



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

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- ◆◆ 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.
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■ CRITICAL CARE MEDICINE

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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*

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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.
- CME **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.

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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.

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