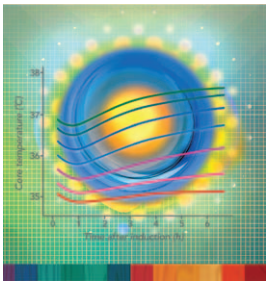
ANESTHESIOLOGY



ON THE COVER:

Forced-air warming during surgery is now routine, yet we know little about core temperature patterns in patients warmed with forced air. The effects of transient and mild intraoperative hypothermia on patient outcomes are unknown. In this issue of ANESTHESIOLOGY, Sun and colleagues analyzed data from almost 59,000 adults having surgery lasting more than an hour, and demonstrated that core temperatures decreased during the first hour of surgery, rising thereafter to an average final temperature of 36.3°C. Hypothermia significantly increased transfusion requirements and duration of hospitalization. In an accompanying Editorial View, Hopf discusses the evolution of our understanding of the physiology of intraoperative hypothermia and its consequences and calls for new standards for prevention and identification of hypothermia in the operating room.

- *Sun et al.*: Intraoperative Core Temperature Patterns, Transfusion Requirement, and Hospital Duration in Patients Warmed with Forced Air, p. 276
- Hopf: Perioperative Temperature Management: Time for a New Standard of Care?, p. 229

◆ THIS MONTH IN ANESTHESIOLOGY 1A

■ SCIENCE, MEDICINE, AND THE ANESTHESIOLOGIST 21A

■ INFOGRAPHICS IN ANESTHESIOLOGY 23A

◆ EDITORIAL VIEWS

CME **Perioperative Temperature Management: Time for a New Standard of Care?** 229
H.W. Hopf

Tilting at Aortocaval Compression 231
C.M. Palmer

Sodium Bicarbonate for Kidney Protection in Cardiac Surgery: Demise of Yet Another Magic Bullet? 233
D.N. Wijeysundera and C.R. Parikh

Bleeding and the New Anticoagulants: Strategies and Concerns 236
C.M. Samama and J.H. Levy

Mesenchymal Stem Cell Therapy for Acute Respiratory Distress Syndrome: A Light at the End of the Tunnel? 238
J.-W. Lee, P.R.M. Rocco, and P. Pelosi

◇ Refers to This Month in Anesthesiology
◆ Refers to Editorial Views
H This article is from the Harvard Medical System
See Supplemental Digital Content
CME CME Article

CONTENTS

PRACTICE PARAMETERS

◇ 🌐 **Practice Guidelines for Perioperative Blood Management: An Updated Report by the American Society of Anesthesiologists Task Force on Perioperative Blood Management** 241

The American Society of Anesthesiologists Committee on Standards and Practice Parameters and the Task Force on Perioperative Blood Management presents an updated report of the Practice Guidelines for Perioperative Blood Management. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

PERIOPERATIVE MEDICINE

CLINICAL SCIENCE

CME ◇◆ **Intraoperative Core Temperature Patterns, Transfusion Requirement, and Hospital Duration in Patients Warmed with Forced Air** 276

Z. Sun, H. Honar, D.I. Sessler, J.E. Dalton, D. Yang, K. Panjasawatwong, A.F. Deroee, V. Salmasi, L. Saager, and A. Kurz

In almost 59,000 adults having surgery lasting more than an hour, core temperatures decreased during the first hour of surgery, thereafter rising to an average final temperature of 36.3°C. Hypothermia significantly increased both transfusion requirements and duration of hospitalization, but only the increase in transfusions was clinically important.

◇◆ **Effect of Lateral Tilt Angle on the Volume of the Abdominal Aorta and Inferior Vena Cava in Pregnant and Nonpregnant Women Determined by Magnetic Resonance Imaging** 286

H. Higuchi, S. Takagi, K. Zhang, I. Furui, and M. Ozaki

In 10 singleton parturients at term without anesthesia, the aorta at the mid- to upper lumbar disk levels was not compressed, although the inferior vena cava was. Tilt of 30°, but not 15°, partially relieved the inferior vena caval compression.

◇◆ **Sodium Bicarbonate and Renal Function after Cardiac Surgery: A Prospectively Planned Individual Patient Meta-analysis** 294

M. Bailey, S. McGuinness, M. Haase, A. Haase-Fielitz, R. Parke, C.L. Hodgson, A. Forbes, S.M. Bagshaw, and R. Bellomo

The authors have performed a novel, prospectively planned individual patient data meta-analysis of the double-blind randomized trials in this important field. Urinary alkalinization with sodium bicarbonate infusion is not associated with a significant reduction in the overall risk of acute kidney injury in cardiac surgery patients. However, urinary alkalinization was associated with significant renal protection in the subgroup of patients undergoing elective coronary artery bypass graft surgery suggesting that further investigation in these patients is warranted.

🌐 **Neurophysiological Correlates of Sevoflurane-induced Unconsciousness** 307

S. Blain-Moraes, V. Tarnal, G. Vanini, A. Alexander, D. Rosen, B. Shortal, E. Janke, and G.A. Mashour

In human volunteers, sevoflurane-induced unconsciousness was not consistently correlated with anteriorization of alpha rhythms or frontal cross-frequency coupling patterns, but rather disrupted phase relationships between frontal and posterior brain structures. Since other agents induce disrupted phase relationships, network fragmentation may be a common correlate or cause of anesthetic-induced unconsciousness. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

Factors Associated with Improved Survival after Resection of Pancreatic Adenocarcinoma: A Multivariable Model 317

T.R. Call, N.L. Pace, D.B. Thorup, D. Maxfield, B. Chortkoff, J. Christensen, and S.J. Mulvihill

A model based on retrospective analysis of the records of 144 patients who underwent resection of pancreatic adenocarcinoma between 2001 and 2011 predicted median survival of patients to whom dexamethasone is administered and who have epidural analgesia would be increased from 370 days to 651 days compared to similar patients receiving neither dexamethasone nor epidural analgesia.

CONTENTS

BASIC SCIENCE

◇ 🌐 **Discovery of a Novel General Anesthetic Chemotype Using High-throughput Screening** 325
A.R. McKinstry-Wu, W. Bu, G. Rai, W.A. Lea, B.P. Weiser, D.F. Liang, A. Simeonov, A. Jadhav, D.J. Maloney, and R.G. Eckenhoff

A high-throughput assay based on competitive binding to a soluble protein model was used to screen a library of more than 350,000 compounds for anesthetic-like binding activity. A novel chemotype, the 6-phenylpyridazin-3(2H)-ones, exhibited general anesthetic activity in secondary assays and ultimately in mice. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

Overexpression of Cyclic Adenosine Monophosphate Effluent Protein MRP4 Induces an Altered Response to β-Adrenergic Stimulation in the Senescent Rat Heart 334
A. Carillion, S. Feldman, C. Jiang, F. Atassi, N. Na, N. Mougenot, S. Besse, J.-S. Hulot, B. Riou, and J. Amour

MRP4 is overexpressed in the senescent rat heart and is involved in the limited positive inotropic response of the senescent heart to β-adrenergic stimulation. MRP4 may be a therapeutic target for altering the inotropic reserve of elderly patients.

🌐 **Possible Pathogenic Mechanism of Propofol Infusion Syndrome Involves Coenzyme Q** 343
A.V. Vanlander, J.G. Okun, A. de Jaeger, J. Smet, E. De Latter, B. De Paepe, G. Dacremont, B. Wuyts, B. Vanheel, P. De Paepe, P.G. Jorens, N. Van Regenmortel, and R. Van Coster

In eight rats sedated for up to 20 h with gradually increasing doses of propofol, succinate cytochrome c reductase (complex II+III) was the most sensitive to inhibition by propofol. The activities of complex II and complex III were not decreased when tested individually, suggesting propofol interferes with coenzyme Q, which transfers electrons from complex II to complex III. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

■ CRITICAL CARE MEDICINE

BASIC SCIENCE

◇◆ **Reversal of Dabigatran Effects in Models of Thrombin Generation and Hemostasis by Factor VIIa and Prothrombin Complex Concentrate** 353
M. Hoffman, Z. Volovyk, and D.M. Monroe

Using a cell-based coagulation model, the ability of either prothrombin complex concentrate or recombinant factor VIIa to restore hemostasis in the presence of dabigatran depends on the dose of procoagulant used and the level of dabigatran present and may explain the inconsistency of effects in different models and when used off label for treating bleeding.

◆🌐 **Therapeutic Efficacy of Human Mesenchymal Stromal Cells in the Repair of Established Ventilator-induced Lung Injury in the Rat** 363
M. Hayes, C. Masterson, J. Devaney, F. Barry, S. Elliman, T. O'Brien, D. O' Toole, G.F. Curley, and J.G. Laffey

Rats with ventilator-induced lung injury who received human mesenchymal stromal cells had enhanced lung repair and improved oxygenation compared to rats who received vehicle or fibroblasts. Mesenchymal stromal cell treatment was also associated with improved lung compliance, decreased alveolar edema, and restored lung architecture. The mechanism for improvement appeared to be in part decreased inflammation and decreased alveolar cell neutrophil. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

Hepatic Hepcidin Protects against Polymicrobial Sepsis in Mice by Regulating Host Iron Status 374
C. Zeng, Q. Chen, K. Zhang, Q. Chen, S. Song, and X. Fang

Disruption of mouse hepatic hepcidin expression led to significant increases in organ damage and mortality when sepsis was produced. Decreasing the iron levels in these mice improved survival.

Effective Reversal of Edoxaban-associated Bleeding with Four-factor Prothrombin Complex Concentrate in a Rabbit Model of Acute Hemorrhage 387
E. Herzog, F. Kaspereit, W. Krege, B. Doerr, J. Mueller-Cohrs, I. Pragst, Y. Morishima, and G. Dickneite

In a rabbit model of acute hemorrhage, a four-factor prothrombin complex concentrate also significantly decreased edoxaban-associated bleeding and improved hemostatic activation.

CONTENTS

PAIN MEDICINE

CLINICAL SCIENCE

◇ **Effect of Minocycline on Lumbar Radicular Neuropathic Pain: A Randomized, Placebo-controlled, Double-blind Clinical Trial with Amitriptyline as a Comparator** 399
P. Vanelderen, J. Van Zundert, T. Kozicz, M. Puylaert, P. De Vooght, R. Mestrum, R. Heylen, E. Roubos, and K. Vissers

In a controlled trial of 60 patients with subacute lumbar radicular pain, a 2-week treatment with minocycline or amitriptyline reduced pain compared to placebo. Reductions in pain over this short time period were small and unlikely to be clinically significant.

Phase 1 Safety Assessment of Intrathecal Oxytocin 407
J.C. Eisenach, C. Tong, and R. Curry

Subarachnoid injections of oxytocin did not produce any major adverse events or complications. In a limited protocol for testing analgesia, no analgesic effects were apparent.

p.L1612P, a Novel Voltage-gated Sodium Channel Nav1.7 Mutation Inducing a Cold Sensitive Paroxysmal Extreme Pain Disorder 414
M.R. Suter, Z.A. Bhuiyan, C.J. Laedermann, T. Kuntzer, M. Schaller, M.W. Stauffacher, E. Roulet, H. Abriel, I. Decosterd, and C. Wider

A new mutation, p.L1612P, was found in four family members suffering from Paroxysmal Extreme Pain Disorder. The mutant ion channel possesses unique electrophysiological characteristics, and a pharmacological profile distinct from other known mutations.

BASIC SCIENCE

5-HT$_{1A}$ Receptor Agonist Befiradol Reduces Fentanyl-induced Respiratory Depression, Analgesia, and Sedation in Rats 424
J. Ren, X. Ding, and J.J. Greer

In conscious rats, administration of the 5-HT$_{1A}$ receptor agonist, befiradol, reversed fentanyl-induced respiratory depression, but also antinociception, and caused abnormal behaviors that may limit clinical efficacy.

EDUCATION

IMAGES IN ANESTHESIOLOGY

Near-complete Upper Airway Obstruction from a Grape 435
J.J. Lamberg and K.S. Donahue

GlideScope Cobalt Videolaryngoscope: Mirrors and Illusions 436
J.E. Fiadjoe, R.S. Isserman, H. Gurnaney, and P.G. Kovatsis
SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT

CLINICAL CONCEPTS AND COMMENTARY

Ultrasound for "Lung Monitoring" of Ventilated Patients 437
B. Bouhemad, S. Mongodi, G. Via, and I. Rouquette

In the intensive care unit, patient lung ultrasound provides accurate information on lung morphology with diagnostic and therapeutic relevance. It enables clinicians easy, rapid, and reliable evaluation of lung aeration and its variations at the bedside. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

REVIEW ARTICLE

◇ H **Acute and Perioperative Care of the Burn-injured Patient** 448
E.A. Bittner, E. Shank, L. Woodson, and J.A.J. Martyn

Major burn injury affects almost every organ. Understanding the complex and often paradoxical pathophysiological responses in the early and late phases of injury is imperative to provide expert care in the acute and perioperative period.
SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT

CONTENTS

MIND TO MIND

Finding a Place for Grief in the Workplace 465
S. Crowe

"I, Am a Person" 468
J.K. Pearson

CORRESPONDENCE

Management of Difficult Airways: Which Is the Safest Approach after Reviewing Virtual Laryngo-tracheo-bronchoscopy Imaging? 469
F. Sanfilippo, F. Sgalambro, and M. Astuto

In Reply
S. Agarwal and M. Castresana

Duration of Hypotension (Still) Matters 470
Wolf H. Stapelfeldt

In Reply
M.D. Kertai, W.D. White, and T.J. Gan

Aspiration during Monitored Anesthesia Care 471
J.K. Bohman

In Reply
J. Savilampi, R. Ahlstrand, H. Geijer, and M. Wattwil

Role of Recruitment Maneuvers for Lung-protective Ventilation in the Operating Room Remains Unclear 472
T.A. Treschan and M. Beiderlinden

In Reply
N.M. Goldenberg, B.E. Steinberg, W.L. Lee, D.N. Wijeysundera, and B.P. Kavanagh

ANESTHESIOLOGY REFLECTIONS FROM THE WOOD LIBRARY-MUSEUM

From Paris to Tunis: Bellon Advertising Xylocaine 324
George S. Bause

SPAR(klet) WARS: Erie's Duncan *et al.* *vs.* Cleveland's Hingson *et al.* 386
George S. Bause

A Floridian Salute to a Clevelander: Liberty Ship SS *Harvey Cushing* 406
George S. Bause

REVIEWS OF EDUCATIONAL MATERIAL 475

ANNOUNCEMENTS 477

CAREERS & EVENTS 29A

CONTENTS

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 © 2015, the American Society of Anesthesiologists, Inc.

Annual Subscription Rates: *United States*—$799 Individual, $1566 Institution, $319 In-training. *Rest of World*—$843 Individual, $1739 Institution, $319 In-training. Single copy rate $145. 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 ($257) and persons in training ($257) 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 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.