



Anesthesiology



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Excellence in Research Award 777
Alex S. Evers

■ CLINICAL INVESTIGATIONS

- ◆ A Model of the Ventilatory Depressant Potency of
Remifentanyl in the Non-steady State 779
*Thomas Bouillon, Joergen Bruhn, Lucian Radu-Radulescu,
Corina Andresen, Carol Cohane, and Steven L. Shafer*

Remifentanyl is a potent ventilatory depressant. The C_{50} for suppression of carbon dioxide elimination from non-steady state data above, at, and below the metabolic hyperbola is 0.92 ng/ml, in excellent agreement with C_{50} s derived from isohypercapnic designs.

- ◆ Pharmacodynamic Effect of Morphine-6-glucuronide
versus Morphine on Hypoxic and Hypercapnic Breathing
in Healthy Volunteers 788
Raymonda Romberg, Erik Olofson, Elise Sarton, Luc Teppema, and Albert Dahan

In humans, morphine is 19-50 times more potent in depressing ventilation than morphine's metabolite, morphine-6-glucuronide. Whereas a lesser morphine concentration is needed to obtain a similar level of depression of hypoxic breathing and hypercapnic breathing, the reverse is true for morphine-6-glucuronide.

- ◇ Mouth Opening: A New Angle 799
*Ian Calder, John Picard, Martin Chapman, Caoimhe O'Sullivan, and
H. Alan Crockard*

Mouth opening and craniocervical movement are interrelated.



- Ability of the Bispectral Index, Autoregressive Modelling with Exogenous Input-derived Auditory Evoked Potentials, and Predicted Propofol Concentrations to Measure Patient Responsiveness during Anesthesia with Propofol and Remifentanyl** **802**

Michel M. R. F. Struys, Hugo Vereecke, Annelies Moerman, Erik Weber Jensen, David Verhaeghen, Nicolaas De Neve, Frank J. E. Dumortier, and Eric P. Mortier

Although the Bispectral Index, A-line autoregressive model with an exogenous input index, and propofol effect-site concentration were influenced by remifentanyl during propofol administration, their ability to detect Observer's Assessment of Alertness/Sedation Scale score and loss of eyelash reflex remained accurate. Improved performance is obtained when the Bispectral Index and A-line autoregressive model with an exogenous input index are measured in conjunction with drug effect-site concentrations. Remifentanyl decreases the ability of these independent variables to detect loss of response to noxious stimulus.

- Effect of Auditory Evoked Potential Index Monitoring on Anesthetic Drug Requirements and Recovery Profile after Laparoscopic Surgery: A Clinical Utility Study** **813**

Alejandro Recart, Paul F. White, Agnes Wang, Irina Gasanova, Stephanie Byerly, and Stephanie B. Jones

The addition of auditory evoked potential monitoring during maintenance of general anesthesia reduced the intraoperative anesthetic (desflurane) and analgesic (fentanyl) requirements, contributing to a decreased duration of recovery room stay and reduced incidence of postoperative nausea and vomiting. This clinical utility study suggests that auditory evoked potential monitoring may be a useful supplement to standard clinical monitors for facilitating the recovery process after laparoscopic surgical procedures.

- Participation of Children in Clinical Research: Factors that Influence a Parent's Decision to Consent** **819**

Alan R. Tait, Terri Voepel-Lewis, and Shobha Malviya

This study examines factors that influence parents to consent to their child's participation in clinical research.

- Sevoflurane Provides Greater Protection of the Myocardium than Propofol in Patients Undergoing Off-pump Coronary Artery Bypass Surgery** **826**

Peter F. Conzen, Susanne Fischer, Christian Detter, and Klaus Peter

Sevoflurane was associated with lower release of cardiac troponin I and better recovery of cardiac function than propofol in patients undergoing off-pump coronary artery surgery.

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High-dose Remifentanyl Does Not Impair Cerebrovascular Carbon Dioxide Reactivity in Healthy Male Volunteers 834

Walter Klimscha, Roman Ullrich, Christian Nasel, Wolfgang Dietrich, Udo M. Illievich, Eckart Wildling, Edda Tschernko, Claudia Weidekamm, Leopold Adler, Georg Heikenwalder, Gyongyi Horvath, and Robert N. Sladen

High-dose remifentanyl decreases cerebral blood flow without impairing cerebrovascular reactivity to acute alterations in arterial carbon dioxide tension. This, together with its short duration of action, suggests that remifentanyl could be a useful agent in the intensive care unit when sedation that can be titrated rapidly is required.

Total Oxygen Uptake with Two Maximal Breathing Techniques and the Tidal Volume Breathing Technique: A Physiologic Study of Preoxygenation 841

Jaideep J. Pandit, Thomas Duncan, and Peter A. Robbins

This study compares three common methods of preoxygenation using total oxygen uptake as measured by breath-by-breath net gas exchange at the mouth as the endpoint.

Cardiopulmonary Bypass Has Minimal Effects on the Pharmacokinetics of Fentanyl in Adults 847

Robert J. Hudson, Ian R. Thomson, Rajive Jassal, David J. Peterson, Aaron D. Brown, and Jeffrey I. Freedman

Pharmacokinetic models for fentanyl that allowed for step-changes in parameters at the start and/or end of cardiopulmonary bypass did not significantly improve overall predictive ability compared to a simple, three-compartment model that was not adjusted for cardiopulmonary bypass. This simple model had good predictive ability when tested prospectively in a second series of patients.

Effect of Nitroglycerin Inhalation on Patients with Pulmonary Hypertension Undergoing Mitral Valve Replacement Surgery 855

Nurgul Yurtseven, Pelin Karaca, Mehmet Kaplan, Vedat Ozkul, Abdullah K. Tuygun, Tamer Aksoy, Sevim Canik, and Ercument Kopman

Nitroglycerin inhalation produced a significant reduction in both mean pulmonary artery pressure and pulmonary vascular resistance in patients who underwent mitral valve operations without reducing mean arterial pressure and systemic vascular resistance.



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Jonathan B. Lesser, Kevin V. Sanborn, Rytis Valskys, and Max Kuroda

■ LABORATORY INVESTIGATIONS

- ◆ Calreticulin Mediates Anesthetic Sensitivity in *Drosophila melanogaster* 867

Sumiko Gamo, Junya Tomida, Katsuyuki Dodo, Dai Keyakidani, Hitoshi Matakatsu, Daisuke Yamamoto, and Yoshiharu Tanaka

The authors describe a hypersensitive mutant for diethylether anesthesia caused by low expression of calreticulin gene in *Drosophila melanogaster*.

- ◇ The Neuroprotective Effect of Xenon Administration during Transient Middle Cerebral Artery Occlusion in Mice 876

H. Mayumi Homi, Noriko Yokoo, Daqing Ma, David S. Warner, Nicholas P. Franks, Mervyn Maze, and Hilary P. Grocott

Xenon administration improved both functional and histologic outcome in a model of transient focal cerebral ischemia in mice.

- Isoflurane Reduction of Carbachol-evoked Cytoplasmic Calcium Transients Is Dependent on Caffeine-sensitive Calcium Stores 882

Alexandra Corrales, Fang Xu, Zayra Garavito-Aguilar, Thomas J. J. Blanck, and Esperanza Recio-Pinto

Isoflurane reduction of the carbachol-evoked $[Ca^{2+}]_{cyt}$ increase requires full caffeine-sensitive Ca^{2+} stores and Ca^{2+} release from the caffeine-sensitive stores through the ryanodine-sensitive Ca^{2+} release channels. This study demonstrates that isoflurane interferes with muscarinic Ca^{2+} signaling through a mechanism downstream from the muscarinic receptors.

- Activation of α_{2B} -Adrenoceptors Mediates the Cardiovascular Effects of Etomidate 889

Andrea Paris, Melanie Philipp, Peter H. Tonner, Markus Steinfath, Martin Lohse, Jens Scholz, and Lutz Hein

Investigations in gene-targeted mice lacking α_2 -adrenoceptors show that the α_{2B} -adrenoceptor mediates a transient hypertensive response of etomidate after intravenous injection. The sedative effects of etomidate are not altered in α_2 -adrenoceptor-deficient mice.



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Isoflurane Pretreatment Has Immediate and Delayed Protective Effects against Cytokine-induced Injury in Endothelial and Vascular Smooth Muscle Cells 896

Manuela J. M. de Klaver, Mary-Gordon Buckingham, and George F. Rich

Isoflurane pretreatment has immediate and delayed protective effects against cytokine-induced injury in endothelial and vascular smooth muscle cells that are modulated *via* mitochondrial adenosine triphosphate-sensitive potassium channels.

◇ Comparison of Intracarotid and Intravenous Propofol for Electroencephalographic Silence in Rabbits 904

Mei Wang, Shailendra Joshi, and Ronald G. Emerson

Intracarotid propofol resulted in electroencephalographic silence at a fraction of the intravenous dose that was not associated with systemic hypotension or a sustained reduction in ipsilateral cerebral blood flow. Intracarotid anesthetics could be potentially useful for providing electroencephalographic silence when cerebral perfusion is at risk.

Effects of Antidepressants on G Protein-coupled Receptor Signaling and Viability in *Xenopus laevis* Oocytes 911

Danja Strümper, Marcel E. Durieux, Barbara Tröster, Klaus Hahnenkamp, Cristina Vitan, Christel G. den Bakker, and Markus W. Hollmann

Although antidepressants are being investigated as local anesthetics, it is not clear if their molecular and cellular effects are similar to those of local anesthetics. This article shows that some antidepressants do not inhibit G protein-coupled signaling (as local anesthetics do) but induce profound cellular toxicity.

■ PAIN AND REGIONAL ANESTHESIA

Use of a Continuous Local Anesthetic Infusion for Pain Management after Median Sternotomy 918

Paul F. White, Shivani Rawal, Paige Latham, Scott Markowitz, Tijani Issioui, Lei Chi, Suzanne Dellaria, Chen Shi, Lisa Morse, and Caleb Ing

This study demonstrated that the use of a local anesthetic infusion of bupivacaine 0.5% reduced chest pain and the need for opioid analgesic medication after median sternotomy procedures. In addition, the local anesthetic infusion improved patient satisfaction with their pain management and reduced the length of hospital stay.



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Acetazolamide Reduces Referred Postoperative Pain after Laparoscopic Surgery with Carbon Dioxide Insufflation 924

Harvey J. Woehlick, Mary Otterson, Hyun Yun, Lois A. Connolly, Daniel Eastwood, and Krista Colpaert

Intravenous acetazolamide (5 mg/kg) given intraoperatively reduced referred pain scores after laparoscopic surgery. The benefit was limited to the time shortly after surgery within the recovery room.

⊕ Pharmacokinetics of an Implanted Osmotic Pump Delivering Sufentanil for the Treatment of Chronic Pain 929

Dennis M. Fisher, Norma Kellett, and Rainer Lenhardt

When administered subcutaneously as a concentrated solution in benzyl alcohol, sufentanil's bioavailability does not differ from 100% and its absorption half-life is 16 h.

Immunoneutralization of c-Fos Using Intrathecal Antibody Electroporation Attenuates Chronic Constrictive Injury-induced Hyperalgesia and Regulates Preprodynorphin Expression in Rats 938

Chen-Yu Lan, Ping-Heng Tan, Jiin-Tsuey Cheng, Hsiao-Feng Lu, Ming-Wei Lin, Po-Ni Hsiao, and Chung-Ren Lin

c-Fos antibody was successfully transferred into rat spinal cords by intrathecal electroporation. This provides an effective method to alleviate hyperalgesia and allodynia in mononeuropathic rats.

Brain Stem Opioidergic and GABAergic Neurons Mediate the Antinociceptive Effect of Nitrous Oxide in Fischer Rats 947

Yoko Ohashi, Tianzhi Guo, Ryo Orii, Mervyn Maze, and Masahiko Fujinaga

N₂O-induced opioid peptide release leads to inhibition of γ -aminobutyric acid-mediated neurons *via* opioid receptors by multiple mechanisms in the brain stem that work in concert. The descending noradrenergic inhibitory neurons, which are tonically inhibited by γ -aminobutyric acid-mediated neurons, are activated and modulate pain processing in the spinal cord.

Inhibition of Inflammatory Hyperalgesia by Activation of Peripheral CB₂ Cannabinoid Receptors 955

Aline Quartilho, Heriberto P. Mata, Mohab M. Ibrahim, Todd W. Vanderah, Frank Porreca, Alexandros Makriyannis, and T. Philip Malan, Jr.

Selective activation of peripheral CB₂ cannabinoid receptors inhibits inflammatory pain.

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Comparative Neurotoxicity of Intrathecal and Epidural Lidocaine in Rats 961

Yumiko Kirihara, Yoji Saito, Shinichi Sakura, Keishi Hashimoto, Tomomune Kishimoto, and Yukihiko Yasui

Epidural lidocaine induces less severe functional impairment and morphologic damage in the rat than does intrathecal lidocaine.

Synergistic Antinociceptive Effects of Ketamine and Morphine in the Orofacial Capsaicin Test in the Rat 969

Pedro Alvarez, Gloria Saavedra, Alejandro Hernández, Carlos Paeile, and Teresa Pelissier

Antinociceptive effects of ketamine, morphine, and the interaction of both drugs were studied in the orofacial capsaicin test in rats. Whereas each drug on its own exhibited antinociceptive effects, the ketamine + morphine association was superadditive in this model of acute tonic orofacial pain.

Orally Administered Paracetamol Does Not Act Locally in the Rat Formalin Test: Evidence for a Supraspinal, Serotonin-dependent Antinociceptive Mechanism 976

Jérôme Bonnefont, Abdelkrim Alloui, Eric Chapuy, Eric Clottes, and Alain Eschaliér

Orally administered paracetamol seems to exert no relevant local action in the rat formalin test, but it might activate the serotonergic bulbospinal pathways *via* a supraspinal site of action, that remains to be elucidated.

■ REVIEW ARTICLE

◆ A Systematic Review of the Safety and Effectiveness of Fast-track Cardiac Anesthesia 982

Paul S. Myles, David J. Daly, George Djaiani, Anna Lee, and Davy C. H. Cheng

This systematic review of randomized controlled trials shows that fast-track techniques result in a shorter length of stay in the intensive care unit and are at least equal in terms of 30-day mortality and major morbidity rates, when compared with traditional high-dose opioid techniques in cardiac anesthesia.

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The Instructions for Authors are published in the January and July issues and are available at www.anesthesiology.org. Please refer to the Instructions for the preparation of any material for submission to ANESTHESIOLOGY.

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