

ON THE COVER:

Neuromuscular-blocking agents (NMBAs) allow for surgical procedures that would be difficult or impossible without induced paralysis. In this issue of ANESTHESIOLOGY, McLean and his colleagues demonstrate a dose-dependent association between intermediate-acting NMBAs and postoperative respiratory complications. In an accompanying Editorial View, Brull and Prielipp make a plea to all clinicians: to reduce complications, use objective measurement of neuromuscular function in *all* patients receiving NMBAs to guide the timing and dosing of neuromuscular blockade and its reversal.

- McLean *et al.*: Dose-dependent Association between Intermediate-acting Neuromuscular-blocking Agents and Postoperative Respiratory Complications, p. 1201
- Brull and Prielipp: Reversal of Neuromuscular Blockade: "Identification Friend or Foe," p. 1183

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Reversal of Neuromuscular Blockade: "Identification Friend or Foe"

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Intraoperative Glycemic Control to Prevent Delirium after Cardiac Surgery: Steering a Course between Scylla and Charybdis

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 CME Article

 Best Abstract article originally presented at ANESTHESIOLOGY 2014

■ PERIOPERATIVE MEDICINE

CLINICAL SCIENCE

-  **Dose-dependent Association between Intermediate-acting Neuromuscular-blocking Agents and Postoperative Respiratory Complications** 1201
D. J. McLean, D. Diaz-Gil, H. N. Farhan, K. S. Ladha, T. Kurth, and M. Eikermann
- In a review of nearly 50,000 subjects, use of intermediate-acting neuromuscular blockers was associated with a dose-dependent increase in pulmonary complications. Neostigmine also was associated with a dose-dependent increase in pulmonary complications although exploratory analysis suggested that this reflected lack of neostigmine dose adjustment using neuromuscular transmission monitoring.
- ◆◆ **Intraoperative Tight Glucose Control Using Hyperinsulinemic Normoglycemia Increases Delirium after Cardiac Surgery** 1214
L. Saager, A. E. Duncan, J.-P. Yared, B. D. Hesler, J. You, A. Deogaonkar, D. I. Sessler, and A. Kurz
- Intraoperative hyperinsulinemic–normoglycemia augments the risk of delirium after cardiac surgery, but not its severity.
- ◆ **Preexisting Cognitive Impairment Is Associated with Postoperative Cognitive Dysfunction after Hip Joint Replacement Surgery** 1224
B. Silbert, L. Evered, D. A. Scott, S. McMahon, P. Choong, D. Ames, P. Maruff, and K. Jamrozik
- Preexisting cognitive dysfunction was identified in approximately a third of the patients before surgery. Preexisting cognitive dysfunction is a good predictor of cognitive dysfunction 1 yr after surgery. However, there is no evidence that anesthesia and surgery *per se* contribute to cognitive dysfunction 1 yr after surgery.
- Effect of Therapeutic Hypercapnia on Inflammatory Responses to One-lung Ventilation in Lobectomy Patients** 1235
W. Gao, D.-D. Liu, D. Li, and G.-x. Cui
- Fifty patients undergoing lobectomy under intravenous anesthesia randomly received carbon dioxide at partial pressures of 35 to 45 mmHg or 60 to 70 mmHg for approximately 210 min. The bronchoalveolar lavage fluid from the patients in the higher carbon dioxide group had decreased the total number of cells, total protein, and some cytokines after surgery.
- ◆ **Effects of Morphine and Midazolam on Pharyngeal Function, Airway Protection, and Coordination of Breathing and Swallowing in Healthy Adults** 1253
A. I. Hårdemark Cedborg, E. Sundman, K. Bodén, H. Witt Hedström, R. Kuylensstierna, O. Ekberg, and L. I. Eriksson
- By simultaneous recordings of breathing, videoradiography, and pharyngeal manometry in healthy adult volunteers, this study is the first to elucidate pharyngeal dysfunctions in conjunction with altered coordination between breathing and swallowing as possible mechanisms for pulmonary aspiration during sedation with midazolam or morphine.
- Monitoring Obstetric Anesthesia Safety across Hospitals through Multilevel Modeling** 1268
J. Guglielminotti and G. Li
- In an analysis of nearly 500,000 labor and delivery records from 144 hospitals in New York, multilevel modeling substantially improved the reliability in the estimated rates of obstetric anesthesia-related adverse events across hospitals compared with the traditional risk-adjustment method.
- ◆ **Comparison of Surgical Pleth Index–guided Analgesia with Conventional Analgesia Practices in Children: A Randomized Controlled Trial** 1280
J. H. Park, B. G. Lim, H. Kim, I. O. Lee, M. H. Kong, and N. S. Kim
- Children assigned to surgical pleth index guidance received less intraoperative fentanyl. However, they suffered more emergence agitation, had more postoperative pain, and required more rescue fentanyl.

BASIC SCIENCE

Opioid-induced Respiratory Depression Is Only Partially Mediated by the preBötzinger Complex in Young and Adult Rabbits *In Vivo*

1288

A. G. Stucke, J. R. Miller, I. Prkic, E. J. Zuperku, F. A. Hopp, and E. A. E. Stuth

In an *in vivo* rabbit model, the preBötzinger Complex partially mediates opioid effects on respiratory phase timing. The preBötzinger Complex does not mediate the opioid-induced depression of respiratory rate.

Activation of Adenosine Triphosphate-regulated Potassium Channels during Reperfusion Restores Isoflurane Postconditioning-induced Cardiac Protection in Acutely Hyperglycemic Rabbits

1299

J. Raphael, Y. Gozal, N. Navot, and Z. Zuo

Adenosine triphosphate-regulated potassium channel activation restored anesthetic postconditioning-induced myocardial protection under acute hyperglycemia. This effect occurred without increasing protein kinase B (Akt) or endothelial nitric oxide synthase phosphorylation, suggesting that adenosine triphosphate-regulated potassium channels are located downstream to Akt and endothelial nitric oxide synthase in the pathway of isoflurane-induced myocardial postconditioning.

Xenon Treatment Protects against Remote Lung Injury after Kidney Transplantation in Rats

1312

H. Zhao, H. Huang, R. Ologunde, D. G. Lloyd, H. Watts, M. P. Vizcaychipi, Q. Lian, A. J. T. George, and D. Ma

Xenon given to kidney transplant recipients after receiving the ischemic renal grafts decreased pulmonary damage and inflammation. The molecular mechanisms involved in the pulmonary protection are likely due to the mammalian target of rapamycin-hypoxia-inducible factor-1 α pathway activation and the high-mobility group protein-1/Toll-like receptor-4/nuclear factor- κ B signaling pathway inhibition by xenon.

■ CRITICAL CARE MEDICINE

BASIC SCIENCE

Valproic Acid Attenuates Acute Lung Injury Induced by Ischemia-Reperfusion in Rats

1327

S.-Y. Wu, S.-E. Tang, F.-C. Ko, G.-C. Wu, K.-L. Huang, and S.-J. Chu

The administration of valproic acid decreased all the parameters of lung injury, oxidative stress, apoptosis, and inflammation and some of its protection appeared to occur by increasing heme oxygenase-1 activity.

BA TRPV4 Is Required for Hypoxic Pulmonary Vasoconstriction

1338

N. M. Goldenberg, L. Wang, H. Ranke, W. Liedtke, A. Tabuchi, and W. M. Kuebler

A role for the calcium-permeant transient receptor potential channel TRPV4 in hypoxic pulmonary vasoconstriction was demonstrated in mouse models *in vivo* and *in vitro* both pharmacologically and in Trpv4^{-/-} mice. TRPV4 is critical for hypoxia-induced pulmonary vasoconstriction, in contrast to its vasodilatory roles in renal and mesentery arteries.

Relationship between Autophagy and Ventilator-induced Diaphragmatic Dysfunction

1349

I. Azuelos, B. Jung, M. Picard, F. Liang, T. Li, C. Lemaire, C. Giordano, S. Hussain, and B. J. Petrof

Autophagy was rapidly induced in the diaphragm in a mouse model of ventilator-induced diaphragmatic dysfunction, but the autophagic process was not responsible for diaphragmatic weakness.

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■ PAIN MEDICINE

CLINICAL SCIENCE

- Computational Analysis of Kilohertz Frequency Spinal Cord Stimulation for Chronic Pain Management** 1362
S. F. Lempka, C. C. McIntyre, K. L. Kilgore, and A. G. Machado

Using a computational model, it was shown that kilohertz frequency spinal cord stimulation (KFSCS) used at clinical intensities probably does not cause the direct activation or conduction block of dorsal column or dorsal root fibers. Possible sites of action for KFSCS to be explored include synaptic terminals, cell bodies, and dendrites. Computational analyses suggest that KFSCS for pain management may not function through direct activation or conduction block of spinal cord fibers, and alternative concepts should be explored and evaluated.

BASIC SCIENCE

- ◆◆ **Targeting p38 Mitogen-activated Protein Kinase to Reduce the Impact of Neonatal Microglial Priming on Incision-induced Hyperalgesia in the Adult Rat** 1377
F. Schwaller, S. Beggs, and S. M. Walker

In rats, incisional surgery in adulthood resulted in greater phosphorylation of the signaling enzyme, p38 mitogen-activated protein (MAP) kinase in spinal cord microglia of animals which had received incisional surgery in the neonatal period. A p38 MAP kinase inhibitor reduced pain behaviors after surgery in adults with previous neonatal surgery, suggesting this enzyme may be a target to reduce exaggerated pain responses after surgery in individuals with a history of neonatal surgery.

- ◆◆ **Surgical Injury in the Neonatal Rat Alters the Adult Pattern of Descending Modulation from the Rostroventral Medulla** 1391
S. M. Walker, M. Fitzgerald, and G. J. Hathway

In rats, neonatal incisional surgery to the paw resulted in reduced sensitivity to mechanical or thermal stimuli in adulthood and changed the effect of rostroventral medulla stimulation from a bimodal pattern of facilitation and inhibition, to only inhibition. Regional anesthesia at the time of neonatal surgery prevented these changes in adulthood.

- Adenosine Monophosphate-activated Protein Kinase Regulates Interleukin-1 β Expression and Glial Glutamate Transporter Function in Rodents with Neuropathic Pain** 1401
D. W. Maixner, X. Yan, M. Gao, R. Yadav, and H.-R. Weng

Nerve injury reduced adenosine monophosphate-activated protein kinase (AMPK) activity, increased inflammation, reduced glutamate transporter expression in the spinal cord, and induced thermal hyperalgesia. Activation of AMPK increased glutamate transporter activity and reduced neuropathic pain; by contrast, knockdown of AMPK induced allodynia. These data indicate that AMPK plays an important role in nociceptive processing in the spinal cord and extend the novel possibility of manipulation of AMPK activity as a therapeutic target in experimental models of pain.

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- ◆◆ **The Role of Dendritic Signaling in the Anesthetic Suppression of Consciousness** 1415
K. Meyer

General anesthetics suppress signal conduction along the apical dendrites of cortical pyramidal neurons. Thereby, they interfere with corticocortical top-down signals and cause a breakdown of the continuous predictive process that is core to conscious perception.

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