



# Anesthesiology



The Journal of the American Society of Anesthesiologists, Inc.  
 American Society of Critical Care Anesthesiologists  
 Society for Obstetric Anesthesia and Perinatology



## CONTENTS

- ◇ THIS MONTH IN ANESTHESIOLOGY 5A
- Does Bispectral Index Monitoring Reduce Recovery Times after Surgical Anesthesia?  
 Effects of Spinal Cord Injury on Anesthetic Requirements in Rats  
 Effective Doses Determined for Intrathecal Spinal-Epidural Analgesics in Labor  
 Intrathecal Ropivacaine and Levobupivacaine Compared as Analgesics in Early Labor
- ◆ EDITORIAL VIEWS
- 🌐 Special Issue on Pharmacogenomics and Anesthesia: Work Presented at the 2004 Journal Symposium 493  
*Evan D. Kharasch*
- Anesthesia and the Human Genome Project: The Quest for Accurate Prediction of Drug Responses 494  
*Paul D. Allen*
- 2004 JOURNAL SYMPOSIUM PHARMACOGENOMICS
- Genetic Predisposition to Latex Allergy: Role of *Interleukin 13* and *Interleukin 18* 496  
*Robert H. Brown, Robert G. Hamilton, Margaret Mintz, Anne E. Jedlicka, Alan L. Scott, and Steven R. Kleeberger*
- An association was found between *IL13* and *IL18* promoter polymorphisms with latex allergy suggesting a potential location for genetic control in the induction of latex allergy. This extends the understanding of the genetic basis for the induction of immediate-type hypersensitivity in healthcare workers occupationally exposed to natural rubber latex.

- ◇ Refers to This Month in Anesthesiology  
 ◆ Refers to Editorial Views  
 🌐 See Web Site enhancement  
 CME CME Article

Continued on page 10A



**Response to Mivacurium in Patients Carrying the K Variant in the Butyrylcholinesterase Gene** **503**

*Mona R. Gätke, Jørgen Viby-Mogensen, Doris Østergaard, and Jens R. Bundgaard*

The K allele in the butyrylcholinesterase gene prolongs the duration of action of mivacurium.

**Increased Sensitivity to Thermal Pain and Reduced Subcutaneous Lidocaine Efficacy in Redheads** **509**

*Edwin B. Liem, Teresa V. Joiner, Kentaro Tsueda, and Daniel I. Sessler*

Redheaded women are more sensitive to thermal pain than women with dark hair and are resistant to the analgesic effects of subcutaneous lidocaine. These findings extend the previous observation that redheads are resistant to volatile anesthetics. Mutations of the melanocortin-1 receptor, or as a consequence thereof, therefore seem to modulate pain sensitivity.

**Screening of the Entire Ryanodine Receptor Type 1 Coding Region for Sequence Variants Associated with Malignant Hyperthermia Susceptibility in the North American Population** **515**

*Nyamkhashig Sambuughin, Heather Holley, Sheila Muldoon, Barbara W. Brandom, Astrid M. de Bantel, Joseph R. Tobin, Tom E. Nelson, and Lev G. Goldfarb*

The entire ryanodine receptor type 1 (*RYR1*) coding region was studied in 30 North American malignant hyperthermia-susceptible individuals. Denaturing high-performance liquid chromatography screening of samples derived from the biopsied skeletal muscle was followed by sequencing. This analysis revealed nine previously reported and nine unknown *RYR1* mutations in 21 studied patients, increasing the rate of mutation detection to 70% and identifying mutations throughout the entire *RYR1* coding region.

**Polymorphism of  $\mu$ -Opioid Receptor Gene (*OPRM1:c.118A>G*) Does Not Protect Against Opioid-induced Respiratory Depression despite Reduced Analgesic Response** **522**

*Raymonda R. Romberg, Erik Olofsen, Hans Bijl, Peter E. M. Taschner, Luc J. Teppema, Elise Y. Sarton, Jack W. van Kleef, and Albert Dahan*

Heterozygous carriers of the *OPRM1:c.118G* allele of the  $\mu$ -opioid receptor gene showed morphine-6-glucuronide-induced respiratory depression of similar magnitude as observed in subjects homozygous for the *OPRM1:c.118A* allele, despite a sharp reduction in analgesic effect in all *OPRM1:c.118GA* heterozygotes compared with *OPRM1:c.118AA* homozygotes.

*Continued on page 13A*

---



---

## CONTENTS

---



### Genotyping the Butyrylcholinesterase in Patients with Prolonged Neuromuscular Block after Succinylcholine 531

*Soledad Levano, Hans Ginz, Martin Siegemund, Miodrag Filipovic, Evgueni Voronkov, Albert Urwyler, and Thierry Girard*

Sequencing of the butyrylcholinesterase gene revealed multiple mutations even in cases of neuromuscular block of 15 min after succinylcholine administration. Patients with identical butyrylcholinesterase genotypes were substantially different in their clinical presentation.

### Effect of $\alpha_{2B}$ -Adrenoceptor Polymorphism on Peripheral Vasoconstriction in Healthy Volunteers 536

*Pekka Talke, Claudia Stapelfeldt, Errol Lobo, Ronald Brown, Mika Scheinin, and Amir Snapir*

The authors tested the hypothesis that  $\alpha_{2B}$ -adrenoceptor activation induces enhanced vasoconstriction in carriers of the DD genotype compared with carriers of the II genotype. They found no differences in hemodynamic responses to an  $\alpha_2$  agonist between the subjects with II and DD  $\alpha_{2B}$  genotypes.

### The Impact of Pharmacogenomics on Postoperative Nausea and Vomiting: Do CYP2D6 Allele Copy Number and Polymorphisms Affect the Success or Failure of Ondansetron Prophylaxis? 543

*Keith A. Candiotti, David J. Birnbach, David A. Lubarsky, Fani Nhuch, Aimee Kamat, Walter H. Koch, Michele Nikoloff, Lin Wu, and David Andrews*

Patients with three copies of the CYP2D6 gene, a genotype consistent with ultrarapid metabolism, or both have an increased incidence of ondansetron failure for the prevention of postoperative vomiting but not nausea.

### Pharmacogenetic Determinants of Human Liver Microsomal Alfentanil Metabolism and the Role of Cytochrome P450 3A5 550

*Theresa Mariero Klees, Pamela Sheffels, Kenneth E. Thummel, and Evan D. Kharasch*

Alfentanil metabolism was greater in human livers expressing the *CYP3A5 I* allele and containing higher amounts of the native protein cytochrome P4503A5 (CYP3A5) than in livers homozygous for the mutant *CYP3A5 J* allele and containing minimal amounts of CYP3A5. Therefore, alfentanil is metabolized by human liver microsomal CYP3A5 in addition to CYP3A4, and pharmacogenetic variability in CYP3A5 expression significantly influences human liver alfentanil metabolism *in vitro*.

*Continued on page 14A*




---



---

## CONTENTS

---

**Effect of *N*-methyl-D-aspartate Receptor  $\epsilon_1$  Subunit Gene Disruption of the Action of General Anesthetic Drugs in Mice** **557**

*Yuki Sato, Eiji Kobayashi, Takanori Murayama, Masayoshi Mishina, and Norimasa Seo*

*N*-methyl-D-aspartate receptor  $\epsilon_1$  subunit gene disruption attenuates the anesthetic effect of nitrous oxide, propofol, pentobarbital, diazepam, and midazolam but not sevoflurane in mice.

■ **CLINICAL INVESTIGATIONS**

---

**Awakening Concentration of Desflurane Is Decreased in Patients with Obstructive Jaundice** **562**

*Jian-Gang Song, Yun-Fei Cao, Li-Qun Yang, Wei-Feng Yu, Quan Li, Jin-Chao Song, Xiao-Yong Fu, and Qiang Fu*

The minimum alveolar anesthetic concentration (MAC)-awake of desflurane is significantly reduced in obstructive jaundiced patients compared with that of nonjaundiced controls.

◇ **Effects of Bispectral Index Monitoring on Recovery from Surgical Anesthesia in 1,580 Inpatients from an Academic Medical Center** **566**

*Janet D. Pavlin, Karen J. Souter, Jae Y. Hong, Peter R. Freund, T. Andrew Bowdle, and Jan O. Bower*

Recovery time in a postanesthesia care unit was compared in 1,580 patients treated with or without monitoring of the Bispectral Index, a parameter derived from the continuous recording of the processed electroencephalogram. There was a small reduction in end-tidal sevoflurane concentration (4.7%) in the monitored group but no difference in the duration of time spent in the recovery unit compared with the unmonitored group.

**Increased Pulmonary Venous Resistance Contributes to Increased Pulmonary Artery Diastolic-Pulmonary Wedge Pressure Gradient in Acute Respiratory Distress Syndrome** **574**

*Charles Her, Szabolcs Mandy, and Mosses Bairamian*

Pulmonary venous resistance was increased in acute respiratory distress syndrome. There was a good correlation between relative pulmonary venous resistance and pulmonary artery diastolic-pulmonary wedge pressure gradient.

*Continued on page 16A*



## LABORATORY INVESTIGATIONS

- Inhibitory Effects of Lidocaine and Mexiletine on Vasorelaxation Mediated by Adenosine Triphosphate-sensitive  $K^+$  Channels and the Role of Kinases in the Porcine Coronary Artery** **581**

*Yoshiki Kimoto, Hiroyuki Kinoshita, Katsutoshi Nakahata, Mayuko Dojo, and Yoshio Hatano*

Lidocaine and mexiletine inhibit vasorelaxation mediated by adenosine triphosphate-sensitive  $K^+$  channels in the coronary artery. The activation of protein kinase C and tyrosine kinase seems to have a role in this inhibitory effect of mexiletine but not in that of lidocaine. Class Ib antiarrhythmic drugs may reduce coronary vasodilation mediated by these  $K^+$  channels *via* the differential modulator effects on kinases.

- Ketamine Attenuates Acetylcholine-induced Contraction by Decreasing Myofilament  $Ca^{2+}$  Sensitivity in Pulmonary Veins** **588**

*Xueqin Ding, Derek S. Damron, and Paul A. Murray*

Ketamine attenuates acetylcholine-induced contraction in pulmonary veins *via* protein kinase C-dependent effects on myofilament  $Ca^{2+}$  sensitivity.

- Vaporized Perfluorohexane Attenuates Ventilator-induced Lung Injury in Isolated, Perfused Rabbit Lungs** **597**

*Marcelo Gama de Abreu, Beate Wilmink, Matthias Hübler, and Thea Koch*

Administration of 14% perfluorohexane vapor can attenuate the development of ventilator-induced lung injury in isolated, perfused rabbit lung.

- Isoflurane Neuroprotection in Hypoxic Hippocampal Slice Cultures Involves Increases in Intracellular  $Ca^{2+}$  and Mitogen-activated Protein Kinases** **606**

*Jonathan J. Gray, Philip E. Bickler, Christian S. Fahlman, Xinhua Zhan, and Jennifer A. Schuyler*

In organotypic cultures of rat hippocampus, isoflurane reduces neuron death after hypoxia. This protection requires  $Ca^{2+}$  release from intracellular stores, moderate increases in intracellular  $Ca^{2+}$  concentration, and  $Ca^{2+}$ -dependent activation of the mitogen-activated protein kinase kinase Ras-Raf-MEK-ERK pathway. Protection also involves phosphorylation of the antiapoptotic factor Akt.

*Continued on page 17A*

---



---

## CONTENTS

---



**Facilitation of Serotonergic Activity and Amnesia in Rats Caused by Intravenous Anesthetics** **616**

*Kazunori Semba, Naoto Adachi, and Tatsuru Arai*

Anesthetic doses of propofol and midazolam facilitate serotonergic activity in the rat brain, which may be a factor in the retrograde amnesia produced by these agents.

◇ **Drastic Decrease in Isoflurane Minimum Alveolar Concentration and Limb Movement Forces after Thoracic Spinal Cooling and Chronic Spinal Transection in Rats** **624**

*Steven L. Jinks, Carmen L. Dominguez, and Joseph F. Antognini*

Acute spinal cold block and chronic spinal transection leads to decreased isoflurane requirements and decreased force of limb movement in response to noxious stimulation below the level of spinal transection, and this effect occurs despite a lack of a baseline motor depression, or "spinal shock," in the awake state.

■ **PAIN AND REGIONAL ANESTHESIA**

---

**Comparison of the Different Approaches to Saphenous Nerve Block** **633**

*Honorio T. Benzon, Sanjay Sharma, and Arthur Calimaran*

The transsartorial approach is the most effective approach in blocking the saphenous nerve. In subjects with partial numbness, supplementary block of the medial dorsal cutaneous branch of the superficial peroneal nerve results in complete sensory blockade of the medial aspect of the foot.

**Variability of Target-controlled Infusion Is Less Than the Variability after Bolus Injection** **639**

*Chuanpu Hu, Damian J. Horstman, and Steven L. Shafer*

Target-controlled infusion pumps can neither increase nor decrease biologic variability. The maximum variability in concentration occurs after bolus injection. All other forms of drug delivery, including multiple boluses, conventional infusions, and target-controlled infusions, have less variability than that observed after bolus injection.

◇ **Minimum Local Analgesic Doses of Ropivacaine, Levobupivacaine, and Bupivacaine for Intrathecal Labor Analgesia** **646**

*Michela Camorcia, Giorgio Capogna, and Malachy O. Columb*

The authors determined the minimum local analgesic doses of intrathecal ropivacaine, levobupivacaine, and bupivacaine in the first stage of labor and established the intrathecal analgesic potency ratio for these three drugs.

*Continued on page 18A*

---



---

## CONTENTS

---



- ◆ **A Comparison of Median Effective Doses of Intrathecal Levobupivacaine and Ropivacaine for Labor Analgesia** **651**

*Alex T. Sia, Raymond W. Goy, Yvonne Lim, and Cecilia E. Ocampo*

The median effective dose of intrathecal ropivacaine was found to be significantly more than that of levobupivacaine for labor analgesia. However, the impact of this finding is debatable because the quality of analgesia rendered by clinical doses (2.5 and 3 mg) of these agents was indistinguishable.

- $\alpha_2$ -Adrenoceptor Activation by Clonidine Enhances Stimulation-evoked Acetylcholine Release from Spinal Cord Tissue after Nerve Ligation in Rats** **657**

*Hideaki Obata, Xinhui Li, and James C. Eisenach*

Clonidine enhances  $K^+$ -evoked release of acetylcholine in spinal cord synaptosomes and slices from rats with spinal nerve ligation compared with normal rats by an action on  $\alpha_2$  adrenoceptors. This may partly explain the increased analgesic potency of clonidine after nerve injury and its dependency on spinal cholinergic receptor activation for analgesia in the neuropathic pain state.

### ■ REVIEW ARTICLE

---

- ◆ **Pharmacogenetics of Anesthetic and Analgesic Agents** **663**

*Stephen N. Palmer, N. Martin Giesecke, Simon C. Body, Stanton K. Sherman, Amanda A. Fox, and Charles D. Collard*

*Pharmacogenetics* is the study of the molecular mechanisms that underlie individual differences in drug metabolism, efficacy, and side effects. The pharmacogenetics of commonly used anesthetic and analgesic agents are reviewed.

### ■ SPECIAL ARTICLE

---

- Gerard W. Ostheimer “What’s New in Obstetric Anesthesia” Lecture** **672**

*Lawrence C. Tsen*

Four advances important to the clinical care and research in the obstetric anesthesia patient are summarized.

### ■ CLINICAL CONCEPTS AND COMMENTARY

---

- Cervical Spine Considerations When Anesthetizing Patients with Down Syndrome** **680**

*Tara Hata and Michael M. Todd*

This article reviews what is still unknown about the risk of spinal cord injury when anesthetizing patients with Down syndrome. It also makes specific suggestions for evaluating patients with Down syndrome preoperatively.

*Continued on page 20A*



---



---

**CONTENTS**


---



---


**■ CASE REPORTS**


---

- Intrathecal Catheter Tip Inflammatory Mass: A Failure of Clonidine to Protect** **687**

*James D. Toombs, Kenneth A. Follett, Richard W. Rosenquist, and Lisa M. Benton*

- Diaphragmatic Paralysis after Endovascular Stent Grafting of a Thoracoabdominal Aortic Aneurysm** **690**

*Harish S. Lecamwasam, Dean Hess, Robert Brown, Christopher J. Kwolek, and Luca M. Bigatello*

**■ CORRESPONDENCE**


---

- Ultrasound-guided Caudal Epidural Injection** **693**

*Reginald Edward*

- Disadvantages of Ultrasound Guidance in Caudal Epidural Needle Placement** **693**

*Jeffrey Huang*

- In Reply** *Carl P. C. Chen* **693**

- Anesthesia for Outpatient Surgery: How Fast Is Fast?** **694**

*Mark C. Norris*

- In Reply** *Brian A. Williams and Admir Hadzic* **695**

- In Clinical Practice, Coadministration of Sevoflurane or Propofol Could Antagonize Remifentanyl Stimulation of N-methyl-D-aspartate Receptors** **695**

*Vincenzo Fodale and Letterio B. Santamaria*

- In Reply** *Klaus Hahnenkamp and Marcel E. Durieux* **696**

- CobraPLA™ Is the Perilaryngeal Airway** **696**

*David Alfery*

- In Reply** *Joseph Brimacombe* **697**

- Metabolic Acidosis due to Propofol Infusion** **697**

*Ehab Farag, Glenn DeBoer, Bruce H. Cohen, and Julie Niezgodá*

- In Reply** *Michael E. Johnson* **698**

- In Reply** *Jean-Corentin Salengros and Edgard Engelman* **698**

*Continued on page 23A*



---



---

## CONTENTS

---



<b>Cardioprotective Properties of Sevoflurane in Patients Undergoing Coronary Surgery with Cardiopulmonary Bypass Are Related to the Modalities of Its Administration</b>	<b>699</b>
<i>Alimorad G. Djalali and Nicholas Sadovnikoff</i>	
<b>In Reply</b> <i>Stefan G. De Hert, Stefanie Cromheecke, and Philippe J. Van der Linden</i>	<b>700</b>
<b>Tolerance to Miotic Effects of Opioids</b>	<b>701</b>
<i>Joshua P. Kollars and Merlin D. Larson</i>	
<b>Epidural Hematoma after Epidural Steroid Injection in a Patient Withholding Enoxaparin per Guidelines</b>	<b>701</b>
<i>Robert J. Ain and Matthew B. Vance</i>	
<b>Potentially Dangerous Fracture of the Needleless Interlink Vial Access Cannula</b>	<b>703</b>
<i>Neeti Kohli and F. Barry Florence</i>	
<b>In Reply</b> <i>Kenneth B. Kassler-Taub</i>	<b>704</b>
<span style="color: red;">■</span> <b>REVIEWS OF EDUCATIONAL MATERIAL</b>	<b>705</b>
<span style="color: red;">■</span> <b>ANNOUNCEMENTS</b>	<b>707</b>
<span style="color: red;">■</span> <b>ANESTHESIOLOGY CME PROGRAM</b>	<b>709</b>

### INSTRUCTIONS FOR AUTHORS

The most recently updated version of the Instructions for Authors is available at [www.anesthesiology.org](http://www.anesthesiology.org). Please refer to the Instructions for the preparation of any material for submission to ANESTHESIOLOGY.

### WEB SITE ANNOUNCEMENT

Full-text articles are now available on-line at [www.anesthesiology.org](http://www.anesthesiology.org)

*ANESAV is a code word ("coden") used by the Chemical Abstract Service to identify the journal.*

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>). Manuscripts may also be submitted *via* computer disk and mailed to the Editorial Office or *via* e-mail ([anesthesiology@uiowa.edu](mailto:anesthesiology@uiowa.edu)). 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 mailed to David O. Warner, M.D., Department of Anesthesia, Mayo Clinic, 200 First Street SW, Rochester, MN 55905. Requests for permission to duplicate materials published in ANESTHESIOLOGY should be submitted in electronic format, to the Editorial Office ([anesthesiology@uiowa.edu](mailto:anesthesiology@uiowa.edu)). All articles accepted for publication are done so with the understanding that they are contributed exclusively to this Journal and become the property of the American Society of Anesthesiologists, Inc. Statements or opinions expressed in the Journal reflect the views of the author(s) and do not represent official policy of the American Society of Anesthesiologists unless so stated. Advertising and related correspondence should be addressed to Advertising Manager, ANESTHESIOLOGY, Lippincott Williams & Wilkins, 530 Walnut Street, Philadelphia, Pennsylvania 19106 (Web site: <http://www.lww.com/advertisingratecards/>). 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.