  **Poor Performance on a Preoperative Cognitive Screening Test Predicts Postoperative Complications in Older Orthopedic Surgical Patients** 765
D. J. Culley, D. Flaherty, M. C. Fahey, J. L. Rudolph, H. Javedan, C.-C. Huang, J. Wright, A. M. Bader, B. T. Hyman, D. Blacker, and G. Crosby
- In a prospective clinical investigation of patients 65 yr or older without dementia having elective hip or knee replacement, screened preoperatively with the Mini-Cog, 24% were found to have probable cognitive impairment. Patients with probable preoperative cognitive impairment, compared to those patients without, were more likely to be discharged to a place other than home, develop postoperative delirium, and have a longer hospital length of stay. Preoperative cognitive screening of older surgical patients may be valuable for risk assessment and risk stratification in older surgical patients.
- ◆ **Clinical Effectiveness of Intravenous Exenatide Infusion in Perioperative Glycemic Control after Coronary Artery Bypass Graft Surgery: A Phase II/III Randomized Trial** 775
G. Besch, A. Perrotti, F. Mauny, M. Puyraveau, M. Baltres, G. Flicoteaux, L. S. du Mont, B. Barrucand, E. Samain, S. Chocron, and S. Pili-Floury
- Exenatide alone at the dose used was not enough to achieve adequate blood glucose control in coronary artery bypass grafting patients, but it reduced overall consumption of insulin and increased the time to initiation of insulin.
- ◆  **Are Anesthesia and Surgery during Infancy Associated with Decreased White Matter Integrity and Volume during Childhood?** 788
R. I. Block, V. A. Magnotta, E. O. Bayman, J. Y. Choi, J. J. Thomas, and K. K. Kimble
- Children exposed to anesthesia and surgery during infancy had lower whole brain white matter volumes than control subjects. Regional white matter volumes and integrity were also reduced in the exposed children. Although white matter volumes and integrity were reduced in exposed children, no inference about causality can be made, and comorbid conditions may well have contributed to the structural changes that were observed on magnetic resonance imaging. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

BASIC SCIENCE

- ◆ ◆  **Effect of Bronchoconstriction-induced Ventilation–Perfusion Mismatch on Uptake and Elimination of Isoflurane and Desflurane** 800
M. Kretzschmar, A. Kozian, J. E. Baumgardner, J. B. Borges, G. Hedenstierna, A. Larsson, T. Hachenberg, and T. Schilling
- Compared with the fairly insoluble desflurane, the uptake and elimination of the more soluble isoflurane in piglets was less affected by methacholine-induced bronchoconstriction and ventilation/perfusion scatter.
-  **Transient Receptor Potential Vanilloid 1 Antagonists Prevent Anesthesia-induced Hypothermia and Decrease Postincisional Opioid Dose Requirements in Rodents** 813
A. Garami, M. Ibrahim, K. Gilbraith, R. Khanna, E. Pakai, A. Miko, E. Pinter, A. A. Romanovsky, F. Porreca, and A. M. Patwardhan
- The selective transient receptor potential vanilloid 1 antagonists AMG 517 and ABT-102 dose-dependently prevented hypothermia during general anesthesia in rats. These same drugs reduced incisional nociceptive sensitization. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

CONTENTS

◇ **Competitive Antagonism of Anesthetic Action at the γ -Aminobutyric Acid Type A Receptor by a Novel Etomidate Analog with Low Intrinsic Efficacy** 824

C. Ma, E. Pejo, M. McGrath, S. S. Jayakar, X. Zhou, K. W. Miller, J. B. Cohen, and D. E. Raines

Naphthalene–etomidate only weakly potentiated γ -aminobutyric acid–evoked currents. However, it significantly decreased the positive modulatory effects of etomidate, propofol, and pentobarbital at the γ -aminobutyric acid type A receptor. The results suggest that naphthalene–etomidate acts as a competitive antagonist of anesthetics at the γ -aminobutyric acid type A receptor.

Disruption of Hippocampal Multisynaptic Networks by General Anesthetics 838

M.-C. Kuo and L. S. Leung

Monosynaptic and multisynaptic excitatory postsynaptic potentials, and spontaneous local field potentials, in the CA1 sector of the hippocampus were significantly suppressed by isoflurane at low doses and in a dose-dependent manner. The results, which confirm previous *in vitro* work, are consistent with the premise that hippocampal network disruption may underlie isoflurane-induced, hippocampal-dependent cognitive function.

■ CRITICAL CARE MEDICINE

BASIC SCIENCE

◇ ◆ **Reversing Dabigatran Anticoagulation with Prothrombin Complex Concentrate *versus* Idarucizumab as Part of Multimodal Hemostatic Intervention in an Animal Model of Polytrauma** 852

M. Honickel, T. Braunschweig, R. Rossaint, C. Stoppe, H. ten Cate, and O. Grottke

In a porcine polytrauma injury model, blood loss was lower with idarucizumab than with prothrombin complex concentrate (PCC) when administered for dabigatran reversal as part of multimodal therapy. However, survival was 100% in both groups. There were no hypercoagulability effects with idarucizumab, while PCC increased thrombin generation. Without idarucizumab or PCC, tranexamic acid and fibrinogen concentrate were ineffective at reducing bleeding in this model. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

■ PAIN MEDICINE

BASIC SCIENCE

◆ **Bromodomain-containing Protein 4 Activates Voltage-gated Sodium Channel 1.7 Transcription in Dorsal Root Ganglia Neurons to Mediate Thermal Hyperalgesia in Rats** 862

M.-C. Hsieh, Y.-C. Ho, C.-Y. Lai, H.-H. Wang, A.-S. Lee, J.-K. Cheng, Y.-P. Chau, and H.-Y. Peng

Using a rat model of inflammatory pain, it was observed that bromodomain-containing protein 4 expression was increased in dorsal root ganglia. Higher levels of bromodomain-containing protein 4 were associated with the increased expression of voltage-gated sodium channel 1.7, larger transmembrane sodium currents, and more profound hyperalgesia. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

◇ **Src Kinase Inhibition Attenuates Morphine Tolerance without Affecting Reinforcement or Psychomotor Stimulation** 878

F. A. Bull, D. T. Baptista-Hon, C. Sneddon, L. Wright, W. Walwyn, and T. G. Hales

The c-Src inhibitor dasatinib attenuated and reversed morphine-induced tolerance in mice. Dasatinib did not alter the locomotor or use reinforcing effects of morphine in mice.

■ EDUCATION

IMAGES IN ANESTHESIOLOGY

Air Embolism during Cardiac Catheterization and the Role for Anesthesia Use of Bedside Ultrasound 890

A. C. Adler

Lingual Thyroid 891

B. K. Behera, S. Misra, and P. K. Parida

Fulminant Hyperfibrinolysis Diagnosed by Rotational Thromboelastometry 892

J. S. McNeil and A. M. Kleiman

CONTENTS

MIND TO MIND

- Still Beauty** 893
A. L. Thoeny
- Losing My Favorite Anesthesiologist** 894
T. A. Yemen

■ CORRESPONDENCE

- Muscle Relaxation and Lower Airway Characteristics May Affect Tidal Volume during Pressure-controlled Ventilation** 896
Z. Zhou and X. Wang
- Rocuronium Onset May Affect Mask Ventilation** 896
L. Wang and L. Wei
- “Loose Lips Are Actually Good”** 897
C. W. Buffington, C. M. Q. Wells, and R. J. Soose
- In Reply**
S. Isono, S. Sato, M. Hasegawa, M. Okuyama, J. Okazaki, Y. Kitamura, Y. Sato, T. Ishikawa, and Y. Sato

-
- Insulin for Perioperative Glucose Control: Settled Science?** 899
R. Gerlach and A. Tung
- In Reply**
E. W. Duggan and G. E. Umpierrez

-
- When Managing Patients with Left Ventricular Assist Devices Undergoing Noncardiac Surgery, Less Is Not More** 901
R. E. Freundlich and A. J. Kingeter
- Noninvasive Blood Pressure Determination in Left Ventricular Assist Device Patients** 902
D. W. Barbara, T. G. Seelhammer, and W. J. Mauermann
- In Reply**
M. R. Mathis, S. Sathishkumar, and M. C. Engoren

-
- A Deeper Look at Anesthesia Depth** 904
R. M. Knapp

-
- Amendments and Corrections to Mattusch *et al.* (ANESTHESIOLOGY 2015; 122[5]:1047–59), “Impact of Hyperpolarization-activated, Cyclic Nucleotide-gated Cation Channel Type 2 for the Xenon-mediated Anesthetic Effect: Evidence from *In Vitro* and *In Vivo* Experiments”** 905
S. Kratzer, R. Haseneder, P. A. Goldstein, E. Kochs, and G. Rammes

■ REVIEWS OF EDUCATIONAL MATERIAL

911

■ ANESTHESIOLOGY REFLECTIONS FROM THE WOOD LIBRARY-MUSEUM

- Queen Victoria’s Youngest Two Sons: Princes Arthur and Leopold** 740
George S. Bause
- Picturing “Dr. Colton” at the Cooper Institute: His Honorific Doctorate** 743
George S. Bause

CONTENTS

- Awnings before Yawnings: Advertising Anesthetic Stupor at “the Cooper”** 746
George S. Bause
- Sharing “Beta-Eucain” with Schering: Albrecht Schmidt and George Merling** 764
George S. Bause
- Presidential Perforations? James T. Gwathmey, M.D., Modifies Yankauer Masks** 774
George S. Bause
- Chicago Art Institute Alumnus Dalton Stevens Covers a Criminal Chloroforming** 837
George S. Bause

■ CAREERS & EVENTS

20A

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 Alan Jay Schwartz, M.D., M.S.Ed., Director of Education, Department of Anesthesiology and Critical Care Medicine, The Children's Hospital of Philadelphia, 34th Street and Civic Center Blvd., Room 9327, Philadelphia, Pennsylvania 19104-4399. 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, Wolters Kluwer Health, Inc., Two Commerce Square, 2001 Market Street, Philadelphia, Pennsylvania 19103 (Web site: <http://www.wkacenter.com/>). Publication of an advertisement in ANESTHESIOLOGY does not constitute endorsement by the Society or Wolters Kluwer Health, 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 Wolters Kluwer Health, Inc., 14700 Citicorp Drive, Bldg 3, Hagerstown, MD 21742. Business office: Two Commerce Square, 2001 Market Street, Philadelphia, PA 19103. Periodicals postage paid at Hagerstown, MD, and at additional mailing offices. Copyright © 2017, the American Society of Anesthesiologists, Inc.

Annual Subscription Rates: *United States*—\$930 Individual, \$2054 Institution, \$374 In-training. *Rest of World*—\$981 Individual, \$2281 Institution, \$374 In-training. Single copy rate \$207. Subscriptions outside of North America must add \$55 for airfreight delivery. Add state sales tax, where applicable. The GST tax of 7% must be added to all orders shipped to Canada (Wolters Kluwer Health, Inc.'s 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 (\$308) and persons in training (\$308) 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. 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 Wolters Kluwer Health, Inc., 14700 Citicorp Drive, Bldg 3, Hagerstown, MD 21742; phone: 800-638-3030; fax: 301-223-2400. 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 (except Japan): Wolters Kluwer Health, Inc., 14700 Citicorp Drive, Bldg 3, Hagerstown, MD 21742; phone: 800-638-3030; fax: 301-223-2400. In Japan, contact Wolters Kluwer Health Japan Co., Ltd., Forecast Mita Building 5th floor, 1-3-31 Mita Minato-ku, Tokyo, Japan 108-0073; phone: +81 3 5427 1969; email: journal@wkjapan.co.jp.

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, 1061 American Lane, Schaumburg, Illinois 60173-4973; phone: 847-825-5586; fax: 847-825-1692; email: membership@ASAhq.org. For all other membership inquiries, contact Wolters Kluwer Health, Inc., Customer Service Department, P.O. Box 1610, Hagerstown, MD 21740; phone: 800-638-3030; fax: 301-223-2400.

Postmaster: Send address changes to ANESTHESIOLOGY, P.O. BOX 1610, Hagerstown, MD 21740.

Advertising: Please contact Hilary Druker, Advertising Field Sales Representative, Health Learning, Research & Practice, Medical Journals, Wolters Kluwer Health, Inc.; phone: 609-304-9187; e-mail: Hilary.Druker@wolterskluwer.com. For classified advertising: Joe Anzuena, Recruitment Advertising Representative, Wolters Kluwer Health, Inc., Two Commerce Square, 2001 Market Street, Philadelphia, PA 19103; phone: 215-521-8532; fax: 215-701-2410; e-mail: Joe.Anzuena@wolterskluwer.com.