

ON THE COVER:

Cervical radicular pain is a major cause of disability and few studies have examined the role for epidural steroids in treatment. In this issue of ANESTHESIOLOGY, Cohen and his colleagues present a multicenter, randomized, comparative-effectiveness study of epidural steroid injections, conservative treatment, or combination treatment for cervical radicular pain. They demonstrate that conservative, epidural steroid, and combination treatment all produce similar reductions in arm pain. In an accompanying editorial, Rathmell discusses this and other recent trials that have clarified the proper role for epidural steroids in our pain treatment armamentarium. (Cover illustration: J. Rathmell; G. Nelson; A. Johnson, Vivo Visuals. Adapted with permission from Rathmell JP: Atlas of Image-guided Intervention, second edition. Philadelphia, Lippincott Williams & Wilkins, 2012.)

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- Cohen *et al.*: Epidural Steroid Injections, Conservative Treatment, or Combination Treatment for Cervical Radicular Pain: A Multicenter, Randomized, Comparative-effectiveness Study, p. 1045

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■ PERIOPERATIVE MEDICINE

CLINICAL SCIENCE

- ◆ ◆ **Lack of Association between Carotid Artery Stenosis and Stroke or Myocardial Injury after Noncardiac Surgery in High-risk Patients** 922
A. Sonny, H.L. Gornik, D. Yang, E.J. Mascha, and D.I. Sessler
 Of 2,110 patients who had an internal carotid duplex ultrasound performed within 6 months before or 1 month after noncardiac, noncardiac surgery, 5.3% died within 30 days of surgery and 2.6% suffered postoperative in-hospital stroke. The degree of stenosis, as measured by peak systolic velocity, was not associated with risk of stroke or myocardial injury.
- ◆ ◆ **Vasoconstrictor Responses to Vasopressor Agents in Human Pulmonary and Radial Arteries: An *In Vitro* Study** 930
D.A. Currigan, R.J.A. Hughes, C.E. Wright, J.A. Angus, and P.F. Soeding
 Sympathomimetics were potent vasoconstrictors of human radial and pulmonary arteries while vasopressin produced vasoconstriction only in radial arteries suggesting a potential advantage of vasopressin use in patients with pulmonary hypertension.
- ◆ **Prehabilitation *versus* Rehabilitation: A Randomized Control Trial in Patients Undergoing Colorectal Resection for Cancer** 937
C. Gillis, C. Li, L. Lee, R. Awasthi, B. Augustin, A. Gamsa, A.S. Liberman, B. Stein, P. Charlebois, L.S. Feldman, and F. Carli
 Two months after surgery, prehabilitated patients were able to walk significantly further in 6 min.
- Lack of Nephrotoxicity by 6% Hydroxyethyl Starch 130/0.4 during Hip Arthroplasty: A Randomized Controlled Trial** 948
A.S.P. Kancir, L. Pleckaitiene, T.B. Hansen, N.P. Ekeløf, and E.B. Pedersen
 Thirty-eight patients with normal renal function were randomly assigned to receive intraoperative infusions of 6% hydroxyethyl starch (HES) 130/0.4 or 0.9% saline during hip arthroplasty. Measurement of urinary excretion of neutrophil gelatinase-associated lipocalin and albumin as well as plasma creatinine concentrations and creatinine clearance before, during, and after surgery revealed no evidence of a harmful nephrotoxic effect of 6% HES 130/0.4 in patients with previous normal renal function.
- ◆ **Effects of Neostigmine Reversal of Nondepolarizing Neuromuscular Blocking Agents on Postoperative Respiratory Outcomes: A Prospective Study** 959
N. Sasaki, M.J. Meyer, S.A. Malviya, A.B. Stanislaus, T. MacDonald, M.E. Doran, A. Igemshcheva, A.H. Hoang, and M. Eikermann
 Three thousand patients were evaluated in a prospective observational study. Neostigmine reversal did not reduce signs and symptoms of postoperative respiratory failure and was associated with worsened atelectasis. Inappropriate use of neostigmine increased the risk of pulmonary edema and reintubation.
- Effect of Reversal of Neuromuscular Blockade with Sugammadex *versus* Usual Care on Bleeding Risk in a Randomized Study of Surgical Patients** 969
N. Rahe-Meyer, H. Fennema, S. Schulman, W. Klimscha, M. Przemek, M. Blobner, H. Wulf, M. Speck, C.M. Sisk, D. Williams-Herman, T. Woo, and A. Szegedi
 In a randomized double-blind trial performed in patients undergoing hip/knee surgery or hip fracture surgery (n = 1,198) and comparing sugammadex (4 mg/kg) and usual care, sugammadex induced limited (<8% at 10 min) and transient (<1 h) increases in activated partial thromboplastin time and prothrombin time but was not associated with an increased incidence of bleeding (2.9 *vs.* 4.1%; relative risk, 0.70; 95% CI, 0.38–1.29) or increased severity of bleeding.
- 🌐 **A Comparison of Propofol- and Dexmedetomidine-induced Electroencephalogram Dynamics Using Spectral and Coherence Analysis** 978
O. Akeju, K.J. Pavone, M.B. Westover, R. Vazquez, M.J. Prerau, P.G. Harrell, K.E. Hartnack, J. Rhee, A.L. Sampson, K. Habeeb, G. Lei, E.T. Pierce, J.L. Walsh, E.N. Brown, and P.L. Purdon
 Alpha oscillations are more coherent and slow oscillations show up to four-fold larger amplitude in propofol-induced unconsciousness compared with dexmedetomidine sedation. The data suggest that propofol and dexmedetomidine have specific electroencephalogram signatures that can be analyzed in real time, which would allow them to be readily interpreted by anesthesiologists. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

Effects of Sevoflurane and Propofol on Frontal Electroencephalogram Power and Coherence 990

O. Akeju, M.B. Westover, K.J. Pavone, A.L. Sampson, K.E. Hartnack, E.N. Brown, and P.L. Purdon

Both propofol and sevoflurane anesthesia were characterized by alpha oscillations with coherence at 10 Hz and slow oscillations at less than 1 Hz, suggesting a common system-level mechanism with unconsciousness. Unlike propofol, sevoflurane was associated with increased power and coherence in the theta range. Whether this electroencephalogram pattern is unique to sevoflurane anesthesia remains to be determined.

BASIC SCIENCE**Distinctive Recruitment of Endogenous Sleep-promoting Neurons by Volatile Anesthetics and a Nonimmobilizer** 999

B. Han, H.S. McCarren, D. O'Neill, and M.B. Kelz

Within the ventrolateral preoptic area, volatile anesthetics increased activation of γ -aminobutyric acidergic neurons. In the median preoptic area, neuronal activation was independent of hypnosis. Anesthetics do not activate all neurons that regulate sleep, nor do they universally recruit all sleep-promoting neural nuclei.

Endocrine and Neurobehavioral Abnormalities Induced by Propofol Administered to Neonatal Rats 1010

S. Tan, C. Xu, W. Zhu, J. Willis, C.N. Seubert, N. Gravenstein, C. Summers, and A.E. Martyniuk

Propofol, administered to neonatal rats, caused an increase in corticosterone levels immediately after anesthesia and induced behavioral abnormalities and exacerbated endocrine activity at rest in response to stress in adulthood. Increased corticosteroid levels in adulthood were observed in both male and female rodents, but behavioral abnormalities were observed in only male rodents. Findings suggest that propofol-caused increases in levels of corticosteroids and excitatory action of γ -aminobutyric acid at the time of anesthesia may play mechanistic roles in induction of long-term endocrine and behavioral abnormalities in adulthood.

Crystallographic Studies with Xenon and Nitrous Oxide Provide Evidence for Protein-dependent Processes in the Mechanisms of General Anesthesia 1018

J.H. Abraini, G. Marassio, H.N. David, B. Vallone, T. Prangé, and N. Colloc'h

Crystallographic studies of 10 binding sites in 4 proteins found that the binding of xenon and nitrous oxide do not depend on hydrophobicity alone but on complex processes in which hydrophobicity and volume interact in different ways. Gas, including general anesthetic, binding to proteins should be considered to be due to a fully reversible interaction between a ligand and a receptor. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

CRITICAL CARE MEDICINE**CLINICAL SCIENCE****Increased Diaphragmatic Contribution to Inspiratory Effort during Neurally Adjusted Ventilatory Assistance versus Pressure Support: An Electromyographic Study** 1028

J. Cecchini, M. Schmidt, A. Demoule, and T. Similowski

Increasing levels of pressure support ventilation or neurally adjusted ventilatory assist both reduced diaphragmatic electromyographic activity and the inspiratory activity of the scalene and *alae nasi* muscles. Compared with pressure support ventilation, neurally adjusted ventilatory assist led to a larger contribution of the diaphragm to inspiratory efforts. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

Pupillary Effects of High-dose Opioid Quantified with Infrared Pupillometry 1037

M.D. Rollins, J.R. Feiner, J.M. Lee, S. Shah, and M. Larson

In 10 volunteers administered remifentanyl to the point of clinically significant hypercarbia and hypoxemia, there was evidence of a robust quantifiable light reflex despite small pupil size. These results suggest that the pupillary light reflex remains a valid neurologic assessment in the presence of opioids and hypoventilation.

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CLINICAL SCIENCE

- ◆ ◆ **Epidural Steroid Injections, Conservative Treatment, or Combination Treatment for Cervical Radicular Pain: A Multicenter, Randomized, Comparative-effectiveness Study** 1045
S.P. Cohen, S. Hayek, Y. Semenov, P.F. Pasquina, R.L. White, E. Veizi, J.H.Y. Huang, C. Kurihara, Z. Zhao, K.B. Guthmiller, S.R. Griffith, A.V. Verdun, D.M. Giampetro, and Y. Vorobeychik

This randomized study suggests that conservative, epidural steroid, and combination treatment may all produce similar outcomes in terms of reduction in arm pain. Combination treatment may offer some advantages for other outcomes such as neck and arm pain.

BASIC SCIENCE

- Modeling Individual Recovery after Peripheral Nerve Injury in Rats and the Effects of Parturition** 1056
C.A. Aschenbrenner, T.T. Houle, S. Gutierrez, and J.C. Eisenach

The authors demonstrate a method to measure recovery from pain-related responses after nerve injury. Using this methodology, sex differences were not evident but enhanced recovery was observed in postpartum rats.

- Calcitonin Gene-related Peptide Is Involved in Inflammatory Pain but Not in Postoperative Pain** 1068
K. Ishida, T. Kawamata, S. Tanaka, T. Shindo, and M. Kawamata

Mice deficient in the α isoform of calcitonin gene-related peptide display reduced pain-related behaviors after the injection of complete Freund's adjuvant. No calcitonin gene-related peptide-related differences were observed after incision. Calcitonin gene-related peptide-deficient mice also had reduced spinal cord Fos expression after complete Freund's adjuvant injection. These data distinguish incision- and inflammation-related pain on a biochemical level.

- AMPAkines Have Novel Analgesic Properties in Rat Models of Persistent Neuropathic and Inflammatory Pain** 1080
A.M. Le, M. Lee, C. Su, A. Zou, and J. Wang

Surprisingly, AMPAkines reduced mechanical and cold allodynia and attenuated symptoms of depression associated with chronic pain. Given the combination of analgesia and reduction of opioid-induced hypoventilation, AMPAkines may find utility in the treatment of persistent postoperative and chronic pain.

■ EDUCATION

IMAGES IN ANESTHESIOLOGY

- Pediatric Tongue Injury after Transesophageal Echocardiography for Cardiac Transplantation** 1091
M.D. Fritock, L.G. Segura, and C.F. Viozzi

- 🌐 **Laryngeal Papillomatosis** 1092
L.R. Kelly Ugarte and C. Munoz-San Julian

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CLINICAL CONCEPTS AND COMMENTARY

- 📺 ◆ **Perioperative Management of the Patient with a Coronary Artery Stent** 1093
T.R. Vetter, R.T. Short III, M.T. Hawn, and M.B. Marques

The need for the preoperative continuation of chronic antiplatelet therapy with coronary artery stents can be challenging and remains controversial.

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A. Monsel, Y.-g. Zhu, S. Gennai, Q. Hao, J. Liu, and J.W. Lee

There are currently more than 350 clinical trials utilizing the adult stem cell, mesenchymal stem or stromal cells. The review summarizes the underlying rationale and preclinical studies using mesenchymal stem cells for acute organ injury.
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