

ON THE COVER:

There is marked variation in use of neuraxial anesthesia for hip fracture surgery. In this issue of *ANESTHESIOLOGY*, McIsaac *et al.* report a population-based cohort study using administrative data in Ontario, Canada, to examine the association of utilization of neuraxial anesthesia with 30-day survival, length of stay, and costs. In an accompanying Editorial View, Chen and Neuman discuss these new research findings and their relationship to how we identify high-quality anesthetic care. Illustration by Sara Jarret, C.M.I.

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- Chen and Neuman: Do Anesthetic Choices Signal Quality? p. 429

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■ PERIOPERATIVE MEDICINE

CLINICAL SCIENCE

- ◆ ◆ **Association of Hospital-level Neuraxial Anesthesia Use for Hip Fracture Surgery with Outcomes: A Population-based Cohort Study** 480
  *D. I. McIsaac, D. N. Wijeyesundera, A. Huang, G. L. Bryson, and C. van Walraven*
 Across hospitals in Ontario, Canada, the rate of neuraxial anesthesia use for hip fracture surgery varied from 0 to 100%. Hospitals performing neuraxial anesthesia for more than 20 to 25% of their patients demonstrated improved survival compared to hospitals performing below that threshold.
- ◆ ◆  **Prediction of Bispectral Index during Target-controlled Infusion of Propofol and Remifentanyl: A Deep Learning Approach** 492
H.-C. Lee, H.-G. Ryu, E.-J. Chung, and C.-W. Jung
 An empirical model was developed from propofol and remifentanyl dosing histories and demographic data to predict bispectral index during total intravenous anesthesia target-controlled infusions using a deep learning approach. The deep learning model had less error in predicting bispectral index during anesthesia induction, maintenance, and recovery periods than the response surface model. The generalizability of the deep learning model is very dependent on the training data set. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*
- ◆ ◆   **Temporal Trends in Difficult and Failed Tracheal Intubation in a Regional Community Anesthetic Practice** 502
R. A. Schroeder, R. Pollard, I. Dhakal, M. Cooter, S. Aronson, K. Grichnik, W. Buhrman, M. D. Kertai, J. P. Mathew, and M. Stafford-Smith
 The rate of difficult and failed tracheal intubation has decreased significantly from 2002 to 2015. The role of specific devices, techniques, algorithms, and other practice changes requires further investigation.
- ◆ **Effect of Thoracic Epidural Ropivacaine versus Bupivacaine on Lower Urinary Tract Function: A Randomized Clinical Trial** 511
S. A. Girsberger, M. P. Schneider, L. M. Löffel, F. C. Burkhard, and P. Y. Wuethrich
 Postvoid bladder volume was less with ropivacaine than bupivacaine, and urine flow was better maintained. Ropivacaine is preferable to bupivacaine for bladder function and may prevent catheterization in some patients.
- Four Types of Pulse Oximeters Accurately Detect Hypoxia during Low Perfusion and Motion** 520
A. Louie, J. R. Feiner, P. E. Bickler, L. Rhodes, M. Bernstein, and J. Lucero
 This study determined the performance of four pulse oximeters (Masimo Radical-7, USA; Nihon Kohden OxyPal Neo, Japan; Nellcor N-600, USA; and Philips Intellivue MP5, USA) in 10 healthy adult volunteers. All oximeters detected hypoxemia during motion and low-perfusion conditions, but motion impaired performance at all ranges, with less accuracy at lower arterial oxygen saturation. Lower perfusion degraded performance in all but the Nihon Kohden instrument.
-  **Physiologic Evaluation of Ventilation Perfusion Mismatch and Respiratory Mechanics at Different Positive End-expiratory Pressure in Patients Undergoing Protective One-lung Ventilation** 531
S. Spadaro, S. Grasso, D. S. Karbing, A. Fogagnolo, M. Contoli, G. Bollini, R. Ragazzi, G. Cinnella, M. Verri, N. G. Cavallesco, S. E. Rees, and C. A. Volta
 Shunt fraction and ventilation/perfusion ratio (\dot{V}/\dot{Q}) distribution was measured in 41 patients undergoing one-lung anesthesia. Positive end-expiratory pressure at 5 or 10 cm H₂O, applied in random order, resulted in lower shunt fraction and driving pressure, without increasing dead space. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

BASIC SCIENCE

Bupivacaine Indirectly Potentiates Glutamate-induced Intracellular Calcium Signaling in Rat Hippocampal Neurons by Impairing Mitochondrial Function in Cocultured Astrocytes 539

Y. Xing, N. Zhang, W. Zhang, and L.-M. Ren

At clinically relevant concentrations, bupivacaine impaired mitochondrial function and reduced mitochondrial membrane potential in astrocytes but not in neurons. Astrocyte glutamate uptake was decreased by bupivacaine. The results suggest that, by reducing astrocyte glutamate uptake, bupivacaine increases neuronal exposure to glutamate, thereby causing excitotoxic injury.

Sevoflurane Blocks the Induction of Long-term Potentiation When Present during, but Not When Present Only before, the High-frequency Stimulation 555

J. Liu, L. Yang, D. Lin, J. E. Cottrell, and I. S. Kass

Sevoflurane administration during the stimulation that induces long-term potentiation also reduced long-term potentiation, a model for memory formation, in the hippocampus. Long-term potentiation was not blocked if sevoflurane was discontinued before the stimulus that induces long-term potentiation. The results suggest that sevoflurane can suppress memory formation only during its administration. The persistent effects on signal transduction do not prevent the recovery of memory formation.

■ CRITICAL CARE MEDICINE

BASIC SCIENCE

L-arginine and Arginase Products Potentiate Dexmedetomidine-induced Contractions in the Rat Aorta 564

E. S. W. Wong, R. Y. K. Man, K. F. J. Ng, S. W. S. Leung, and P. M. Vanhoutte

These results suggest that when vascular nitric oxide homeostasis is impaired, the potentiation of the vasoconstrictor effect of dexmedetomidine by L-arginine depends on arginase activity and the production of urea and ornithine.

 **Astrocytic N-Myc Downstream-regulated Gene-2 Is Involved in Nuclear Transcription Factor κ B-mediated Inflammation Induced by Global Cerebral Ischemia** 574

Y. Deng, Y. Ma, Z. Zhang, L. Zhang, H. Guo, P. Qin, Y. Hou, Z. Gao, and W. Hou

In *in vitro* cocultures of astrocytes and neurons, inhibition of nuclear transcription factor κ B (NF- κ B) or knockdown of N-Myc downstream-regulated gene-2 (NDRG2) in astrocytes reduced neuronal apoptosis. Similarly, inhibition of NF- κ B *in vivo* reduced neuronal injury and better preserved learning and memory function in rodents. The results suggest that suppression of astrocyte-mediated inflammation can improve neuronal survival and that NDRG2 may serve as a pharmacologic target for the improvement of outcome after cerebral ischemia. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

■ PAIN MEDICINE

CLINICAL SCIENCE

  **Targeted Genotyping Identifies Susceptibility Locus in Brain-derived Neurotrophic Factor Gene for Chronic Postsurgical Pain** 587



Y. Tian, X. Liu, M. Jia, H. Yu, P. Lichtner, Y. Shi, Z. Meng, S. Kou, I. H. T. Ho, B. Jia, B. C. P. Cheng, C. K. M. Lam, S. Tsang, S. H. Wong, J. Yu, C. H. K. Cheng, T. Gin, W. K. K. Wu, Z. Chen, M. T. V. Chan; for the Persistent Pain after Surgery Study Investigators

Among more than 1,000 surgical patients, 21% reported chronic postsurgical pain 12 months after surgery. Patients were genotyped for 638 single nucleotide polymorphisms in 54 pain-related genes, with 23 and 19 polymorphisms associated with increased and decreased pain, respectively, including a polymorphism in brain-derived neurotrophic factor associated with lower risk. Mice with the brain-derived neurotrophic factor polymorphism had less nociceptive response to a surgical incision compared with wild-type animals. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

Using Activity Trackers to Quantify Postpartum Ambulation: A Prospective Observational Study of Ambulation after Regional Anesthesia and Analgesia Interventions

598

J. Ma, R. Martin, B. Chan, M. Gofeld, M. P. Geary, J. G. Laffey, and F. W. Abdallah

This study objectively demonstrates that vaginal delivery is associated with greater early ambulation and functional recovery compared to cesarean delivery. It also establishes the feasibility of using activity trackers to evaluate early postoperative ambulation after neuraxial anesthesia and analgesia.

BASIC SCIENCE

Pharmacodynamics and Pharmacokinetics of Lidocaine in a Rodent Model of Diabetic Neuropathy

609

W. ten Hoope, M. W. Hollmann, K. de Bruin, H. J. Verberne, A. O. Verkerk, H. L. Tan, C. Verhamme, J. Horn, M. Rigaud, S. Picardi, and P. Lirk

Rats with neuropathy secondary to type 2 diabetes had prolonged nerve block duration compared to control rats. Radiolabeled lidocaine concentrations were higher in the nerves of diabetic rats 60 min after nerve block, when most diabetic nerves are still blocked. The ED₅₀ of lidocaine for motor block in diabetic rats was 64% of that of control animals. The *in vitro* inhibitory effect of a given lidocaine concentration was much more pronounced in primary sensory neurons harvested from diabetic rats.

Transcriptional Changes in Dorsal Spinal Cord Persist after Surgical Incision Despite Preemptive Analgesia with Peripheral Resiniferatoxin

620

S. J. Raithel, M. R. Sapio, D. M. LaPaglia, M. J. Iadarola, and A. J. Mannes

Using a rat model of postsurgical pain, it was shown that a single localized injection of resiniferatoxin reduced evoked and nonevoked pain-related behaviors over the entire period of postoperative recovery. Analysis of spinal cord dorsal horn tissue revealed that resiniferatoxin pretreatment did not block most changes in gene expression, including the expression of genes associated with microglia, despite reducing pain-related behaviors. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

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ORIGINAL INVESTIGATION IN EDUCATION

Relaxation before Debriefing during High-fidelity Simulation Improves Memory Retention of Residents at Three Months: A Prospective Randomized Controlled Study

638

M. Lilot, J.-N. Evain, C. Bauer, J.-C. Cejka, A. Faure, B. Balança, O. Vassal, C. Payet, B. Bui Xuan, A. Duclos, J.-J. Lehot, and T. Rimmelé

This investigation tested whether residents in a simulation would better recall critical key messages at three months when a relaxation break occurred before debriefing. More residents (71 vs. 46%) recalled three or more messages at three months when there was a relaxation break compared with controls. Results suggest that relaxation as a cognitive technique may enhance learning. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

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- ◇ **Use of Uncrossmatched Erythrocytes in Emergency Bleeding Situations** 650
M. H. Yazer, J. H. Waters, P. C. Spinella; on behalf of the AABB (formerly known as the American Association of Blood Banks)/Trauma Hemostasis Oxygenation Resuscitation Network (THOR) Working Party


Transfusion of uncrossmatched erythrocytes is lifesaving in patients who are severely bleeding when crossmatched erythrocytes are unavailable. The hemolysis risk after uncrossmatched erythrocyte administration to appropriate patients is very low. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

REVIEW ARTICLE

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J. H. Levy, A. Koster, Q. J. Quinones, T. J. Milling, and N. S. Key

Fibrinolysis is important for hemostatic balance, but after trauma or surgery may contribute to coagulopathy and bleeding. Antifibrinolytic agents reduce bleeding and transfusions, and tranexamic acid is the agent most extensively studied and administered.

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