



ON THE COVER:

This issue is the 2nd annual special issue featuring research from a pioneering institution in our field. The cover is a compilation of images presented in Washington University research published in this issue.

THIS MONTH IN ANESTHESIOLOGY

9A

EDITORIAL VIEWS

- WUA** **Washington University and the Why of Anesthesiology** 1145
James C. Eisenach
- WUA** **Memories and Dreams: Building an Academic Department at Washington University in St. Louis** 1147
Alex S. Evers and William D. Owens
- WUA** **Depth of Anesthesia: Perhaps the Patient Isn't a Submarine** 1149
Jamie W. Sleigh
- From Bedside to Bench and Back: Perfecting Lipid Emulsion Therapy for Local Anesthetic Toxicity** 1151
Peter V. Killoran and Davide Cattano

PERIOPERATIVE MEDICINE

- WUA** **Perioperative Pharmacokinetics of Methadone in Adolescents** 1153
Anshuman Sharma, Danielle Tallchief, Jane Blood, Thomas Kim, Amy London, and Evan D. Kharasch
- This investigation determined the pharmacokinetics of intravenous methadone in adolescents undergoing surgery. Methadone disposition was similar to that in healthy adults.
- WUA** **A Gain-of-function Mutation in Adenylate Cyclase Confers Isoflurane Resistance in *Caenorhabditis elegans*** 1162
Owais Saifee, Laura B. Metz, Michael L. Nonet, and C. Michael Crowder
- A gain-of-function mutation in an adenylate cyclase gene was discovered in the nematode *Caenorhabditis elegans* that strongly reduces the potency of isoflurane. This mutation acts in neurons to regulate neurotransmitter release and isoflurane sensitivity.

- ◇ Refers to This Month in Anesthesiology
- ◆ Refers to Editorial Views
- WUA This article is from or about Washington University
- 🌐 See Supplemental Digital Content
- CME CME Article

- CME** **Perioperative Nerve Injury after Total Hip Arthroplasty: Regional Anesthesia Risk during a 20-year Cohort Study** **1172**
Adam K. Jacob, Carlos B. Mantilla, Hans P. Sviggum, Darrell R. Schroeder, Mark W. Pagnano, and James R. Hebl
 This cohort study determined the overall incidence of perioperative nerve injury after total hip arthroplasty to be 0.72%. Use of neuraxial or peripheral regional anesthesia techniques did not increase the risk for perioperative nerve injury.
- First-line Therapy with Coagulation Factor Concentrates Combined with Point-of-Care Coagulation Testing Is Associated with Decreased Allogeneic Blood Transfusion in Cardiovascular Surgery: A Retrospective, Single-center Cohort Study** **1179**
Klaus Görlinger, Daniel Dirkmann, Alexander A. Hanke, Markus Kamler, Eva Kottenberg, Matthias Thielmann, Heinz Jakob, and Jürgen Peters
 First-line fibrinogen and/or prothrombin complex concentrate administration combined with point-of-care testing (thromboelastometry, impedance aggregometry) was associated with a markedly decreased incidence of allogeneic blood transfusion and of thrombotic/thromboembolic events in cardiovascular surgery.
- Pharmacogenomic Strain Differences in Cardiovascular Sensitivity to Propofol** **1192**
Thomas A. Stekiel, Stephen J. Contney, Richard J. Roman, Craig A. Weber, Anna Stadnicka, Zeljko J. Bosnjak, Andrew S. Greene, and Carol Moreno
 There is a pharmacogenomic difference in Dahl Salt Sensitive rats compared with Brown Norway control rats manifesting as enhanced cardiovascular sensitivity to propofol. This is attributable to altered renin gene function in the Dahl strain.
- WUA** **Use of Recombinant Factor VIIa in Patients with Amniotic Fluid Embolism: A Systematic Review of Case Reports** **1201**
Barbara L. Leighton, Michael H. Wall, Ellen M. Lockhart, Louise E. Phillips, and Amanda J. Zatta
 Amniotic fluid embolism patients who received recombinant factor VIIa had significantly worse outcomes than cohorts who did not receive recombinant factor VIIa. Death and major organ thrombosis were common in patients receiving recombinant factor VIIa.
- WUA** **◆ Relationship between Bispectral Index Values and Volatile Anesthetic Concentrations during the Maintenance Phase of Anesthesia in the B-Unaware Trial** **1209**
Elizabeth L. Whitlock, Alexander J. Villafranca, Nan Lin, Ben J. Palanca, Eric Jacobsohn, Kevin J. Finkel, Lini Zhang, Beth A. Burnside, Heiko A. Kaiser, Alex S. Evers, and Michael S. Avidan
 Individual and population concentration response characteristics limit the feasibility of titrating volatile anesthetic administration against processed electroencephalographic indices such as the Bispectral Index.
- ◆ Lipid Resuscitation of Bupivacaine Toxicity: Long-chain Triglyceride Emulsion Provides Benefits over Long- and Medium-chain Triglyceride Emulsion** **1219**
Zhengqian Li, Yun Xia, Xiaoxi Dong, Hongfei Chen, Fangfang Xia, Xianqin Wang, Huimin Dong, Zhousheng Jin, Xili Ding, Thomas J. Papadimos, and Xuzhong Xu
 The results of resuscitation effects of two commercially available lipid emulsions of different compositions on the recovery from bupivacaine toxicity in rats displayed long-chain triglyceride emulsion's superiorities over long- and medium-chain triglyceride emulsion.

CONTENTS

■ CRITICAL CARE MEDICINE

Neuroprotective Effect of Curcumin in an Experimental Rat Model of Subarachnoid Hemorrhage 1229

Chang-Po Kuo, Chueng-He Lu, Li-Li Wen, Chen-Hwan Cherng, Chih-Shung Wong, Cecil O. Borel, Da-Tong Ju, Chun-Mei Chen, and Ching-Tang Wu

Treatment with multiple doses of curcumin after subarachnoid hemorrhage reduced mortality rate and improved functional and histological outcomes. Possible mechanisms include attenuation of glutamate level by preservation of glutamate transporter-1 protein expression and attenuation of oxidant stress.

■ PAIN MEDICINE

WUA Metabotropic Glutamate Receptor 5 Antagonism with Fenobam: Examination of Analgesic Tolerance and Side Effect Profile in Mice 1239

Michael C. Montana, Beth A. Conrardy, Laura F. Cavallone, Benedict J. Kolber, Lesley K. Rao, Suellen C. Greco, and Robert W. Gereau IV

Daily administration of the mGlu5 antagonist fenobam for up to 2 weeks does not result in tolerance to fenobam's analgesic effects and is well tolerated in mice.

WUA Buprenorphine Metabolites, Buprenorphine-3-glucuronide and Norbuprenorphine-3-glucuronide, Are Biologically Active 1251

Sarah M. Brown, Michael Holtzman, Thomas Kim, and Evan D. Kharasch

Buprenorphine-3-glucuronide and norbuprenorphine-3-glucuronide had moderate to high affinity for human μ , δ , and/or nociceptin receptors, and elicited mild analgesic responses. Norbuprenorphine-3-glucuronide but not buprenorphine-3-glucuronide caused sedation and decreased tidal volume. Glucuronide metabolites may contribute to buprenorphine effects.

WUA Isozyme-specific Effects of Protein Kinase C in Pain Modulation 1261

Chengshui Zhao, Michael Leitges, and Robert W. Gereau IV

This study utilizes a panel of genetically modified mice to demonstrate the diverse roles of the α , β , γ , and δ isoforms of protein kinase C in mediating hypersensitivity after inflammation or nerve injury.

Rewarding Electrical Brain Stimulation in Rats after Peripheral Nerve Injury: Decreased Facilitation by Commonly Abused Prescription Opioids 1271

Eric E. Ewan and Thomas J. Martin

Spinal nerve ligation in rats suppresses opioid facilitation of rewarding brain stimulation in a manner that is distinct from analgesia-related manipulations.

Shifts in Cell-type Expression Accompany a Diminishing Role of Spinal P38-Mapkinase Activation over Time during Prolonged Postoperative Pain 1281

Liang Huang, Yong-Jing Gao, Jeffrey Wang, and Gary Strichartz

During prolonged, postoperative pain, expression of activated mitogen-activated protein kinase p38 shifts from microglia to neurons. Inhibition of P-p38 at early times prevents later postoperative pain, but later inhibition causes only transient pain relief.

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■ EDUCATION

CASE SCENARIO

- WUA** ♦ **Opioid Association with Serotonin Syndrome: Implications to the Practitioners** **1291**
Rahul Rastogi, Robert A. Swarm, and Trusharth A. Patel

Serotonin syndrome is an uncommon but potentially life-threatening drug-induced toxicity, from interaction of opioids to other serotonergic agents. This toxic reaction can either be avoided, through knowing a patient's detailed medicinal history, or be diagnosed early to prevent severe morbidity and mortality. It is even more critical for a practicing anesthesiologist to understand this entity, as the syndrome will be even more difficult to diagnose if secondary to overlapping symptoms from anesthetic. This case scenario focused on serotonin syndrome pathophysiology and management, and its association to routinely used opioids.

IMAGES IN ANESTHESIOLOGY

- WUA** 🌐 **Inflammatory Myofibroblastic Tumor within Intrahepatic Inferior Vena Cava** **1299**
Andrea Vannucci, Lan Chi Tran, and Ivan M. Kangrga

- WUA** **Subglottic Airway Foreign Body: A Near Miss** **1300**
Jacob AuBuchon, Catherine Krucylak, and David J. Murray

- WUA** **Necrotizing Fasciitis after Cesarean Delivery** **1301**
Kathleen W. Nissman, Daniel B. Nissman, Barbara L. Leighton, Swarup S. Varaday, and Ellen M. Lockhart

- WUA** **Pus in the Ventricles of a Patient with a Lumbar Cerebrospinal Fluid Drain for a Thoracoabdominal Aneurysm Repair** **1302**
Jonathan E. Charnin, Brian T. Bateman, and Edward A. Bittner

- ANESTHESIA LITERATURE REVIEW** **1303**

ORIGINAL INVESTIGATIONS IN EDUCATION

- WUA** ♦ **Simulation-based Assessment of Pediatric Anesthesia Skills** **1308**
James J. Fehr, John R. Boulet, William B. Waldrop, Rebecca Snider, Megan Brockel, and David J. Murray

A multiple scenario simulation-based assessment of pediatric perioperative care demonstrated that anesthesia residents with more training achieved higher scores, with a wide range of ability among subjects.

REVIEW ARTICLES

- WUA** ♦ **Genetic Variation, β -blockers, and Perioperative Myocardial Infarction** **1316**
Peter Nagele and Stephen B. Liggett

Perioperative myocardial infarction (MI) is a common and potentially fatal complication after noncardiac surgery. The use of β -adrenergic receptor blocking drugs for prevention and treatment of perioperative MI has become controversial. Interindividual genetic variation may determine the clinical response to β -blocker therapy. This article reviews the molecular, cellular, and physiologic consequences of polymorphisms in the adrenergic signaling pathway and CYP2D6 gene, and shows that these are likely relevant factors influencing efficacy, safety, and toxicity of β -blocker therapy in prevention and treatment of perioperative MI.

- WUA** **Use of Concatemers of Ligand-Gated Ion Channel Subunits to Study Mechanisms of Steroid Potentiation** **1328**
Joe Henry Steinbach and Gustav Akk

Neurosteroids potentiate responses to neurotransmitter at multiple sites on receptors. The authors review the use of covalently linked channel subunits to characterize the sites individually and provide insights into the mechanisms of neurosteroid potentiation.

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- WUA** **Structural Studies of the Actions of Anesthetic Drugs on the γ -Aminobutyric Acid Type A Receptor** 1338
Gustav Akk and Joe Henry Steinbach

The γ -aminobutyric acid type A receptor is the major target for many clinically used anesthetic drugs. The authors describe the current state of knowledge of the structural rearrangements taking place during receptor activation and modulation.

- WUA** **Advances in the Management of Sepsis and the Understanding of Key Immunologic Defects** 1349
Lee P. Skrupky, Paul W. Kerby, and Richard S. Hotchkiss

Anesthesiologists increasingly face the difficult challenge of managing patients with sepsis both in the operating room and intensive care unit. This review discusses advances in current therapy and an evolving immunologic understanding of sepsis.

- WUA** **Molecular Mechanisms of Opioid Receptor-dependent Signaling and Behavior** 1363
Ream Al-Hasani and Michael R. Bruchas

This review highlights the recent advances in opioid receptor signaling and discusses their potential for the development of novel opioids in the treatment of pain and neurologic disorders.

- MIND TO MIND**
“... And I Was Born” 1382
Ezzat I. Abouleish

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- New Dreams: Back to the Future** 1388
Louis Jacobson and Anthony J. Mariano

- Pain Treatment and Opioids** 1389
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- WUA** **🌐 Intraoperative Transesophageal Echocardiography Guides Liver Transplant Surgery in a Patient with Thrombosed Transjugular Intrahepatic Portosystemic Shunt** 1389
Andrea Vannucci, Joshua Johnston, Truman M. Earl, Majella Doyle, and Ivan M. Kangranga

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