



ON THE COVER:

Management of perioperative fluid impacts gastrointestinal function. In this issue of ANESTHESIOLOGY, Gómez-Izquierdo *et al.* randomized patients undergoing laparoscopic colorectal surgery within an Enhanced Recovery After Surgery program to receive intraoperative goal-directed fluid therapy or fluid therapy based on traditional principles and assessed the impact on postoperative ileus. Intraoperative goal-directed fluid therapy did not reduce postoperative ileus, suggesting that previously demonstrated benefits might have been offset by advancements in perioperative care.

- Gómez-Izquierdo *et al.*: Goal-directed Fluid Therapy Does Not Reduce Primary Postoperative Ileus after Elective Laparoscopic Colorectal Surgery: A Randomized Controlled Trial, p. 36

◆ THIS MONTH IN ANESTHESIOLOGY

1A

■ SCIENCE, MEDICINE, AND THE ANESTHESIOLOGIST

13A

■ INFOGRAPHICS IN ANESTHESIOLOGY

15A

◆ EDITORIAL VIEWS

Editor's Note: ANESTHESIOLOGY 2017: Expanding the Richness and Reach

E. D. Kharasch

1

Raising the Alarm on Brain Attacks in Surgical Patients: Are We Doing Enough to Prevent and Treat Postoperative Strokes?

L. G. Glance and R. G. Holloway

3

Understanding Potential Drug Side Effects: Can We Translate Molecular Mechanisms to Clinical Applications?

A. Koster and J. H. Levy

6

■ PERIOPERATIVE MEDICINE

CLINICAL SCIENCE

◆◆ Risks of Cardiovascular Adverse Events and Death in Patients with Previous Stroke Undergoing Emergency Noncardiac, Nonintracranial Surgery: The Importance of Operative Timing

9

M. N. Christiansen, C. Andersson, G. H. Gislason, C. Torp-Pedersen, R. D. Sanders, P. Føge Jensen, and M. E. Jørgensen

After emergency noncardiac nonintracranial surgery, risks of 30-day major adverse cardiovascular events (acute myocardial infarction, ischemic stroke, or cardiovascular death) were high for patients with stroke less than 3 months before surgery (odds ratio [OR] = 4.7), 3 to 9 months (OR = 1.9), and more than 9 months (OR = 1.6) compared with no previous stroke. Risks of death (1.6, 1.2, and 1.2) in the same period were also increased. Risk of major adverse cardiovascular events was significantly lower after immediate (1 to 3 days after stroke) compared with early surgery (4 to 14 days). These patterns were similar to that observed in poststroke patients having elective surgery.

◆ Refers to This Month in Anesthesiology

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◆ Refers to Editorial Views

CME CME Article


🎧 This article has an Audio Podcast

📺 This article has a Video Abstract


🩸 This is a Coagulation 2016 article

- ◆  **A Phase 1, Single-center, Double-blind, Placebo-controlled Study in Healthy Subjects to Assess the Safety, Tolerability, Clinical Effects, and Pharmacokinetics–Pharmacodynamics of Intravenous Cyclopropyl-methoxycarbonylmetomidate (ABP-700) after a Single Ascending Bolus Dose** 20
M. M. R. F. Struys, B. I. Valk, D. J. Eleveld, A. R. Absalom, P. Meyer, S. Meier, I. den Daas, T. Chou, K. van Amsterdam, J. A. Campagna, and S. P. Sweeney
- In a first-in-human study, cyclopropyl-methoxycarbonylmetomidate (ABP-700) was safe and well tolerated up to a maximum tolerated bolus dose of 1.0 mg/kg. Onset of hypnosis after bolus administration was rapid as was recovery. APB-700 did not cause cardiovascular depression, centrally induced respiratory depression, or suppression of the physiologic response of the adrenal axis to adrenocorticotrophic hormone stimulation. Involuntary muscle movements were observed at doses of 0.175 mg/kg and greater.
- ◆  **Goal-directed Fluid Therapy Does Not Reduce Primary Postoperative Ileus after Elective Laparoscopic Colorectal Surgery: A Randomized Controlled Trial** 36
 *J. C. Gómez-Izquierdo, A. Trainito, D. Mirzakandov, B. L. Stein, S. Liberman, P. Charlebois, N. Pecorelli, L. S. Feldman, F. Carli, and G. Baldini*
- This randomized blinded trial assessed effects of goal-directed fluid therapy on primary postoperative ileus after laparoscopic colorectal surgery, within a well-established Enhanced Recovery After Surgery program. The incidence of primary postoperative ileus was identical (22%) in the goal-directed fluid therapy control groups. Previous benefits of goal-directed fluid therapy may have been offset by subsequent improvements in perioperative and surgical care.
- ◆ **Epidural Neostigmine *versus* Fentanyl to Decrease Bupivacaine Use in Patient-controlled Epidural Analgesia during Labor: A Randomized, Double-blind, Controlled Study** 50
J. L. Booth, V. H. Ross, K. E. Nelson, L. Harris, J. C. Eisenach, and P. H. Pan
- Adding neostigmine (2, 4, or 8 µg/ml) to bupivacaine for patient-controlled epidural analgesia during labor did not reduce bupivacaine requirement compared with bupivacaine plus fentanyl.
- ◆  **Neurophysiologic Correlates of Ketamine Sedation and Anesthesia: A High-density Electroencephalography Study in Healthy Volunteers** 58
 *P. E. Vlisides, T. Bel-Bahar, U. Lee, D. Li, H. Kim, E. Janke, V. Tarnal, A. B. Pichurko, A. M. McKinney, B. S. Kunkler, P. Picton, and G. A. Mashour*
- Ketamine had dose-dependent effects on spectral power, functional connectivity, and directed connectivity. Anesthetic doses of ketamine resulted in markedly increased theta power across the cortex as well as increased gamma and delta power. Increased anterior-posterior connectivity in the theta bandwidth and decreased connectivity in the alpha bandwidth were specific for ketamine anesthesia.
- GNAQ TT(-695/-694)GC Polymorphism Is Associated with Increased Gq Expression, Vascular Reactivity, and Myocardial Injury after Coronary Artery Bypass Surgery** 70
U. H. Frey, S. Klenke, A. Mitchell, T. Knüfermann, H. Jakob, M. Thielmann, W. Siffert, and J. Peters
- The GC/GC genotype of the TT(-695/-694)GC polymorphism is associated with increased Gq protein expression, augmented angiotensin II receptor type 1-related vasoconstriction, and increased myocardial injury after coronary artery bypass grafting.
- ◆  **A Systematic Review and Meta-analysis Examining the Impact of Incident Postoperative Delirium on Mortality** 78
G. M. Hamilton, K. Wheeler, J. Di Michele, M. M. Lalu, and D. I. McIsaac
- Patients who develop delirium are at increased risk of death. However, in the studies with reduced bias and adequate control for confounding, an independent association between delirium and mortality was not apparent.

BASIC SCIENCE

- ◆ **High Concentrations of Tranexamic Acid Inhibit Iontropic Glutamate Receptors** 89
 *I. Lecker, D.-S. Wang, K. Kaneshwaran, C. D. Mazer, and B. A. Orser*
- Tranexamic acid inhibits *N*-methyl-D-aspartate receptors likely by reducing the binding of the co-agonist glycine and also inhibits other ionotropic glutamate receptors. Receptor blockade only occurs at high concentrations, similar to those that occur after topical application to peripheral tissues. Inhibition of glutamate receptors in peripheral tissues may contribute to adverse effects observed at high concentrations.


CONTENTS

-  **Triggering Receptor Expressed on Myeloid Cells 2, a Novel Regulator of Immunocyte Phenotypes, Confers Neuroprotection by Relieving Neuroinflammation** 98
Q. Zhai, F. Li, X. Chen, J. Jia, S. Sun, D. Zhou, L. Ma, T. Jiang, F. Bai, L. Xiong, and Q. Wang

In a mouse model of middle cerebral artery occlusion, activation and up-regulation of triggering receptor expressed on myeloid cells 2 (TREM2) promoted microglial switching from the detrimental M1 phenotype to the beneficial M2 phenotype. Administering a TREM2 agonist systemically or delivering TREM2 lentivirus directly into the cerebral ventricle caused neuroprotection in mice. TREM2 regulates microglial phenotype after stroke and may affect short-term outcome after stroke in mice.

■ CRITICAL CARE MEDICINE

CLINICAL SCIENCE

-  **Management of Severe Bleeding in Patients Treated with Direct Oral Anticoagulants: An Observational Registry Analysis** 111
P. Albaladejo, C.-M. Samama, P. Sié, S. Kauffmann, V. Mémier, P. Suchon, A. Viallon, J. S. David, Y. Gruel, L. Bellamy, E. de Maistre, P. Romegoux, S. Thoret, G. Pernod, and J.-L. Bosson, on behalf of the GIHP-NACO Study Group

In a prospective cohort registry study of 732 patients treated with direct oral anticoagulants and hospitalized for severe bleeding, bleeding sites were gastrointestinal in 37% and intracranial in 24% of the cases. Activated or nonactivated prothrombin complex concentrates were administered in 38% of the cases with a day 30 mortality of 13.5% and varied according to bleeding sites but was similar to previous reports. Our report provides a detailed assessment of direct oral anticoagulant-treated patients managed in clinical settings.


BASIC SCIENCE

-  **Iron Loading Exaggerates the Inflammatory Response to the Toll-like Receptor 4 Ligand Lipopolysaccharide by Altering Mitochondrial Homeostasis** 121
K. Hoefft, D. B. Bloch, J. A. Graw, R. Malhotra, F. Ichinose, and A. Bagchi

In rodent and cellular models, iron loading potentiated inflammation caused by lipopolysaccharide. Iron loading in this model increased the production of mitochondrial superoxide and disrupted mitochondrial homeostasis.


■ PAIN MEDICINE

CLINICAL SCIENCE

-  **Pain Catastrophizing Moderates Relationships between Pain Intensity and Opioid Prescription: Nonlinear Sex Differences Revealed Using a Learning Health System** 136
Y. Sharifzadeh, M.-C. Kao, J. A. Sturgeon, T. J. Rico, S. Mackey, and B. D. Darnall

A retrospective study of 1,794 patients with chronic pain seeking initial medical evaluation found a significant relationship between pain intensity and opioid prescription that was much stronger in women, especially those with high levels of pain catastrophizing. Although men and women had similar levels of catastrophizing and opioid prescription, opioid prescriptions were more common at lower levels of catastrophizing for women.

BASIC SCIENCE

-  **DNA Hydroxymethylation by Ten-eleven Translocation Methylcytosine Dioxygenase 1 and 3 Regulates Nociceptive Sensitization in a Chronic Inflammatory Pain Model** 147
Z. Pan, Z.-Y. Xue, G.-F. Li, M.-L. Sun, M. Zhang, L.-Y. Hao, Q.-Q. Tang, L.-J. Zhu, and J.-L. Cao

The knockdown of key DNA demethylating enzyme ten-eleven translocation enzymes (TET1, TET3) reduces nociceptive sensitization induced by inflammation. The effects of TET1/TET3 knockdown may result from alterations in spinal signal transducer and activator of transcription 3 expression.

■ EDUCATION

IMAGES IN ANESTHESIOLOGY

- Torus Palatinus and Airway Management** 164
J. Aron, S. J. Raithel, and A. J. Mannes

- Persistent Left Superior Vena Cava: Unusual Catheter Position on Chest X-ray Film** 165
R. Deshpande, M. Band, and V. Kurup

CLINICAL CONCEPTS AND COMMENTARY

- ◇ **Perioperative Steroid Management: Approaches Based on Current Evidence** 166
M. M. Liu, A. B. Reidy, S. Saatee, and C. D. Collard

Perioperative stress-dose steroid administration remains a controversial topic, with recent studies questioning its necessity. We discuss the current literature, largely published in nonanesthesiology journals, and suggest a practical approach to perioperative steroid management.

REVIEW ARTICLE

- ◇ **Phrenic Nerve Palsy and Regional Anesthesia for Shoulder Surgery: Anatomical, Physiologic, and Clinical Considerations** 173
K. El-Boghdadly, K. J. Chin, and V. W. S. Chan

A review of the anatomical, physiologic, and clinical principles governing phrenic nerve palsy in the context of regional anesthesia for shoulder surgery and the strategies for reducing its incidence and impact.

MIND TO MIND

- Texting under Anesthesia** 192
D. Guardiola, M. Guardiola, and S. D. Cook-Sather

CORRESPONDENCE

- Should Neuromuscular Blocking Agents Always Be Reversed?** 194
M. J. Meyer and M. Eikermann

- Neuromuscular Blockade and Risk of Postoperative Pneumonia** 195
A. Cumberworth

- Accounting for Planned Postoperative Intubation** 195
T. M. Austin and H. Lam

- Risk of Postoperative Pneumonia with Neuromuscular Blockade: Keep It Simple!** 196
L. J. Caruso, H. Reed, and R. V. Zhang

- Science or Fiction? Risk of Postoperative Pneumonia with Neuromuscular Blockade** 197
R. V. Zhang, H. Reed, and L. J. Caruso

- In Reply**
C. M. Bulka and J. M. Ehrenfeld

- In Reply**
A. S. Kopman and G. S. Murphy

-
- Assessing Success of Rescue Intubation Techniques after Failed Direct Laryngoscopy** 198
F.-S. Xue, G.-Z. Yang, and H.-X. Li

- Is Airway Management Better?** 200
A. Maslow and S. Panaro

- Apneic Intubation: Video Laryngoscopy Lacks the Continuous Ventilation Offered by Other Airway Management Techniques** 201
S. T. Herway and J. L. Benumof

- In Reply**
M. F. Aziz, D. W. Healy, A. M. Brambrink, and S. Kheterpal
-

Calculating Ideal Body Weight: Keep It Simple 203
O. Moreault, Y. Lacasse, and J. S. Bussières

In Reply
G. Hedenstierna and L. Edmark

Evaluation of Nitrous Oxide in the Gas Mixture for Anesthesia II (ENIGMA II) Revisited: Patients Still Vomiting 204
E. C. K. Li, L. D. Balbuena, and J. J. Gamble

In Reply
P. S. Myles and J. Kasza

Promoting Sustainable Practices *via* Art 206
K. L. Zuegge, M. E. Warren, B. L. Muldowney, and A. T. B. Kron

■ ERRATUM

208

■ CAREERS & EVENTS

17A

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