



ON THE COVER:

In this issue of ANESTHESIOLOGY, James C. Eisenach, M.D., ANESTHESIOLOGY's Editor-in-Chief from 2007 to this issue of the journal, discusses the contributions of Emery Rovenstine to the evolution of the practice of our specialty. Several other articles appear in this issue that highlight the evolution of ethics in our specialty, including the evolution of the intraoperative anesthetic record from the handwritten record of Robert Dripps shown on the cover (Johnstone and Fleisher) to ethics in modern education (Schwartz) and patients' perspectives on giving informed consent for research on the morning of surgery (Murphy *et al.*). In addition, Huffmyer and her colleagues raise the problem faced by modern anesthesiology training programs by demonstrating that lapses in driving performance are common after overnight work in the hospital.

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- Johnstone and Fleisher: A 1966 Anesthetic Administered by Robert D. Dripps, M.D., Demonstrated His Experimental Style of Clinical Care, p. 1218
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SPECIAL ARTICLES

- ◆◆ **A 1966 Anesthetic Administered by Robert D. Dripps, M.D., Demonstrated His Experimental Style of Clinical Care** 1218
R. E. Johnstone and L. A. Fleisher

An anesthesia record of Robert Dripps, M.D., from 1966 illustrates his philosophy that clinical anesthetics are research studies. This philosophy led in 1967 to criticisms over patient consents, which changed his teaching.

- 49 Mathoura Road: Geoffrey Kaye's Center of Excellence for the Australian Society of Anaesthetists** 1222
M. L. Edwards and D. B. Waisel

Through letters written by Geoffrey Kaye to Paul Wood (1939 to 1955) and to Gwenifer Wilson (1981 to 1983), we present Kaye's design and intent for his Australian center of excellence, and his views regarding its failure.

PERIOPERATIVE MEDICINE

CLINICAL SCIENCE

- CMR ◆◆ **Effects of Volatile Anesthetics on Mortality and Postoperative Pulmonary and Other Complications in Patients Undergoing Surgery: A Systematic Review and Meta-analysis** 1230
C. Uhlig, T. Bluth, K. Schwarz, S. Deckert, L. Heinrich, S. De Hert, G. Landoni, A. Serpa Neto, M. J. Schultz, P. Pelosi, J. Schmitt, and M. Gama de Abreu

In this systematic literature review and meta-analysis conducted for 68 randomized controlled trials including 7,104 patients, it was found that in cardiac, but not in noncardiac, surgery, compared to total intravenous anesthesia, general anesthesia with volatile anesthetics was associated with major benefits in outcome, including reduced mortality, as well as lower incidence of pulmonary and other complications. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

- ◆ **Consent for Anesthesia Clinical Trials on the Day of Surgery: Patient Attitudes and Perceptions** 1246
G. S. Murphy, J. W. Szokol, M. J. Avram, S. B. Greenberg, T. D. Shear, J. S. Vender, and E. Landry

In a survey distributed to 200 patients who provided informed consent for anesthesia research on the day of surgery, 96% of respondents were satisfied with the consent process, and most disagreed that they were anxious, felt obligated to participate, or had regrets about participation.

- Postoperative Urinary Catheterization Thresholds of 500 versus 800 ml after Fast-track Total Hip and Knee Arthroplasty: A Randomized, Open-label, Controlled Trial** 1256
L. S. Bjerregaard, U. Hornum, C. Trolborg, S. Bogoe, P. Bagi, and H. Kehlet

Eight hundred patients having major orthopedic surgery were randomized, with 721 providing per-protocol results. Thirteen percent of patients assigned to the 800-ml threshold were catheterized, whereas 32% were in the 500-ml group. Urinary complications did not differ. An 800-ml catheterization threshold thus appears preferable.

- ◆ **Convergent Validity of Three Methods for Measuring Postoperative Complications** 1265
B. A. Fritz, K. E. Escallier, A. Ben Abdallah, J. Oberhaus, J. Becker, K. Geczi, S. McKinnon, D. L. Helsten, A. Sharma, T. S. Wildes, and M. S. Avidan

In a study of over 1,500 subjects more than 30 days after surgery, patient-reported outcomes, compared to automated or manual chart review, demonstrated poor-to-moderate positive agreement (0 to 58%) and excellent negative agreement (82 to 100%). Discrepancies frequently reflected patients reporting events that occurred outside the time period of interest, suggesting that more effective in-hospital communication and thoughtful survey design may improve the value of patient-reported outcomes. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

- Anticoagulant Effect of Sugammadex: Just an *In Vitro* Artifact** 1277
D. Dirkmann, M. W. Britten, H. Pauling, J. Weidle, L. Volbracht, K. Görlinger, and J. Peters

Sugammadex affects various coagulation assays by the binding of phospholipids by the cyclodextrin molecules, and this represents an *in vitro* artifact observed in commercial phospholipid-dependent assays such as the activated partial thromboplastin time.

Management of One-lung Ventilation: Impact of Tidal Volume on Complications after Thoracic Surgery

1286

R. S. Blank, D. A. Colquhoun, M. E. Durieux, B. D. Kozower, T. L. McMurry, S. P. Bender, and B. I. Naik

Analysis from 1,019 patients undergoing one-lung ventilation indicated that low tidal volume in the presence of low positive end-expiratory pressure is associated with increased pulmonary complications. This suggests that low tidal volume during one-lung ventilation is protective only when accompanied by adequate positive end-expiratory pressure.

BASIC SCIENCE

◆◆ Proteomic Profiling Reveals Adaptive Responses to Surgical Myocardial Ischemia–Reperfusion in Hibernating Arctic Ground Squirrels Compared to Rats

1296

Q. J. Quinones, Z. Zhang, Q. Ma, M. P. Smith, E. Soderblom, M. A. Moseley, J. Bain, C. B. Newgard, M. J. Muehlbauer, M. Hirschey, K. L. Drew, B. M. Barnes, and M. V. Podgoreanu

Applying gene ontology analysis to hibernating arctic ground squirrels, the authors have found that the natural cardiac protective adaptations of hibernators involve metabolic shifts in fatty acid metabolism proteins, reductions in toxic lipid metabolites, and up-regulation of sirtuins. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

General Anesthesia Causes Epigenetic Histone Modulation of c-Fos and Brain-derived Neurotrophic Factor, Target Genes Important for Neuronal Development in the Immature Rat Hippocampus

1311

L. Dalla Massara, H. P. Osuru, A. Oklopic, D. Milanovic, S. M. Joksimovic, V. Caputo, M. R. DiGrucchio, C. Ori, G. Wang, S. M. Todorovic, and V. Jevtovic-Todorovic

Exposure to general anesthesia during critical stages of synaptogenesis modulated expression and function of the key transcription factors, cAMP-responsive element-binding protein (CREB) and CREB-binding protein. CREB-binding protein and CREB modulation may, in turn, cause epigenetic changes manifested as histone hypoacetylation, leading to down-regulated transcription of the target genes cellular Finkel-Biskis-Jenkins murine sarcoma virus osteosarcoma oncogene and brain-derived neurotrophic factor, which play an important role in neuronal development.

Lipid-free Fluoropolymer-based Propofol Emulsions and Lipid Reversal of Propofol Anesthesia in Rats

1328

C. L. Parks, W. Tucker, C. A. Amlong, S. Mecozzi, and R. A. Pearce

Three propofol nanoemulsions prepared using novel semifluorinated surfactants were as effective and as potent as Diprivan in impairing the righting reflex of rats with bolus dosing, without apparent toxic effects. A bolus of lipid emulsion accelerated clearance of propofol from its effect site after an induction dose of either lipid-based Diprivan or lipid-free fluoropolymer-based emulsions but was more effective for the lipid-free emulsion.

■ CRITICAL CARE MEDICINE


CLINICAL SCIENCE

Influence of Diaphragmatic Motion on Inferior Vena Cava Diameter Respiratory Variations in Healthy Volunteers

1338

L. Gignon, C. Roger, S. Bastide, S. Alonso, L. Zieleskiewicz, H. Quintard, L. Zoric, X. Bobbia, M. Raux, M. Leone, J.-Y. Lefrant, and L. Muller

In 52 spontaneously breathing healthy adults, respiratory variation of collapsibility of central vena cava (cIVC) was associated with inspiratory effort and diaphragmatic motion. This study identified a gray zone of the diaphragmatic motion ranging from 25 to 43 mm for predicting cIVC more than or equal to 40%. This study suggests, although not tested, inaccuracy of cIVC for determining fluid responsiveness when the diaphragmatic motion is more than 25 mm.

-  **Differential Perceptions of Noninvasive Ventilation in Intensive Care among Medical Caregivers, Patients, and Their Relatives: A Multicenter Prospective Study—The PARVENIR Study** 1347
M. Schmidt, E. Boutmy-Deslandes, S. Perbet, N. Mongardon, M. Dres, K. Razazi, E. Guerot, N. Terzi, P. Andrivet, M. Alves, R. Sonnevill, C. Cracco, V. Peigne, F. Collet, B. Sztrymf, C. Rafat, D. Reuter, X. Fabre, V. Labbe, G. Tachon, C. Minet, M. Conseil, E. Azoulay, T. Similowski, and A. Demoule

A large-sample questionnaire (396 patients, 1,063 clinicians, and 145 relatives) from 32 intensive care units revealed that concerns about noninvasive ventilation were greatest among nurses (workload) and patients (dyspnea, anxiety). Future research may reveal how to improve the effectiveness and acceptance of noninvasive ventilation. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

BASIC SCIENCE

-  **Therapeutic Whole-body Hypothermia Protects Remote Lung, Liver, and Kidney Injuries after Blast Limb Trauma in Rats** 1360
J. Ning, L. Mo, B. Yi, J. Gu, K. Lu, Y. Zhou, X. Lai, H. Zhao, and D. Ma


Whole-body hypothermia for 3 h immediately after injury in an experimental animal model provides multiorgan protection for traumatic injury after blast trauma. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

■ PAIN MEDICINE

CLINICAL SCIENCE

- Liposome Bupivacaine Femoral Nerve Block for Postsurgical Analgesia after Total Knee Arthroplasty** 1372
A. Hadzic, H. S. Minkowitz, T. I. Melson, R. Berkowitz, A. Uskova, F. Ringold, J. Lookabaugh, and B. M. Ilfeld

In a two-part clinical study designed to meet the U.S. Food and Drug Administration standard for approval of analgesic agents, femoral nerve block with liposome bupivacaine after total knee arthroplasty resulted in modestly reduced average pain and opioid use in the first 72 h after surgery compared with placebo. Side effects were similar in both groups, supporting further investigation.

-  **Injury and Liability Associated with Implantable Devices for Chronic Pain** 1384
D. R. Fitzgibbon, L. S. Stephens, K. L. Posner, E. Michna, J. P. Rathmell, K. A. Pollak, and K. B. Domino


Claims related to surgical implantation of devices involved infection, inadequate pain relief, trauma to the cord or cauda equina, and retained catheter fragments. Claims related to implanted drug delivery system maintenance tended to involve more serious outcomes associated with medication administration errors and failure to recognize granuloma formation.

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J. L. Huffmyer, M. Moncrief, J. A. Tashjian, A. M. Kleiman, D. C. Scalzo, D. J. Cox, and E. C. Nemergut

Resident physicians have greater difficulty controlling speed and driving performance in the driving simulator after six consecutive night shifts. Reaction times are also increased with emphasis on increases in minor and major lapses in attention after six consecutive night shifts.

CLINICAL CONCEPTS AND COMMENTARY

- ◇ **Epiglottitis: It Hasn't Gone Away** 1404
J. L. Lichtor, M. Roche Rodriguez, N. L. Aaronson, T. Spock, T. R. Goodman, and E. D. Baum

Due to the potentially unforgiving nature of epiglottitis and supraglottitis, the clinician should have a firm understanding of the presentation, work up, and management of a patient presenting with worrisome symptoms.

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