Anesthesiology

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

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■ CLINICAL INVESTIGATION

◆ Use of Perflubron Emulsion to Decrease Allogeneic Blood Transfusion in High-blood-loss Non-Cardiac Surgery: Results of a European Phase 3 Study **1338**

Donat R. Spahn, Klaus F. Waschke, Thomas Standl, Johann Motsch, Léone Van Huynegem, Martin Welte, Hans Gombotz, Pierre Coriat, Lev Verkh, Simon Faithfull, Peter Keipert, and the European Perflubron Emulsion in Non-Cardiac Surgery Study Group

Perflubron emulsion in combination with augmented acute normovolemic hemodilution reduced the need for allogeneic blood transfusion in the intent-to-treat population at 24 h in patients undergoing major noncardiac surgery, but not until day of discharge. In a protocol-defined target population, *i.e.*, patients with a blood loss of 20 ml/kg or greater, both avoidance of allogeneic blood and its use was significantly reduced through day of hospital discharge.

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Non–steady State Analysis of the Pharmacokinetic Interaction between Propofol and Remifentanil **1350**

Thomas Bouillon, Joergen Bruhn, Lucian Radu-Radulescu, Edward Bertaccini, Sang Park, and Steven Shafer

Coadministration of remifentanil does not alter propofol pharmacokinetics in the clinical relevant concentration range, but coadministration of propofol decreases the central volume of distribution and distributional clearance of remifentanil by 41% and elimination clearance by 15%.

◇🌐 Propofol: Relation between Brain Concentrations, Electroencephalogram, Middle Cerebral Artery Blood Flow Velocity, and Cerebral Oxygen Extraction during Induction of Anesthesia **1363**

Guy L. Ludbrook, Elizabeth Visco, and Arthur M. Lam

Prolonged distribution between the blood and the brain has been demonstrated in humans, with a close relation between brain concentrations and bispectral index.

Validation Study of Two-microphone Acoustic Reflectometry for Determination of Breathing Tube Placement in 200 Adult Patients **1371**

David T. Raphael, Maxim Benbassat, Dimiter Arnaudov, Alex Bohorquez, and Bita Nasseri

Acoustic reflectometry is a rapid, noninvasive method by which to determine whether breathing tube placement is correct (tracheal) or incorrect (esophageal). Reflectometry determination of tube placement may be useful in airway emergencies, particularly in cases where visualization of the glottic area is not possible and capnography fails, as may occur in patients with cardiac arrest.

Modeling of the Sedative and Airway Obstruction Effects of Propofol in Patients with Parkinson Disease undergoing Stereotactic Surgery **1378**

Neus Fábregas, Javier Rapado, Pedro L. Gambús, Ricard Valero, Enrique Carrero, Lydia Salvador, Miguel A. Nalda-Felipe, and Iñaki F. Trocóniz

The modeling of sedation and airway obstruction effects allowed to define a steady state plasma concentration of propofol that assures adequate sedation with minor respiratory effects in patients with Parkinson disease undergoing functional stereotactic surgery.

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◇ Comparison of Acustimulation and Ondansetron for the Treatment of Established Postoperative Nausea and Vomiting **1387**

Margarita Coloma, Paul F. White, Babatunde O. Ogunnaike, Scott D. Markowitz, Philip M. Brown, Alex Q. Lee, Sally B. Berrisford, Cynthia A. Wakefield, Tijani Issioui, Stephanie B. Jones, and Daniel B. Jones

The ReliefBand® acustimulation device was not significantly different from ondansetron (4 mg intravenously) in treating postoperative nausea and vomiting after ambulatory surgery. However, ondansetron further improved the efficacy of the ReliefBand® in the treatment of established postoperative nausea and vomiting.

Pharmacokinetics of Propofol Infusions in Critically Ill Neonates, Infants, and Children in an Intensive Care Unit **1393**

Ann E. Rigby-Jones, Judith A. Nolan, Melanie J. Priston, Peter M. C. Wright, J. Robert Sneyd, and Andrew R. Wolf

Propofol pharmacokinetics are altered in critically ill neonates and infants. Increased peripheral distribution volume and reduced clearance following cardiac surgery causes prolonged elimination.

Pharmacodynamics and Pharmacokinetics of Propofol in a Medium-Chain Triglyceride Emulsion **1401**

Denham S. Ward, J. Russell Norton, Pol-Henri Guivarc'h, Ronald S. Litman, and Peter L. Bailey

In a phase 1, double-blind, crossover clinical trial, propofol emulsified in a medium-chain triglyceride vehicle was compared with Diprivan®. No significant differences in the pharmacokinetics or pharmacodynamics between the two formulations were found; however, significant differences between male and female subjects were found for both drugs.

Changes of Electroencephalographic Bicoherence during Isoflurane Anesthesia Combined with Epidural Anesthesia **1409**

Satoshi Hagihira, Masaki Takashina, Takahiko Mori, Takashi Mashimo, and Ikuto Yoshiya

The heights of two peaks in electroencephalographic bicoherence change with good correlation to the isoflurane concentration.

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Propofol and Sevoflurane in Subanesthetic Concentrations Act Preferentially on the Spinal Cord: Evidence from Multimodal Electrophysiological Assessment **1416**

Thomas Kammer, Benno Rehberg, Dieter Menne, Hans-Christian Wartenberg, Ingobert Wenningmann, and Bernd W. Urban

In human volunteers, subanesthetic concentrations of propofol and sevoflurane profoundly affected spinal motor responses and muscle potentials evoked by transcranial magnetic stimulation. Cortical parameters of electroencephalography and auditory evoked responses were only slightly affected.

Conventional Mechanical Ventilation Is Associated with Bronchoalveolar Lavage-induced Activation of Polymorphonuclear Leukocytes: A Possible Mechanism to Explain the Systemic Consequences of Ventilator-induced Lung Injury in Patients with ARDS **1426**

Haibo Zhang, Gregory P. Downey, Peter M. Suter, Arthur S. Slutsky, and V. Marco Ranieri

Exposure of human polymorphonuclear leukocytes to bronchoalveolar lavage collected in acute respiratory distress syndrome patients ventilated for 36 h with a conventional ventilatory strategy up-regulated the surface markers of cell activation and the release of elastase; this was not seen in patients ventilated for 36 h with a protective ventilatory strategy. The elastase release stimulated by the bronchoalveolar lavage correlated with plasma concentration of interleukin 6 and multiple organ failure score.

◇ Evaluation of Anesthesia Residents Using Mannequin-based Simulation: A Multiinstitutional Study **1434**

Howard A. Schwid, G. Alec Rooke, Jan Carline, Randolph H. Steadman, W. Bosseau Murray, Michael Olympio, Stephen Tarver, Karen Steckner, Susan Wetstone, and the Anesthesia Simulator Research Consortium

Ninety-nine anesthesia residents at 10 institutions were graded on their management of four anesthetic critical incidents using standardized grading forms. Even advanced residents were observed to make management errors, indicating that additional attention to these issues is warranted during anesthesia training. Furthermore, measures of validity and reliability indicate that simulation shows promise as a new method to evaluate anesthesia residents.

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Both Local Anesthetics and Salbutamol Pretreatment Affect Reflex Bronchoconstriction in Volunteers with Asthma undergoing Awake Fiberoptic Intubation **1445**

Harald Groeben, Markus Schlicht, Sven Stieglitz, Goran Pavlakovic, and Jürgen Peters

Lidocaine attenuates reflex bronchoconstriction while dyclonine does not. Salbutamol pretreatment does not eliminate this difference, but attenuates the response even further.

LABORATORY INVESTIGATIONS

Inhibition of Mammalian Gq Protein Function by Local Anesthetics **1451**

Markus W. Hollmann, William E. McIntire, James C. Garrison, and Marcel E. Durieux

Local anesthetics have been shown to inhibit Gq protein signaling in amphibian recombinant models. However, it was not known whether mammalian Gq protein is similarly affected. This article shows that local anesthetics block mouse Gq protein to the same degree as they do frog Gq. Gq inhibition may explain in part the inflammatory modulating properties of local anesthetics.

Evidence for the Involvement of Spinal Cord α_1 Adrenoceptors in Nitrous Oxide–induced Antinociceptive Effects in Fischer Rats **1458**

Ryo Orii, Yoko Ohashi, Tianzhi Guo, Laura E. Nelson, Toshikazu Hashimoto, Mervyn Maze, and Masahiko Fujinaga

The antinociceptive effect of N_2O in rats is partly mediated by α_1 adrenoceptor in the spinal cord.

Effect of Local Anesthetic on Neuronal Cytoplasmic Calcium and Plasma Membrane Lysis (Necrosis) in a Cell Culture Model **1466**

Michael E. Johnson, J. Armando Saenz, Assir Daniel DaSilva, Cindy B. Uhl, and Gregory J. Gores

In a neuronal cell culture model exposed to local anesthetic for 60 min, lidocaine and bupivacaine caused an initial transient increase in cytoplasmic calcium, whose source appeared to be the endoplasmic reticulum. Lidocaine less than 1% and bupivacaine less than 0.625% did not cause further major changes in calcium, and did not cause cell death by 60 min. Lidocaine 2.5 and 5% caused a subsequent large sustained increase in cytoplasmic calcium associated with neuronal death within 60 min.

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Myocardial Effects of Halothane and Isoflurane in Senescent Rats **1477**

Sandrine Rozenberg, Sophie Besse, Benoît Vivien, Pierre Coriat, and Bruno Riou

In spite of marked alterations in the myocardium, the inotropic and lusitropic effects of halothane were less important in senescent than in adult rats, whereas the effects of isoflurane were similar. These differences are probably related to differences in sarcoplasmic reticulum function and in the effects of halogenated anesthetics on the sarcoplasmic reticulum.

Mechanism of Preconditioning by Isoflurane in Rabbits: A Direct Role for Reactive Oxygen Species **1485**

Katsuya Tanaka, Dorothee Weihrauch, Franz Kehl, Lynda M. Ludwig, John F. LaDisa, Jr., Judy R. Kersten, Paul S. Pagel, and David C. Warltier

Isoflurane generates reactive oxygen species (ROS) in rabbit ventricular myocardium, and ROS scavengers abolish isoflurane-induced reductions in myocardial infarct size *in vivo*. The results suggest that direct production of ROS by isoflurane plays an important role in the signaling mechanism responsible for anesthetic preconditioning.

Clonidine and Dexmedetomidine Potently Inhibit Peristalsis in the Guinea Pig Ileum *In Vitro* **1491**

Michael K. Herbert, Susanne Roth-Goldbrunner, Peter Holzer, and Norbert Roewer

Clonidine and dexmedetomidine inhibit peristalsis in the guinea pig ileum *in vitro*. The inhibitory action is mediated through α_2 adrenoceptors and, in the case of clonidine, also involves small conductance Ca^{2+}-activated potassium channels and endogenous opioidergic pathways.

General Anesthetics Do Not Affect Release of the Neuropeptide Cholecystokinin from Isolated Rat Cortical Nerve Terminals **1500**

Victor N. Pashkov, Robert I. Westphalen, and Hugh C. Hemmings, Jr.

Representative intravenous and volatile general anesthetics did not affect basal or stimulated release of the neuropeptide cholecystokinin from isolated central nervous system nerve terminals in contrast to the demonstrable effects of certain anesthetics on the release of amino acid and catecholamine transmitters. Thus, the presynaptic effects of general anesthetics are both transmitter specific and agent specific.

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Karine Nouette-Gaulain, François Forestier, Monique Malgat, Roger Marthan, Jean-Pierre Mazat, and François Sztark

Chronic hypoxia impairs cardiac energy metabolism in left ventricles and enhances the depressant effects of bupivacaine on mitochondrial energy metabolism.

Nonhalogenated Alkanes Cyclopropane and Butane Affect Neurotransmitter-gated Ion Channel and G-protein–coupled Receptors: Differential Actions on $GABA_A$ and Glycine Receptors **1512**

Koji Hara, Edmond I. Eger II, Michael J. Laster, and R. Adron Harris

Effects of nonhalogenated alkane anesthetics cyclopropane and butane on eight recombinant receptors were investigated with *Xenopus* oocytes. Glycine and *N*-methyl-D-aspartate receptors, but not γ-aminobutyric acid type A receptors, may contribute to immobility produced by nonhalogenated alkane anesthetics.

Desflurane Improves Neurologic Outcome after Low-flow Cardiopulmonary Bypass in Newborn Pigs **1521**

Andreas W. Loepke, Margaret A. Priestley, Steven E. Schultz, John McCann, Jeffrey Golden, and C. Dean Kurth

Desflurane improves neurologic outcome following hypothermic low-flow cardiopulmonary bypass compared with fentanyl–droperidol in neonatal piglets, as indicated by better functional outcome and less histologic brain damage. Desflurane also seems to confer myocardial protection in the same setting, as suggested by a lower incidence of ventricular fibrillation.

Isoflurane-induced Cerebral Hyperemia Is Partially Mediated by Nitric Oxide and Epoxyeicosatrienoic Acids in Mice *In Vivo* **1528**

Franz Kehl, Hui Shen, Carol Moreno, Neil E. Farber, Richard J. Roman, John P. Kampine, and Anthony G. Hudetz

Nitric oxide and epoxyeisosatrienoic acids contribute to isoflurane-induced cerebral hyperemia in mice, whereas prostaglandins play a minor role. Other mechanisms, presumably direct vasorelaxant effects on vascular smooth muscle, are also involved since combined blockade of all three pathways only blocked 30% of the hyperemic response to isoflurane.

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Baiping Lei, Susanna Popp, Christine Capuano-Waters, James E. Cottrell, and Ira S. Kass

Delayed administration of a clinical antiarrhythmic dose of lidocaine increases the number of intact neurons in the ischemic penumbral and core regions and improves neurological outcome after transient focal cerebral ischemia in rats.

Inhibitory Effects of Isoflurane and Nonimmobilizing Halogenated Compounds on Neuronal Nicotinic Acetylcholine Receptors **1541**

Takayuki Matsuura, Yoshinori Kamiya, Hideki Itoh, Tomoko Higashi, Yoshitsugu Yamada, and Tomio Andoh

Halogenated anesthetic and nonimmobilizing compounds inhibited rat native neuronal nicotinic acetylcholine receptors independently from their ability to produce the anesthetic state, but sensitivity of the receptors was related to amnesic actions of these agents.

Investigation of Systemic Bupivacaine Toxicity using the *In situ* Perfused Working Heart–Brainstem Preparation of the Rat **1550**

Anthony E. Pickering, Hidefumi Waki, P. Max Headley, and Julian F. R. Paton

In a rat decerebrate, artificially perfused working heart–brainstem preparation, systemic bupivacaine selectively inhibited baroreflex function and attenuated respiratory sinus arrhythmia (RSA) by an action within the brainstem. This selective effect on key brainstem cardiovascular regulatory centers may contribute to the severity of bupivacaine toxicity.

Propofol Increases Pulmonary Artery Smooth Muscle Myofilament Calcium Sensitivity: Role of Protein Kinase C **1557**

Satoru Tanaka, Noriaki Kanaya, Yasuyuki Homma, Derek S. Damron, and Paul A. Murray

The propofol-induced increase in myofilament calcium sensitivity in canine pulmonary artery smooth muscle involves the protein kinase C (PKC) signaling pathway.

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PAIN AND REGIONAL ANESTHESIA

Randomized Controlled Trial Comparing Traditional with Two "Mobile" Epidural Techniques: Anesthetic and Analgesic Efficacy **1567**

Comparative Obstetric Mobile Epidural Trial (COMET) Study Group UK

The Comparative Obstetric Mobile Epidural Trial (COMET). A randomized controlled trial comparing traditional epidural analgesia with two forms of "mobile" epidural for labor. Anesthetic and analgesic efficacy.

Postural Stability following Ambulatory Regional Analgesia for Labor **1576**

Jeremy Davies, Roshan Fernando, Andrew McLeod, Sonia Verma, and Philip Found

Using the Balance Master 6.1 Computerised Dynamic Posturography system, the authors found that being pregnant at term significantly affects balance function compared with nonpregnant women. However, receiving initial low-dose spinal epidural analgesia for labor does not impair function further.

Fetal and Maternal Effects of Phenylephrine and Ephedrine during Spinal Anesthesia for Cesarean Delivery **1582**

David W. Cooper, Mark Carpenter, Paul Mowbray, William R. Desira, David M. Ryall, and Manmohan S. Kokri

This study found that using an infusion of phenylephrine to maintain systolic arterial pressure during spinal anesthesia for elective cesarean delivery can decrease fetal acidosis and maternal nausea and vomiting, compared with using ephedrine alone. There was no advantage in combining phenylephrine and ephedrine because it increased maternal nausea and vomiting, and it did not further improve fetal blood gas values, compared with using phenylephrine alone.

Mechanisms of Postoperative Pain: Clinical Indications for a Contribution of Central Neuronal Sensitization **1591**

Jesper Dirks, Steen Møiniche, Karen-Lisa Hilsted, and Jørgen B. Dahl

A significant association was observed between the effect of remifentanil on wound hyperalgesia and heat-induced secondary hyperalgesia in surgical patients.

Microinjection of an Adenosine A_1 Agonist into the Medial Pontine Reticular Formation Increases Tail Flick Latency to Thermal Stimulation **1597**

Diana Tanase, Helen A. Baghdoyan, and Ralph Lydic

An adenosine A_1 receptor agonist caused antinociception when microinjected into pontine reticular formation regions known to regulate sleep.

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Shao-Rui Chen, Kristi L. Sweigart, Joan M. Lakoski, and Hui-Lin Pan

The [^{35}S]GTPγS binding stimulated by the μ opioid receptor agonist, DAMGO, is significantly reduced in the spinal cord dorsal horn of diabetic rats. However, [^{35}S]GTPγS bindings stimulated by several other G protein-coupled receptor agonists and the expression of G_i and G_o proteins in the dorsal spinal cord are not significantly altered in diabetic rats.

REVIEW ARTICLE

Anesthesia Safety: Model or Myth?: A Review of the Published Literature and Analysis of Current Original Data **1609**

Robert S. Lagasse

The medical literature and current original data do not support the claim that anesthesia-related mortality rates have improved dramatically over the past three decades.

CLINICAL CONCEPTS AND COMMENTARY

Perioperative Atrial Tachyarrhythmias **1618**

David Amar

Rapid atrial arrhythmias affect close to one million elderly Americans who undergo cardiac or noncardiac operations annually. This commentary focuses on the pathophysiology and management of this complication in the perioperative period.

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