



ON THE COVER:

Médecins Sans Frontières is an international, medical humanitarian organization that delivers emergency aid to people affected by armed conflict, epidemics, and natural disasters and exclusion from health care. Anesthesia is integral to improving surgical care in these low-resource settings. In this issue of ANESTHESIOLOGY, Ariyo and his colleagues present a retrospective analysis of 75,536 anesthetics performed at Médecins Sans Frontières facilities from July 2008 to June 2014. They show that a wide range of anesthetics can be carried out safely in resource-limited settings and they discuss the risks and outcomes associated with administering anesthesia in these settings.

- Ariyo *et al.*: Providing Anesthesia Care in Resource-limited Settings: A 6-year Analysis of Anesthesia Services Provided at Médecins Sans Frontières facilities, p. 561
- McQueen: Realities of Anesthesia Care in Resource-limited Settings, p. 521

◆ THIS MONTH IN ANESTHESIOLOGY	1A
■ SCIENCE, MEDICINE, AND THE ANESTHESIOLOGIST	19A
■ INFOGRAPHICS IN ANESTHESIOLOGY	21A
◆ EDITORIAL VIEWS	
Realities of Anesthesia Care in Resource-limited Settings <i>K. McQueen</i>	521
Predicting In-hospital Postoperative Mortality for the Practitioner: Beyond the Numbers <i>E. J. Mascha and V. Mazo</i>	523
Cautious Optimism: Can Preoperative Ultrasound Predict Postinduction Hypotension? <i>B. Subramaniam and K. Subramaniam</i>	526
Arterial Line Placement: Safety First <i>A. Dahan, D. P. Engberts, and M. Niesters</i>	528
Are Epigenetic Changes the Key to the Elusive Mechanism for the Long-lasting Effects of Anesthetic Drugs that Persist after Emergence? <i>V. Degos and P. Flood</i>	530
The Goldilocks Principle, Carbon Dioxide, and Acute Respiratory Distress Syndrome: Too Much, Too Little, or Just Right? <i>G. F. Curley</i>	532

◆ Refers to This Month in Anesthesiology

◆ Refers to Editorial Views



This article has an Audio Podcast



This is an Accelerated Recovery article



See Supplemental Digital Content



CME Article



This article has a Video Abstract

CONTENTS

■ PRACTICE PARAMETERS

- ◆◆ Practice Guidelines for the Prevention, Detection, and Management of Respiratory Depression Associated with Neuraxial Opioid Administration: An Updated Report by the American Society of Anesthesiologists Task Force on Neuraxial Opioids and the American Society of Regional Anesthesia and Pain Medicine 535

The American Society of Anesthesiologists Committee on Standards and Practice Parameters and the Task Force on Neuraxial Opioids and the American Society of Regional Anesthesia and Pain Medicine present an updated report of the Practice Guidelines for the Prevention, Detection, and Management of Respiratory Depression Associated with Neuraxial Opioid Administration. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

■ SPECIAL ARTICLES

- “Gentlemen! This Is No Humbug”: Did John Collins Warren, M.D., Proclaim These Words on October 16, 1846, at Massachusetts General Hospital, Boston? 553
R. P. Haridas

The proclamation, “Gentlemen! This is no humbug,” was not identified in any contemporaneous eyewitness report of William T. G. Morton’s October 16, 1846, demonstration of ether at Massachusetts General Hospital.

■ PERIOPERATIVE MEDICINE

CLINICAL SCIENCE

- ◆◆ Providing Anesthesia Care in Resource-limited Settings: A 6-year Analysis of Anesthesia Services Provided at Médecins Sans Frontières Facilities 561
P. Ariyo, M. Trelles, R. Helmand, Y. Amir, G. H. Hassani, J. Mftavyanka, Z. Nzeyimana, C. Akemani, I. B. Ntawukiruwabo, A. Charles, Y. Yana, K. Moussa, M. Kamal, M. L. Suma, M. Ahmed, M. Abdullahi, E. G. Wong, A. Kushner, and A. Latif

Médecins Sans Frontières (MSF; Doctors Without Borders) anesthesia providers include physician anesthesiologists, nurse anesthetists, and local nurses trained by MSF to provide anesthesia. A standardized set of essential equipment and medications is provided for each mission to enable anesthesia care delivery and management of potential complications. A retrospective review of anesthetic procedures performed at MSF facilities from 2008 until 2014 found that a wide range of anesthesia procedures can be carried out safely in resource-limited settings with resources such as those provided by MSF.

- ◆◆◆ Preoperative Score to Predict Postoperative Mortality (POSPOM): Derivation and Validation 570
Y. Le Manach, G. Collins, R. Rodseth, C. Le Bihan-Benjamin, B. Biccard, B. Riou, P. J. Devereaux, and P. Landais

This multicenter study examining in-hospital mortality in over 5.5 million patients in France in a 1-yr period identified a 17-variable, highly sensitive, and specific risk calculator for in-hospital mortality. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

- ◆ Inferior Vena Cava Ultrasonography before General Anesthesia Can Predict Hypotension after Induction 580
J. Zhang and L. A. H. Critchley

The authors have shown that preoperative ultrasound of the inferior vena cava can be used to predict significant hypotension after anesthetic induction. The findings expand the potential clinical utility of ultrasound in the perioperative period.

- ◆ **Surgical and Patient Risk Factors for Severe Arterial Line Complications in Adults** 590
G. Nuttall, J. Burckhardt, A. Hadley, S. Kane, D. Kor, M. S. Marienau, D. R. Schroeder, K. Handlogten, G. Wilson, and W. C. Oliver

In a series of 57,787 patients receiving arterial cannulation, 21 patients were identified as having experienced vascular complications or nerve injuries, resulting in a very low complication rate of 3.4/10,000. The rate of complications differed significantly ($P < 0.001$) across the three most common catheter sizes (2.7/10,000 for 20 gauge, 17.2/10,000 for 18 gauge, and 9.4/10,000 for 5 French). Given the low frequency of complications observed, the current study does not have sufficient statistical power to make definitive conclusions regarding the risk factors (listed in the appendix).

- ◇ **Mild Sedation Exacerbates or Unmasks Focal Neurologic Dysfunction in Neurosurgical Patients with Supratentorial Brain Mass Lesions in a Drug-specific Manner** 598
N. Lin, R. Han, J. Zhou, and A. W. Gelb

Mild sedation with propofol and midazolam exacerbated neurologic deficits to a greater extent than fentanyl or dexmedetomidine; the latter had the least effect on neurologic function. The change in neurologic function in patients with preexisting brain lesions is produced in a drug-specific effect and is not due to nonspecific sedation.

- ◇ **Anesthetic Care for Orthopedic Patients: Is There a Potential for Differences in Care?** 608
S. G. Memtsoudis, J. Poeran, N. Zubizarreta, R. Rasul, M. Operer, and M. Mazumdar

In a review of more than 1 million hip and knee arthroplasty procedures in the Premier Perspective database, use of neuraxial anesthesia was considerably less (odds ratio [OR], 0.35) in teaching *versus* nonteaching hospitals and moderately less for black patients (OR, 0.88), those on Medicaid (OR, 0.78), and those without insurance (OR, 0.89).

BASIC SCIENCE

- ◆ **Epigenetic Manipulation of Brain-derived Neurotrophic Factor Improves Memory Deficiency Induced by Neonatal Anesthesia in Rats** 624
J. Wu, B. Bie, and M. Naguib

The authors found a substantial reduction of hippocampal brain-derived neurotrophic factor resulting from the transcriptional factors–mediated epigenetic modification in the promoter region of *Bdnf* exon IV in rats exposed postnatally to anesthetic drugs. This brain-derived neurotrophic factor reduction led to the insufficient drive for the synthesis of synaptic proteins, thus contributing to the hippocampal synaptic and cognitive dysfunction induced by neonatal anesthesia. These effects were mitigated by the exposure to an enriched environment.

- G-protein–gated Inwardly Rectifying Potassium Channels Modulate Respiratory Depression by Opioids** 641
G. Montandon, J. Ren, N. C. Victoria, H. Liu, K. Wickman, J. J. Greer, and R. L. Horner

By using genetic, pharmacological, and physiological approaches in rodents, this article identifies G-protein–gated inwardly rectifying potassium channels in the respiratory network of the ventrolateral medulla. G-protein–gated inwardly rectifying potassium channels contribute to respiratory depression by μ -opioid receptors and opioid analgesics.

- γ -Aminobutyric Acid Type A Receptor Modulation by Etomidate Analogs** 651
E. Pejo, P. Santer, L. Wang, P. Dershwitz, S. S. Husain, and D. E. Raines

By using both *in vitro* and *in vivo* assays of etomidate action, γ -aminobutyric acid type A receptor and hypnotic potencies of etomidate and 22 etomidate analogs were significantly correlated, supporting a direct role for receptor activation in etomidate-induced hypnosis. Molecular modeling computational techniques were used to build pharmacophore models that revealed multiple structural elements associated with high-potency binding-site interactions of etomidate.

- 🌐 **Common Anesthetic-binding Site for Inhibition of Pentameric Ligand-gated Ion Channels** 664
M. N. Kinde, W. Bu, Q. Chen, Y. Xu, R. G. Eckenhoff, and P. Tang

Using ELIC, a prokaryotic pentameric ligand-gated ion channel (pLGIC) *Erwinia chrysanthemi*, as a model, propofol is shown to bind in a transmembrane intrasubunit pocket that overlaps anesthetic-binding sites previously identified in other pLGICs. The functional relevance of this binding site is demonstrated by analysis of chimeric receptors, which suggests that the transmembrane intrasubunit site is a common binding site for anesthetic inhibition of cationic pLGICs.
 SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT

CONTENTS

■ CRITICAL CARE MEDICINE

BASIC SCIENCE

- ◆◆◆ **Extracorporeal Carbon Dioxide Removal Enhanced by Lactic Acid Infusion in Spontaneously Breathing Conscious Sheep** 674
V. Scaravilli, S. Kreyer, S. Belenkiy, K. Linden, A. Zanella, Y. Li, M. A. Dubick, L. C. Cancio, A. Pesenti, and A. I. Batchinsky

In a study of six spontaneously breathing conscious sheep connected to a minimally invasive circuit, extracorporeal blood acidification with lactic acid (acid load carbon dioxide removal) increased extracorporeal carbon dioxide removal by 50% compared with standard extracorporeal carbon dioxide removal. Although lactic acid infusion increased overall energy expenditure, feasibility safety and efficiency of acid load carbon dioxide removal were proved. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

■ PAIN MEDICINE

CLINICAL SCIENCE

- ◆ **IV and Perineural Dexmedetomidine Similarly Prolong the Duration of Analgesia after Interscalene Brachial Plexus Block: A Randomized, Three-arm, Triple-masked, Placebo-controlled Trial** 683
F. W. Abdallah, T. Dwyer, V. W. S. Chan, A. U. Niazi, D. J. Ogilvie-Harris, S. Oldfield, R. Patel, J. Oh, and R. Brull

In 99 patients receiving interscalene block with 15 ml ropivacaine, 0.5%, with 0.5 µg/kg dexmedetomidine prolonged the blockade and reduced the 24-h opioid use compared with placebo control, and these effects were similar whether dexmedetomidine was administered intravenously or perineurally.

- ◆ **Perioperative Dextromethorphan as an Adjunct for Postoperative Pain: A Meta-analysis of Randomized Controlled Trials** 696
M. R. King, K. S. Ladha, A. M. Gelineau, and T. A. Anderson

This meta-analysis identified 21 studies describing the effects of dextromethorphan on postoperative pain and opioid consumption. Dextromethorphan was found to reduce pain from 1 to 24 h postoperatively and was found to reduce morphine requirements 24 to 48 h after surgery.

BASIC SCIENCE

- Activation of Peripheral µ-opioid Receptors by Dermorphin [D-Arg2, Lys4] (1-4) Amide Leads to Modality-preferred Inhibition of Neuropathic Pain** 706
V. Tiwari, F. Yang, S.-Q. He, R. Shechter, C. Zhang, B. Shu, T. Zhang, V. Tiwari, Y. Wang, X. Dong, Y. Guan, and S. N. Raja

By using a model of male and female rats with spinal nerve ligation-induced neuropathic pain, the authors demonstrated that systemic administration of dermorphin [d-Arg2, Lys4] (1-4) amide, a highly selective µ-receptor agonist, attenuated both neuropathic mechanical and heat hypersensitivity through activation of µ-receptor at peripheral but not central sites. Further, the efficacy of dermorphin [d-Arg2, Lys4] (1-4) amide to inhibit heat hypersensitivity is greater than that to inhibit mechanical hypersensitivity.

■ EDUCATION

IMAGES IN ANESTHESIOLOGY

- An Unexpected Embolism during a Craniotomy** 721
A. Serdiuk, F. Khalil, and J. B. Cohen
- Severe Bilateral Ocular Hypotony after Emergent Coronary Artery Bypass Graft Surgery Complicated with Cardiogenic Shock** 722
G. Munoz, S. Agarwal, and M. R. Castresana

CONTENTS

REVIEW ARTICLE

- ◇ **Survival after Perioperative Cardiopulmonary Resuscitation: Providing an Evidence Base for Ethical Management of Do-not-resuscitate Orders** 723

S. Kalkman, L. Hooft, J. M. Meijerman, J. T. A. Knape, and J. J. M. van Delden

The probability of surviving perioperative cardiopulmonary resuscitation is at least twice as high as in other settings, warranting reevaluation of do-not-resuscitate orders during the perioperative period in a preoperative conversation with the patient.

MIND TO MIND

- Doctor Patient** 731

J. S. Rose

- Post Something-or-other Syndrome** 733

S. M. Picca

■ CORRESPONDENCE

- Conclusions on Ventilator-induced Mechanical Injuries Associated with Ventilation Using Abnormally Large Tidal Volume** 736

F. Formenti

In Reply

M. Cressoni, C. Chiurazzi, and L. Gattinoni

■ ANESTHESIOLOGY REFLECTIONS FROM THE WOOD LIBRARY-MUSEUM

- A “Nitrous Oxide Gas” Advertising Bookmark from Dr. A. K. Harroun** 579

George S. Bause

- Porter’s Pain King: Ether in Alcohol “for Man and Beast”** 640

George S. Bause

- Legacies of Charles Bernard Pittinger, M.D., M.S., F.A.C.A., D.A.B.A. (1913–1990)** 730

George S. Bause

■ REVIEWS OF EDUCATIONAL MATERIAL 738

■ ERRATUM

- Association between Intraoperative Hypotension and Hypertension and 30-day Postoperative Mortality in Noncardiac Surgery: Erratum** 741

■ ANNOUNCEMENTS 743

■ 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 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, Lippincott Williams & Wilkins, Two Commerce Square, 2001 Market Street, Philadelphia, Pennsylvania 19103 (Web site: <http://www.wkadcenter.com/>). 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 © 2016, the American Society of Anesthesiologists, Inc.

Annual Subscription Rates: *United States*—\$835 Individual, \$1714 Institution, \$335 In-training. *Rest of World*—\$881 Individual, \$1904 Institution, \$335 In-training. Single copy rate \$152. Subscriptions outside of North America must add \$53 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 (\$285) and persons in training (\$285) 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@lwwis.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, 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 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 Mike Prinzi, Field Sales Rep, Medical Journals, Lippincott Williams & Wilkins, 333 Seventh Avenue, 19th Floor, New York, NY 10001; tel: (800) 933-6525, fax: (646) 607-5479, e-mail: Mike.Prinzi@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.