



Anesthesiology



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- ◆ Clinical Pharmacology of GW280430A in Humans 768
Matthew R. Belmont, Cynthia A. Lien, Joseph Tjan, Eleanor Bradley, Brenna Stein, Sanjay S. Patel, and John J. Savarese
- GW280430A, a new nondepolarizing relaxant, shows fast onset, an ultrashort duration, a good safety margin, and a lack of cumulative neuromuscular properties in this first study of the drug in human volunteers.

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Intracarotid Verapamil Decreases both Proximal and Distal Human Cerebrovascular Resistance 774

Shailendra Joshi, Philip M. Meyers, John Pile-Spellman, Mei Wang, and Daniel H. Sahlein

The authors describe a novel method to investigate segmental vascular resistance in human cerebral circulation. The method involves measurement of pressure at two points within the arterial tree and ^{133}Xe cerebral blood flow measurements. They show that intracarotid infusion of verapamil, a calcium channel-blocking drug, decreases the resistance of both the proximal-conductance and the distal-arteriolar resistance.

Long-term Effects of Different Humidification Systems on Endotracheal Tube Patency: Evaluation by the Acoustic Reflection Method 782

Samir Jaber, Jérôme Pigeot, Redouane Fodil, Salvatore Maggiore, Alain Harf, Daniel Isabey, Laurent Brochard, and Bruno Louis

The long-term impact of two humidification systems on the endotracheal tube patency was assessed during long-term mechanical ventilation. A comparison of the two systems using the acoustic reflection method suggests that heated humidifier systems are more efficient than heat and moisture exchangers for long-term mechanical ventilation.

Histomorphologic Examination of Skeletal Muscle Preparations Does Not Differentiate between Malignant Hyperthermia-Susceptible and -Normal Patients 789

Franziska von Breunig, Frank Wappler, Christian Hagel, Verena von Richthofen, Marko Fiege, Ralf Weisshorn, Dimitrios Stavrou, and Jochen Schulte am Esch

Myopathologic examinations did not reveal any specific alterations in malignant hyperthermia. Therefore, these examinations can neither improve the diagnosis of malignant hyperthermia nor contribute to a better definition of the malignant hyperthermia status.

Mixed-effects Modeling of the Influence of Alfentanil on Propofol Pharmacokinetics 795

Martijn J. Mertens, Erik Olofsen, Anton G. L. Burm, James G. Bovill, and Jaap Vuyk

Alfentanil decreases the elimination clearance, the distribution clearance, and the peripheral volume of distribution of propofol. The introduction of cardiac output and heart rate as covariates, in addition to plasma alfentanil concentration, significantly improves the pharmacokinetic model of propofol.

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- ◇ Recurrent Hypoxemia in Young Children with Obstructive Sleep Apnea Is Associated with Reduced Opioid Requirement for Analgesia **806**

Karen A. Brown, André Laferrière, and Immanuela Ravé Moss

Young age and preoperative oxygen desaturation in children with obstructive sleep apnea are correlated with decreased analgesic morphine dosage after adenotonsillectomy.

- Does the Use of Electroencephalographic Bispectral Index or Auditory Evoked Potential Index Monitoring Facilitate Recovery after Desflurane Anesthesia in the Ambulatory Setting? **811**

Paul F. White, Hong Ma, Jun Tang, Ronald H. Wender, Alexander Sloninsky, and Robert Kariger

Cerebral monitoring using the Bispectral Index or auditory evoked index value for titrating desflurane during ambulatory anesthesia decreased the intraoperative desflurane requirement, contributing to an improved recovery profile and earlier discharge compared with standard clinical monitoring practices alone.

- Electroencephalographic Bicoherence Is Sensitive to Noxious Stimuli during Isoflurane or Sevoflurane Anesthesia **818**

Satoshi Hagihira, Masaki Takashina, Takahiko Mori, Hiroshi Ueyama, and Takashi Mashimo

During volatile anesthesia, peak heights of electroencephalographic bicoherence were decreased by noxious stimuli, and the effect was reversed by fentanyl.

- ◇🌐 Perioperative Cardiorespiratory Complications in Adults with Mediastinal Mass: Incidence and Risk Factors **826**

Philippe Béchar, Louis Létourneau, Yves Lacasse, Dany Côté, and Jean S. Bussières

Obstruction of the airway in an adult with a mediastinal mass is a rare event in the intraoperative period; nevertheless, caution should be observed for the occurrence of early life-threatening respiratory complications. Patients at risk of complications can be identified by cardiopulmonary signs and symptoms at the initial presentation, pulmonary function test results, and computed tomography scan findings.

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■ LABORATORY INVESTIGATIONS

- ◆ Preclinical Pharmacology of GW280430A (AV430A) in the Rhesus Monkey and in the Cat: A Comparison with Mivacurium 835

John J. Savarese, Matthew R. Belmont, Mir A. Hashim, Robert A. Mook, Jr., Eric E. Boros, Vicente Samano, Sanjay S. Patel, Paul L. Feldman, Jan-Ake I. Schultz, Michael McNulty, Timothy Spitzer, Douglas L. Cohn, Philip Morgan, and William B. Wastila

GW280430A (AV430A) is a representative of a new class of chemically degradable nondepolarizing relaxants called *asymmetric mixed-onium chlorofumarates*. The duration of action is shorter than mivacurium in the cat and in the monkey. There is a wide separation of the neuromuscular blocking dose range from doses that cause autonomic cardiovascular side effects. The dose ratio for histaminoid phenomena (ED Hist:ED₉₅ Neuromuscular Block) is four times greater than that of mivacurium in the monkey (53 *vs.* 13), indicating a considerable reduction of this side effect. Clinical studies are anticipated.

- ◆ Cardiopulmonary Effects of the Novel Neuromuscular Blocking Drug GW280430A (AV430A) in Dogs 846

Paul M. Heerdt, Richard Kang, Andrew The', Mir Hashim, Robert J. Mook, Jr., and John J. Savarese

The ultrashort neuromuscular blocking drug GW280430 does not produce cardiovascular effects in the anesthetized dog until doses far in excess of the ED₉₅ are administered as a bolus.

- Time-dependent Inhibition of G Protein-coupled Receptor Signaling by Local Anesthetics 852

Markus W. Hollmann, Susanne Herroeder, Katrin S. Kurz, Christian W. Hoenemann, Danja Struemper, Klaus Hahnenkamp, and Marcel E. Durieux

Inhibition of G protein-coupled receptor signaling by local anesthetics was found to be time dependent and reversible. Critically requiring Gαq-protein function, this effect is located downstream of guanosine diphosphate-guanosine triphosphate exchange and is not dependent on increased guanosine triphosphatase activity, phosphatases, or protein kinases.



Acute Hyperinsulinemia Restrains Endotoxin-induced Systemic Inflammatory Response: An Experimental Study in a Porcine Model **861**

Vibeke Brix-Christensen, Søren Kæseleer Andersen, René Andersen, Annette Mengel, Thomas Dyhr, Niels Trolle Andersen, Anders Larsson, Ole Schmitz, Hans Ørskov, and Else Tønnesen

Exogenous insulin decreases the cytokine response and glucagon secretion in endotoxin-induced sepsis.

◇ **Influence of Fluid Infusion Associated with High-volume Blood Loss on Plasma Propofol Concentrations** **871**

Tadayoshi Kurita, Tomiei Kazama, Koji Morita, Shunsuke Fujii, Masahiro Uraoka, Kotaro Takata, and Shigehito Sato

The pseudo-steady state concentration of propofol is influenced differently depending on the method of fluid infusion associated with high-volume blood loss.

Sevoflurane Inhibits Angiotensin II-induced, Protein Kinase C-mediated but Not Ca²⁺-elicited Contraction of Rat Aortic Smooth Muscle **879**

Jingui Yu, Yasuyuki Tokinaga, Koji Ogawa, Shizue Iwahashi, and Yoshio Hatano

This study indicates that Ca²⁺ and Ca²⁺-dependent protein kinase C are involved in the angiotensin II-induced contraction of rat aortic smooth muscle. Sevoflurane dose-dependently inhibited the angiotensin II-stimulated, Ca²⁺-dependent protein kinase C-mediated but not Ca²⁺-elicited contraction of rat aortic smooth muscle.

Hemorrhage during Isoflurane-Nitrous Oxide Anesthesia: Effects of Endothelin-A or Angiotensin II Receptor Blockade or Both **885**

Claudia Höhne, Pia Vogler, Ilka Frerking, Roland C. E. Francis, Erik R. Swenson, Gabriele Kaczmarczyk, and Willehad Boemke

Endothelin A receptor inhibition became apparent by lower blood pressure and cardiac output values after prolonged hypovolemia and by a blunted blood pressure recovery after blood replacement, indicating that endothelins seem to have a place especially in long-term (hours range) cardiovascular regulation. In contrast, angiotensin II receptor blockade impaired both short- and long-term blood pressure regulation during anesthesia and after hemorrhage.

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Dexmedetomidine Enhances Analgesic Action of Nitrous Oxide: Mechanisms of Action 894

Cecilia Dawson, Daqing Ma, Andre Chow, and Mervyn Maze

The synergistic analgesic interaction between nitrous oxide and dexmedetomidine within the spinal cord is obscured by a supraspinal antagonism when dexmedetomidine is administered systemically in the pretolerant state. After tolerance to nitrous oxide develops, supraspinal functional antagonism no longer occurs.

■ PAIN AND REGIONAL ANESTHESIA

◆ Antiallodynic Effects of Systemic and Intrathecal Morphine in the Spared Nerve Injury Model of Neuropathic Pain in Rats 905

Chengshui Zhao, Jill M. Tall, Richard A. Meyer, and Srinivasa N. Raja

Systemic and intrathecal morphine dose-dependently produced antiallodynic effects in the spared nerve injury model of neuropathic pain in rats, indicating that neuropathic pain is not resistant to opioids.

Nerve Injury Induces a Tonic Bilateral μ -Opioid Receptor-mediated Inhibitory Effect on Mechanical Allodynia in Mice 912

Heikki Mansikka, Chengshui Zhao, Rishi N. Sheth, Ichiro Sora, George Uhl, and Srinivasa N. Raja

Mice lacking the μ -opioid receptor gene were used to examine the role of μ -opioid receptors in neuropathic pain. After unilateral spinal nerve injury, more profound and bilateral allodynia developed to mechanical stimuli in μ -opioid knockout mice compared with control animals. Similar results were obtained with naloxone administration in wild-type mice, suggesting that μ -opioid receptors exhibit a tonic bilateral inhibitory role after nerve injury.

Can Ropivacaine and Levobupivacaine Be Used as Test Doses during Regional Anesthesia? 922

Medge D. Owen, Philippe Gautier, and David D. Hood

Plain ropivacaine and levobupivacaine (25 mg) solutions produce inadequate central nervous system symptoms with intravenous injection to warrant routine use as test doses during regional anesthesia.



Intrathecal Anesthesia and Recovery from Radical Prostatectomy: A Prospective, Randomized, Controlled Trial **926**

Daniel R. Brown, Roger E. Hofer, David E. Patterson, Paul J. Fronapfel, Pamela M. Maxson, Bradly J. Narr, John H. Eisenach, Michael L. Blute, Darrell R. Schroeder, and David O. Warner

The addition of intrathecal analgesia to anesthetized patients undergoing radical retropubic prostatectomy does not improve chronic pain or long-term functional status. Addition of intrathecal analgesia in this patient population may decrease the duration of hospital stay.

Analgesic Effects of Gabapentin after Spinal Surgery **935**

Alparslan Turan, Beyhan Karamanlioğlu, Dilek Memiş, Mustafa Kemal Hamamcioglu, Barış Tükenmez, Zafer Pamukçu, and Imran Kurt

Preoperative oral gabapentin reduced morphine consumption and pain in patients undergoing spinal surgery.

Dissociable Brain Activation Responses to 5-Hz Electrical Pain Stimulation: A High-field Functional Magnetic Resonance Imaging Study **939**

Michael T. Alkire, Nathan S. White, Raymond Hsieh, and Richard J. Haier

High-field functional magnetic resonance imaging in humans, coupled with stimulus intensity–response function modeling and a statistical conjunction analysis, was used to reveal dissociable regional responses to tonic aching electrical pain. The results reveal that the primary sensory cortex and the insula are involved with encoding stimulus intensity information, whereas the secondary sensory cortex encodes pain intensity information, and the cingulate activates with high pain intensity.

Meperidine Suppresses the Excitability of Spinal Dorsal Horn Neurons **947**

Matthias Wolff, Andrea Olschewski, Werner Vogel, and Gunter Hempelmann

In clinically relevant concentrations, meperidine reduces the firing frequency of spinal dorsal horn neurons by blocking voltage-gated Na⁺ and K⁺ currents.



Repeated Dosing with Oral Allosteric Modulator of Adenosine A1 Receptor Produces Tolerance in Rats with Neuropathic Pain **956**

Xinhui Li, Carsten Bantel, Dawn Conklin, Steven R. Childers, and James C. Eisenach

Chronic oral administration of the allosteric adenosine modulator, T62 (2-amino-3-(4-chlorobenzoyl)-5,6,7,8-tetrahydrobenzothiothiophene), at 50 and 100 mg/kg, reduces allodynia in spinal nerve-ligated rats, with minor side effects but with rapid development of tolerance. Radioligand binding studies show that adenosine A1 receptor number is decreased after 4 weeks of chronic exposure to T62, suggesting receptor down-regulation as one mechanism of tolerance.

Possible Mechanism of Irreversible Nerve Injury Caused by Local Anesthetics: Detergent Properties of Local Anesthetics and Membrane Disruption **962**

Norihito Kitagawa, Mayuko Oda, and Tadahide Totoki

Local anesthetics form molecular aggregations, resulting in the appearance of detergent properties and consequent disruption of membranes, or solubilization. Irreversible neurologic injury induced by highly concentrated local anesthetics might be because of the detergent nature of these agents.

Background Infusion Is Not Beneficial during Labor Patient-controlled Analgesia with 0.1% Ropivacaine plus 0.5 $\mu\text{g/ml}$ Sufentanil **968**

Emmanuel Boselli, Richard Debon, Yann Cimino, Thomas Rimmelé, Bernard Allaouchiche, and Dominique Chassard

The results of this study suggest that the use of a background infusion with 0.1% ropivacaine and 0.5 $\mu\text{g/ml}$ sufentanil administered *via* patient-controlled epidural analgesia during labor leads to a greater consumption of anesthetic solution without improving the comfort and satisfaction of parturients.

Epidural Ropivacaine *versus* Epidural Morphine and the Catabolic Response to Colonic Surgery: Stable Isotope Kinetic Studies in the Fasted State and during Infusion of Glucose **973**

Thomas Schricker, Linda Wykes, Leopold Eberhart, Ralph Lattermann, and Franco Carli

The catabolic response to colonic surgery was not suppressed by epidural ropivacaine or epidural morphine, either under fasting conditions or during administration of 4 $\text{mg} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ glucose.

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Influence of Sensory and Proprioceptive Impairment on the Development of Phantom Limb Syndrome during Regional Anesthesia **979**

Xavier Paqueron, Morgan Leguen, Marc E. Gentili, Bruno Riou, Pierre Coriat, and Jean Claude Willer

Parallel assessment of sensorimotor impairment and phantom limb syndrome during the onset of a peripheral nerve block showed that phantom limb position is related to both abolition of proprioception and initial position of the anesthetized limb.

■ **REVIEW ARTICLE**

Drugs and Human Memory (Part 1): Clinical, Theoretical, and Methodologic Issues **987**

Mohamed M. Ghoneim

This article provides a review of issues related to drugs and human memory.

■ **SPECIAL ARTICLE**

A Historical Perspective on Use of the Laryngoscope as a Tool in Anesthesiology **1003**

Christopher M. Burkle, Fernando A. Zepeda, Douglas R. Bacon, and Steven H. Rose

Interest in visualizing the larynx for medical purposes dates back to at least the 18th century. The adoption of the laryngoscope as a tool used in the practice of anesthesia played a significant role in the development of the specialty.

■ **CLINICAL CONCEPTS AND COMMENTARY**

High-frequency Oscillatory Ventilation **1007**

Jean-Christophe Bouchut, Jean Godard, and Olivier Claris

High-frequency oscillatory ventilation is a widely used lung-protective strategy in preterm infants and neonates. The effects of high-frequency oscillatory ventilation on oxygenation and ventilation may be beneficial for those infants during surgery. The article provides an overview of the physiologic basis and reports that enhance this hypothesis.

■ **CLASSIC PAPERS REVISITED**

🌐 **The Birth of Opioid Anesthesia** **1013**

Edward Lowenstein

This article is a revisiting of original material published as follows: Lowenstein E, Hallowell P, Levine F, Daggett WM, Austen WG, Laver MB: Cardiovascular response to large doses of intravenous morphine in man. *N Engl J Med* 1969; 281:1389-93.

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