



## ON THE COVER:

This month we highlight the history of the specialty, focusing on the failed attempt to create an historical museum-library in Australia, but the success of the Wood Library and its recent move to a spectacular facility open to all anesthesiologists. The pen and ink image shows the historical Massachusetts General Hospital, and this month includes several articles from the Harvard Medical System (designated in the table of contents with an “H”) submitted specifically for this issue that demonstrate the ongoing legacy of research in these institutions.

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**CME** CME Article

**H** This article is from the Harvard Medical System

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### SPECIAL ARTICLES

- ◆ **H** **49 Mathoura Road: Geoffrey Kaye's Letters to Paul M. Wood, 1939–1955** 1150  
*M.L. Edwards and D.B. Waisel*

Geoffrey Kaye, a prominent Australian anesthetist, started a center of excellence for Australian anesthetists in 1951. The center failed by 1955. Through letters written by Kaye, we see his perception about why it failed.

### PERIOPERATIVE MEDICINE

#### CLINICAL SCIENCE

- ◆ **H** **Opioid Abuse and Dependence during Pregnancy: Temporal Trends and Obstetrical Outcomes** 1158

*A. Maeda, B.T. Bateman, C.R. Clancy, A.A. Creanga, and L.R. Leffert*

In a review of over 57 million American women admitted for obstetric delivery in the Nationwide Inpatient Sample, the prevalence of opioid abuse and dependence more than doubled between 1998 and 2011. Opioid abuse and dependence was associated with a 4.6-fold increased risk of maternal death during hospitalization and was present in 1.5% of deliveries complicated by maternal death. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

- ◆ **H** **Application of Process Improvement Principles to Increase the Frequency of Complete Airway Management Documentation** 1166

*L.K. McCarty, D. Saddawi-Konefka, L.M. Gargan, W.D. Driscoll, J.L. Walsh, and R.A. Peterfreund*

At the Massachusetts General Hospital, a combination of iterative improvements through Plan-Do-Study-Act cycles, change management, standardization of work flow, and data sharing improved the frequency of “complete airway management documentation” from a baseline of 13.2% to over 90% of records in 13 months. Systematic study and application of formal process improvement strategies may similarly enable improvement in other institutes and in other areas of anesthesia practice.

- ◆ **H** **Anesthesia and Increased Hypercarbic Drive Impair the Coordination between Breathing and Swallowing** 1175

*O.M. D'Angelo, D. Diaz-Gil, D. Nunn, J.C.P. Simons, C. Gianatasio, N. Mueller, M.J. Meyer, E. Pierce, C. Rosow, and M. Eikermann*

In 11 healthy adult volunteers, this study demonstrated that compared to wakefulness, sevoflurane and propofol anesthesia decreased spontaneous swallowing frequency ( $28.0 \pm 22.3$  vs.  $1.7 \pm 3.3$  per hour) and increased proportion of pathological swallows (swallowing during inspiration or followed by an inspiration) ( $4.9$  vs.  $25.9\%$ ). Mild hypercapnia under general anesthesia augmented this pattern of swallowing impairment.

#### BASIC SCIENCE

- An Enantiomerically Pure Formulation of Esmolol Attenuates Hypotension and Preserves Heart Rate Control in Dogs** 1184

*J.S. McKee, B.E. Rabinow, J.R. Daller, B.D. Brooks, B. Baumgartner, and P. Rohatgi*

An esmolol formulation containing only the S-enantiomer achieved the same degree of heart rate control as the RS-esmolol formulation when infused at half the rate of RS-esmolol in a large animal model but with less-associated hypotension.

- Equipotent Subanesthetic Concentrations of Sevoflurane and Xenon Preventing Cold-stimulated Vocalization of Neonatal Rats** 1194

*H. Gill, M. Thoresen, S. Bishop, E. Smit, X. Liu, L. Walloe, and J. Dingley*

The effective concentrations of sevoflurane and xenon that prevented cold-induced vocalization were 0.46 and 20.15%, respectively; this indicates that sevoflurane is approximately 43 times more potent than xenon in neonatal rodents. The use of cold-stimulated vocalization can be used as a measure of anesthetic potency. As such, the research adds to our armamentarium a method of measuring anesthetic potency, especially in the study of the effects of subanesthetic concentrations of inhaled agents.

## **H** Advancing Novel Anesthetics: Pharmacodynamic and Pharmacokinetic Studies of Cyclopropyl-methoxycarbonyl Metomidate in Dogs 1203

*J.A. Campagna, K. Pojasek, D. Grayzel, J. Randle, and D.E. Raines*

Recovery of dogs from the hypnotic effect of cyclopropyl-methoxycarbonyl metomidate was rapid, with recovery times that were independent of infusion duration. Adrenocortical recovery was faster after cyclopropyl-methoxycarbonyl metomidate infusion than after etomidate infusion. Adrenocortical responsiveness 90 min after cyclopropyl-methoxycarbonyl metomidate infusion did not differ from that after propofol infusion.

## **🌐** Postoperative Hyperoxia (60%) Worsens Hepatic Injury in Mice 1217

*Q. Zangl, A. Martignoni, S.H. Jackson, A. Ohta, B. Klaunberg, I. Kaufmann, D. Lukashev, J.M. Ward, M. Sitkovsky, M. Thiel, and A. Choukèr*

In anesthetized mice subjected to ischemia–reperfusion injury of their livers, the provision of 60% inspired oxygen postoperatively led to significantly more cell-driven (polymorphonuclear and Kupffer cells) induced tissue injury. Elimination of either polymorphonuclear or Kupffer cells abolished the oxygen-induced damage. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

### ■ CRITICAL CARE MEDICINE

#### CLINICAL SCIENCE

## **🌐 H** Tracheal Tube Obstruction in Mechanically Ventilated Patients Assessed by High-resolution Computed Tomography 1226

*C. Mietto, R. Pinciroli, A. Piriyapatsom, J.G. Thomas, L. Bry, M.L. Delaney, A. Du Bois, J. Truelove, J.B. Ackman, G.R. Wojtkiewicz, M. Nahrendorf, R.M. Kacmarek, and L. Berra*

High-resolution computed tomography scan accurately determines reduction of cross-sectional area due to mucus accumulation. The partial occlusion is common even in the absence of clinical signs while it significantly increases airway resistance. The partial occlusion is often overlooked by the standard computed tomography scan. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

#### BASIC SCIENCE

## **🔹 H** Importance of Toll-like Receptor 2 in Mitochondrial Dysfunction during Polymicrobial Sepsis 1236

*Y. Gong, L. Zou, Y. Feng, D. Li, J. Cai, D. Chen, and W. Chao*

In a mouse model of polymicrobial sepsis, mice lacking toll-like receptor 2 showed improved mitochondrial function during sepsis compared with wild-type mice. These data support a critical role for toll-like receptor 2 in mediating mitochondrial dysfunction during sepsis.

## **H** Sodium Thiosulfate Attenuates Acute Lung Injury in Mice 1248

*M. Sakaguchi, E. Marutani, H.-S. Shin, W. Chen, K. Hanaoka, M. Xian, and F. Ichinose*

Using an experimental model of acute lung injury in mice challenged with intratracheal lipopolysaccharide or subjected to cecal ligation and puncture with or without sodium thiosulfate, it was shown that sodium thiosulfate exerts robust antiinflammatory effects in mice lung and vascular endothelium.

## **🌐 H** Role of Cardiac- and Myeloid-MyD88 Signaling in Endotoxin Shock: A Study with Tissue-specific Deletion Models 1258

*Y. Feng, L. Zou, C. Chen, D. Li, and W. Chao*

Both cardiac- and myeloid-MyD88 signaling play an important role in the mortality and cardiomyopathy after a lethal dose of lipopolysaccharide. Moreover, myeloid-MyD88 signaling plays a predominant role in mediating systemic and cardiac cytokine responses, whereas cardiomyocyte-MyD88 signaling is mainly responsible for mediating myocardial inducible nitric oxide synthase induction during endotoxin shock. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

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- H** **Toll-like Receptor 4 Is Essential to Preserving Cardiac Function and Survival in Low-grade Polymicrobial Sepsis** 1270  
*M. Zhang, L. Zou, Y. Feng, Y.-J. Chen, Q. Zhou, F. Ichinose, and W. Chao*
- Deletion of toll-like receptor 4 in mice results in attenuated neutrophil function, decreased bacterial clearance, deleterious cardiac dysfunction and kidney/liver injury, and markedly increased mortality during low-grade polymicrobial sepsis. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

### ■ PAIN MEDICINE

#### CLINICAL SCIENCE

- Cyclosporine-inhibitable Cerebral Drug Transport Does Not Influence Clinical Methadone Pharmacodynamics** 1281  
*K. Meissner, J. Blood, A.M. Francis, V. Yermolenka, and E.D. Kharasch*
- Pretreatment of healthy volunteers with either oral or intravenous cyclosporine had no effect on the methadone concentration *versus* miosis relationship, suggesting there is no role for P-glycoprotein or other cyclosporine-inhibitable transporters in methadone brain access or pharmacodynamics in humans.
- H** **Distraction Analgesia in Chronic Pain Patients: The Impact of Catastrophizing** 1292  
*K.L. Schreiber, C. Campbell, M.O. Martel, S. Greenbaum, A.D. Wasan, D. Borsook, R.N. Jamison, and R.R. Edwards*
- In 149 chronic pain patients, pain reporting during temporal summation was decreased by distraction to a greater extent in those with high catastrophizing. Analgesia from conditioned pain modulation was inversely related to that from distraction, suggesting these rely on different mechanisms.
- ◇ **The Analgesic Effects of Proximal, Distal, or No Sciatic Nerve Block on Posterior Knee Pain after Total Knee Arthroplasty: A Double-blind Placebo-controlled Randomized Trial** 1302  
*F.W. Abdallah, V.W.S. Chan, R. Gandhi, A. Koshkin, S. Abbas, and R. Brull*
- In a placebo-controlled trial of 60 patients undergoing total knee arthroplasty, both proximal and distal sciatic nerve block reduced rest pain in the posterior and anterior knee more effectively for up to 8 h postoperatively compared to no sciatic nerve block.

#### BASIC SCIENCE

- H** **Cannabinoid Receptor Type 1 Antagonist, AM251, Attenuates Mechanical Allodynia and Thermal Hyperalgesia after Burn Injury** 1311  
*M. Ueda, H. Iwasaki, S. Wang, E. Murata, K.Y.T. Poon, J. Mao, and J.A.J. Martyn*
- Using a rat model of burn-induced pain, it was observed that the cannabinoid receptor 1 antagonist AM251 prevents or inhibits the development of nociceptive behavior. Although astroglial and microglial activity was enhanced in spinal cord tissue, AM251 did not alter that activity suggesting that it works through an alternative mechanism.

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## CLINICAL CONCEPTS AND COMMENTARY

- CME** ♦♦ **Perioperative Management of Elderly Patients with Hip Fracture** 1336  
*J. Boddaert, M. Raux, F. Khiami, and B. Riou*

Hip fracture has devastating consequences in elderly patients with comorbidities. The two main objectives to improve outcome are the needs for early surgery and for a multidisciplinary approach, known as the orthogeriatric concept.

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- Is Less than 50% More Narcotics Really Noninferior?**  
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- In Reply**  
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- Questioning a Relationship between Nitrous Oxide Duration of Exposure and Postoperative Nausea and Vomiting**  
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