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Special Article

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In 1846, William T. G. Morton chose *Letheon* as a commercial name for his preparation containing sulfuric ether. The adjective *Lethean* may have influenced the coinage of the name.

Perioperative Medicine

CLINICAL SCIENCE

◆ ◆ **Population Pharmacodynamics of Propofol and Sevoflurane in Healthy Volunteers Using a Clinical Score and the Patient State Index: A Crossover Study**

M. H. Kuizenga, P. J. Collin, K. M. E. M. Reijntjens, D. J. Touw, H. Nalbat, F. H. Knotnerus, H. E. M. Vereecke, M. M. R. F. Struys1223

A four-period randomized sequence crossover study determined the concentration–effect relationships for both propofol and sevoflurane, both with and without remifentanyl coadministration, with effects measured as tolerance to standard stimuli and by the Patient State Index. The sevoflurane Patient State Index values associated with a 50% probability of tolerance to the standard stimuli were higher for than those for propofol. Adding a 2 ng · ml⁻¹ predicted effect-site remifentanyl concentration increased all Patient State Index values associated with a 50% probability of tolerance to the standard stimuli, but 4 ng · ml⁻¹ produced additional effects only during propofol administration.

◆ ◆ **δ-Oscillation Correlates of Anesthesia-induced Unconsciousness in Large-scale Brain Networks of Human Infants**

I. Pappas, L. Cornelissen, D. K. Menon, C. B. Berde, E. A. Stamatakis1239

In infants younger than four months, slow-wave functional connectivity breaks down during general anesthesia and brain networks are less integrated. Functional disconnections in the cortex might be a common marker of anesthesia-induced unconsciousness in infants and adults.

◆ ◆ **Peripheral Nerve Blocks for Ambulatory Shoulder Surgery: A Population-based Cohort Study of Outcomes and Resource Utilization**

G. M. Hamilton, R. Ramlogan, A. Lui, C. J. L. McCartney, F. Abdallah, J. McVicar, D. I. McIsaac1254

Peripheral nerve blocks are associated with a decrease in unplanned admissions after ambulatory shoulder surgery. There is no associated improvement in other postoperative outcomes such as emergency department visits, readmissions, mortality, or costs.

◇ Refers to This Month in ANESTHESIOLOGY

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 CME Article

 This article has a Video Abstract

 Part of the Letheon writing competition

 This article has a Visual Abstract

 Readers' Toolbox



ON THE COVER: It remains unclear how to quantitatively compare the pharmacodynamics of propofol and sevoflurane in the absence or presence of opioids during anesthesia. In this issue of ANESTHESIOLOGY, Kuizenga *et al.* assessed the population pharmacodynamics of propofol and sevoflurane with or without opioids in healthy volunteers. In an accompanying Editorial View, Sleigh puts the new findings into the context of clinical practice where anesthesiologists commonly—and effectively—use more complex combinations of volatile agent, opioid, and infusions of propofol, dexmedetomidine, lidocaine, or ketamine. Cover photo: J. P. Rathmell. Cover illustration: S. M. Jarret, M.F.A., C.M.I.

- Kuizenga *et al.*: Population Pharmacodynamics of Propofol and Sevoflurane in Healthy Volunteers Using a Clinical Score and the Patient State Index: A Crossover Study, p. 1223
- Sleigh: The Art of General Anesthesia: Juggling in a Multidimensional Space, p. 1199

An Automated Software Application Reduces Controlled Substance Discrepancies in Perioperative Areas

N. Shah, A. Sinha, A. Thompson, K. Tremper, A. Meka, S. Kheterpal1264

In a large number of patients studied, a software application that tracks perioperative controlled substance use that is integrated into the electronic health and pharmacy records and database systems is associated with a decrease in management errors.

BASIC SCIENCE

◆ **Drug-selective Anesthetic Insensitivity of Zebrafish Lacking γ -Aminobutyric Acid Type A Receptor $\beta 3$ Subunits**

X. Yang, Y. Jounaidi, K. Mukherjee, R. J. Fantasia, E. C. Liao, B. Yu, S. A. Forman1276

Zebrafish larvae lacking functional $\beta 3$ subunits of the γ -aminobutyric acid type A (GABA_A) receptor displayed selective insensitivity to the same anesthetic drugs (etomidate, propofol, and pentobarbital) as transgenic mice with mutated GABA_A receptor $\beta 3$ subunits. These experiments indicate phylogenetic conservation of $\beta 3$ subunit-containing GABA_A receptors between zebrafish and mice in mediating hypnotic and sedative components of general anesthesia. These observations also suggest that zebrafish can be a valuable experimental model for mechanisms of anesthesia research.

Critical Care Medicine

CLINICAL SCIENCE

◆ **Hydrocortisone Compared with Placebo in Patients with Septic Shock Satisfying the Sepsis-3 Diagnostic Criteria and APROCCHSS Study**

Inclusion Criteria: A *Post Hoc* Analysis of the ADRENAL Trial

B. Venkatesh, S. Finfer, J. Cohen, D. Rajbhandari, Y. Arabi, R. Bellomo, L. Billot, P. Glass, C. Joyce, Q. Li, C. McArthur, A. Perner, A. Rhodes, K. Thompson, S. Webb, J. Myburgh1292

In a *post hoc* analysis of the Adjunctive Glucocorticoid Therapy in Patients with Septic Shock (ADRENAL) trial, in participants who fulfilled either the Sepsis-3 or -2 inclusion criteria or those with severe septic shock, a continuous infusion of hydrocortisone did not result in a lower 90-day mortality than placebo.

BASIC SCIENCE

Sevoflurane Promotes Bactericidal Properties of Macrophages through Enhanced Inducible Nitric Oxide Synthase Expression in Male Mice

T. J. Gerber, V. C. O. Fehr, S. D. S. Oliveira, G. Hu, R. Dull, M. G. Bonini, B. Beck-Schimmer, R. D. Minshall1301

In a lipopolysaccharide model of inflammation, sevoflurane increased mouse macrophage nitric oxide synthase activity and bacteria phagocytosis *in vitro* and *in vivo*. These effects were abolished by pharmacologically inhibiting nitric oxide synthase expression. In endotoxemia in mice, sevoflurane had bactericidal effects.

Pain Medicine

CLINICAL SCIENCE

◆ **Superior Trunk Block Provides Noninferior Analgesia Compared with Interscalene Brachial Plexus Block in Arthroscopic Shoulder Surgery**

◆ *R. Kang, J. S. Jeong, K. J. Chin, J. C. Yoo, J. H. Lee, S. J. Choi, M. S. Gwak, T. S. Hahm, J. S. Ko*1316

When interscalene block was compared with superior trunk block, less frequent hemidiaphragmatic paralysis was seen in the superior trunk block group. Superior trunk block was noninferior to interscalene block in terms of pain scores for up to 24 h postoperatively, and superior trunk block patients were no less satisfied.

◆ **Analgesic and Respiratory Depressant Effects of R-dihydroetorphine: A Pharmacokinetic–Pharmacodynamic Analysis in Healthy Male Volunteers**

E. Olofson, M. Boom, E. Sarton, M. van Velzen, P. Baily, K. J. Smith, A. Oksche, A. Dahan, M. Niesters1327

The effects of four R-dihydroetorphine doses (12.5, 75, 125, and 150 ng/kg) on isohypercapnic ventilation and antinociception were studied in 40 healthy male volunteers. Over the dose range tested, an apparent maximum in respiratory depression to 33% of baseline ventilation was identified, but a maximum in antinociception was not reached. At an R-dihydroetorphine effect-site concentration of 20 pg/ml, the probability of analgesia was 60%, while the probability of analgesia without respiratory depression was 45%. The probability of analgesia increased to 95% at 100 pg/ml, but the probability of analgesia without respiratory depression was reduced to 20%.

Education

IMAGES IN ANESTHESIOLOGY

Holodiastolic Flow Reversal in Descending Aorta with Right Coronary Artery to Coronary Sinus Fistula

Z. Merchant, A. Alfievic1340

Spinal Epidural Hematoma after Interlaminar Cervical Epidural Steroid Injection

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Drug Label Ribbons to Improve Patient Safety in Low-resource Environments

M. Prin, C. E. Algeo, L. Kalonga, C. Mkwezalamba1344

◆ **Seeing Double: The Clinical Conundrum of the Double-barrel Coronary Sinus**

S. J. Hankins1345

REVIEW ARTICLE

- ◇ **Artificial Intelligence and Machine Learning in Anesthesiology**
C. W. Connor1346

Anesthesiologists synthesize data from disparate sources, of varying precision and prognostic value, making life-critical decisions under time pressure. This review describes the evolution of artificial intelligence and machine learning through application to this challenging environment.

MIND TO MIND

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