



ON THE COVER:



Postoperative cognitive dysfunction is common. It remains uncertain if there are long-term adverse cognitive effects that are attributable to surgery combined with anesthesia. In this issue of *ANESTHESIOLOGY*, Dokkedal *et al.* examined the association between exposure to surgery and level of cognitive function in a sample of 8,503 middle-aged and elderly twins. In an accompanying Editorial View, Avidan and Evers argue based on the existing evidence that persistent postoperative dysfunction is largely a fallacy. Their arguments are highlighted in this month's infographic.

- Dokkedal *et al.*: Cognitive Functioning after Surgery in Middle-aged and Elderly Danish Twins, p. 312
- Avidan and Evers: The Fallacy of Persistent Postoperative Cognitive Decline, p. 255
- Infographics in Anesthesiology: Persistent Postoperative Cognitive Decline? A Pyramid of Evidence, p. 21A

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The American Society of Anesthesiologists Committee on Standards and Practice Parameters and the Task Force on Obstetric Anesthesia and the Society for Obstetric Anesthesia and Perinatology present an updated report of the Practice Guidelines for Obstetric Anesthesia. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

- ◆ Refers to This Month in Anesthesiology
- ◆ Refers to Editorial Views

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- ◆ **An Anesthesiologist's Perspective on the History of Basic Airway Management: The "Preanesthetic" Era—1700 to 1846** 301
A. A. Matioc

The modern history of basic airway management started in the early 18th century. The preanesthetic era (1700 to 1846) saw the rise and fall of the positive pressure ventilation and its replacement with negative pressure ventilation.

■ PERIOPERATIVE MEDICINE

CLINICAL SCIENCE

- CME ◆ **Cognitive Functioning after Surgery in Middle-aged and Elderly Danish Twins** 312
U. Dokkedal, T. G. Hansen, L. S. Rasmussen, J. Mengel-From, and K. Christensen

In a study of 8,503 twins, a negligible but statistically significant decrease in a sensitive composite cognitive score was present in twins with at least one major surgery, but there was no difference by intrapair analysis. There was no clinically significant association of major surgery and anesthesia with long-term cognitive dysfunction, suggesting that factors other than surgery and anesthesia are more important.

- ◆ **Prolonged Operative Time to Extubation Is Not a Useful Metric for Comparing the Performance of Individual Anesthesia Providers** 322
E. O. Bayman, F. Dexter, and M. M. Todd

In a review of over 27,000 anesthetics in a university practice, approximately 20% of extubations were prolonged, with 95% confidence bounds spanning less than 1%. By a frequentist approach on this small variance data set, 40% of individual anesthesiologists were outliers, whereas with a Bayesian approach only 1% were. Focusing on changing extubation times only for practitioners who were outliers would have minimal effect on operating room workflow. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

- ◆ **Platelet Counts, Acute Kidney Injury, and Mortality after Coronary Artery Bypass Grafting Surgery** 339
M. D. Kertai, S. Zhou, J. A. Karhausen, M. Cooter, E. Jooste, Y.-J. Li, W. D. White, S. Aronson, M. V. Podgoreanu, J. Gaca, I. J. Welsby, J. H. Levy, M. Stafford-Smith, J. P. Mathew, and M. L. Fontes

The authors performed a retrospective observational study of the association between postoperative nadir platelet counts, acute kidney injury, and mortality in coronary artery bypass grafting (CABG) surgery. The authors found a significant independent association between postoperative nadir platelet counts, acute kidney injury, and mortality after CABG surgery. The work suggests that the potential platelet-related ischemic events during the CABG surgery warrant further investigation. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

- ◆ **Cerebrospinal Fluid Biomarker for Alzheimer Disease Predicts Postoperative Cognitive Dysfunction** 353
L. Evered, B. Silbert, D. A. Scott, D. Ames, P. Maruff, and K. Blennow

There was an association between low preoperative levels of amyloid β in the cerebrospinal fluid and postoperative cognitive dysfunction (POCD) at 3 months; POCD was not observed at 12 months. Patients with Alzheimer's disease neuropathology, identified by low cerebrospinal fluid levels of amyloid β , may be at an increased risk of POCD even in the absence of clinically detectable symptoms.

- Dexmedetomidine versus Propofol Sedation Reduces Delirium after Cardiac Surgery: A Randomized Controlled Trial** 362
G. Djaiani, N. Silverton, L. Fedorko, J. Carroll, R. Styra, V. Rao, and R. Katznelson

When compared with propofol, dexmedetomidine sedation reduced incidence, delayed onset, and shortened duration of postoperative delirium in elderly patients after cardiac surgery.

Severity of Myasthenia Gravis Influences the Relationship between Train-of-four Ratio and Twitch Tension and Run-down of Rat Endplate Potentials

369

K. Takahashi, T. Niiya, Y. Takada, E. Narimatsu, and M. Yamakage

A rat model was developed to study different severities of myasthenia gravis. Phrenic nerve–stimulated diaphragmatic responses to a standardized rocuronium dose were recorded *in vitro*. With increasing myasthenia gravis severity, train-of-four and the first twitch became less reliable indicators of muscle strength during recovery from neuromuscular blockade, indicating that the evaluation of neuromuscular blockade by train-of-four ratio may overestimate the extent of recovery.

In Vitro Comparative Effect of Carbetocin and Oxytocin in Pregnant Human Myometrium with and without Oxytocin Pretreatment

378

N. M. Cole, J. C. A. Carvalho, M. Erik-Soussi, N. Ramachandran, and M. Balki

Oxytocin produced stronger contractions of term pregnant human myometrium *in vitro* than did carbetocin over the entire range of equimolar concentrations studied. Oxytocin pretreatment of term pregnant human myometrium *in vitro* attenuated contractions produced by both oxytocin and carbetocin.

Morbidity and Mortality after High-dose Transfusion

387

D. J. Johnson, A. V. Scott, V. M. Barodka, S. Park, J. O. Wasey, P. M. Ness, T. Gniadek, and S. M. Frank

Mortality increased linearly with erythrocyte dose, reaching 50% in patients given more than 50 units of blood. Infection and thrombotic events were the most common complications.

◆ Impact of Perioperative Epidural Placement on Postdischarge Opioid Use in Patients Undergoing Abdominal Surgery

396

K. S. Ladha, E. Patorno, J. Liu, and B. T. Bateman

In a review of over 6,400 patients who underwent open abdominal surgery, propensity-matched analysis showed no effect of use of epidural analgesia on time to discontinuation of opioids after hospital discharge or dose of opioids administered in the first 90 days after discharge. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

BASIC SCIENCE

Sleep Homeostasis and General Anesthesia: Are Fruit Flies Well Rested after Emergence from Propofol?

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B. Gardner, E. Strus, Q. C. Meng, T. Coradetti, N. N. Naidoo, M. B. Kelz, and J. A. Williams

Propofol produced anesthesia in the fruit fly *Drosophila*, but it did not dissipate sleep debt or satisfy the homeostatic need for sleep in contrast to rodents. Further studies will be required to validate the findings in both rodents and flies and reconcile the apparent species-specific differences in the interactions between natural sleep and general anesthesia.

◆ Inflammation Increases Neuronal Sensitivity to General Anesthetics

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S. Avramescu, D.-S. Wang, I. Lecker, W. T. H. To, A. Penna, P. D. Whissell, L. Mesbah-Oskui, R. L. Horner, and B. A. Orser

The inflammatory cytokine interleukin-1 β increased γ -aminobutyric acidergic inhibitory currents in the presence of etomidate or isoflurane in cultured mouse hippocampal and cortical neurons. In a mouse model of sepsis, behavioral sensitivity to both anesthetics was increased. The clinical relevance of these findings will require studies of specific anesthetic endpoints in patients with systemic inflammation.

Insulin Signaling in Bupivacaine-induced Cardiac Toxicity: Sensitization during Recovery and Potentiation by Lipid Emulsion

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M. R. Fettiplace, K. Kowal, R. Ripper, A. Young, K. Lis, I. Rubinstein, M. Bonini, R. Minshall, and G. Weinberg

In vivo, local anesthetic toxicity altered phosphorylation at targets of glucose metabolism, including Akt, 5'-adenosine monophosphate–activated protein kinase and insulin receptor substrate-1. IV lipid emulsion reduced these local anesthetic–induced changes in phosphorylation.

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Positive end-expiratory pressure decreased dynamic (cyclical) strain and increased static strain in an animal model (six pigs; oleic acid lung injury) and in a study of six patients with acute respiratory distress syndrome.

■ PAIN MEDICINE

CLINICAL SCIENCE

Does Fentanyl Lead to Opioid-induced Hyperalgesia in Healthy Volunteers?: A Double-blind, Randomized, Crossover Trial

453

E. Mauermann, J. Filitz, P. Dolder, K. M. Rentsch, O. Bandschapp, and W. Ruppen

High-dose (10 µg/kg) fentanyl infusion can increase cold pressor test pain threshold and tolerance 4.5 to 6.5 h after infusion. Simultaneously, high-dose fentanyl infusion can increase the area of hyperalgesia caused by electrical burn.

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ORIGINAL INVESTIGATIONS IN EDUCATION

Lack of Association between Blood Pressure Management by Anesthesia Residents and Competence Committee Evaluations or In-training Exam Performance: A Cohort Analysis

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D. I. Sessler, N. Makarova, R. Riveros-Perez, D. L. Brown, and S. Kimatian

In a cohort of 70 anesthesia residents, there was no association between five measures of blood pressure control obtained from electronic anesthesia records and either faculty evaluations of clinical competence or quantitative knowledge testing. While negative, this study provides a novel and important initial attempt to use electronic anesthesia records to evaluate the clinical performance.

CLINICAL CONCEPTS AND COMMENTARY

Differential Opioid Tolerance and Opioid-induced Hyperalgesia: A Clinical Reality

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C. J. Hayhurst and M. E. Durieux

Differential opioid tolerance (different degrees and speed of tolerance to various opioid side effects) and opioid-induced hyperalgesia (increased pain with escalating doses of opioids) potentially complicate postoperative management.

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V. Neudecker, K. S. Brodsky, S. Kreth, A. A. Ginde, and H. K. Eltzschig

MicroRNAs are small, noncoding RNA molecules that have the capability to regulate protein expression at the posttranslational level. They play important roles as modulators of various biological functions including health and disease. This review provides an overview of microRNA biology, and specifically highlights their functional roles for the field of perioperative medicine.

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