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◆◆◆ **Upper Airway Collapsibility during Dexmedetomidine and Propofol Sedation in Healthy Volunteers: A Nonblinded Randomized Crossover Study**

◆ *Å. Lodenius, K. J. Maddison, B. K. Lawther, M. Scheinin, L. I. Eriksson, P. R. Eastwood, D. R. Hillman, M. J. Fagerlund, J. H. Walsh* .....962

At comparable levels of light to moderate sedation, dexmedetomidine and propofol exhibit similar degrees of pharyngeal collapsibility and reductions in ventilatory drive. The findings suggest that sedation with dexmedetomidine does not offer inherent protection against upper airway obstruction or ventilatory depression.

◆◆◆ **Genetic Analysis of Patients Who Experienced Awareness with Recall while under General Anesthesia**

◆ *J. W. Sleigh, K. Leslie, A. J. Davidson, D. J. Amor, P. Diakumis, V. Lukic, P. J. Lockhart, M. Bahlo* .....974

A preliminary study sought to determine whether there is evidence that awareness with recall is caused by a few rare variants with high penetrance in 12 patients who had experienced awareness with recall in the presence of apparently adequate anesthesia. Whole exome sequencing was conducted and identified variants were filtered and prioritized to identify a candidate list that might be suitable for further investigation of causes of awareness with recall. No candidate gene(s) suggestive of a monogenic etiology were identified, possibly because of the application of a filtering strategy, the small sample size, or use of exome sequencing, which does not interrogate potentially important regulatory noncoding sequences.

◆◆◆ **An Assessment of Penetrance and Clinical Expression of Malignant Hyperthermia in Individuals Carrying Diagnostic Ryanodine Receptor 1 Gene Mutations**

◆ *C. A. Ibarra Moreno, S. Hu, N. Kraeva, F. Schuster, S. Johannsen, H. Rueffert, W. Klingler, L. Heytens, S. Riaz* .....983

In a multicenter case-control study of 229 genotype-positive subjects with previous recorded exposure to trigger anesthetics, there were 93 malignant hyperthermia cases, for an overall penetrance for the analyzed *RYR1* mutations of 40.6%. The probability of developing malignant hyperthermia on exposure to triggers was 0.25 among all *RYR1* mutation carriers and 0.76 in survivors of malignant hyperthermia reactions (95% CI of the difference 0.41 to 0.59). Young age, male sex, and the use of succinylcholine were major nongenetic risk factors influencing expression of the *RYR1* mutations conferring malignant hyperthermia susceptibility.

◆ Refers to This Month in ANESTHESIOLOGY

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**ON THE COVER:** Dexmedetomidine is a sedative promoted as having minimal impact on ventilatory drive or upper airway muscle activity. However, more recent study has demonstrated impaired ventilatory drive and induction of apneas in sedated volunteers. In this issue of ANESTHESIOLOGY, Lodenius *et al.* measured upper airway collapsibility during dexmedetomidine sedation and related it to propofol. In an accompanying Editorial View, Ward and Karan review previous comparative studies with this new trial and conclude that light to moderate sedation with dexmedetomidine does not appear to offer any protection from central ventilatory apneas and airway obstructions over propofol. Cover illustration: A. Johnson, Vivo Visuals.


- Lodenius *et al.*: Upper Airway Collapsibility during Dexmedetomidine and Propofol Sedation in Healthy Volunteers: A Nonblinded Randomized Crossover Study, p. 962
- Ward and Karan: Dexmedetomidine and the Upper Airway: Not as Simple as We Hoped, p. 953

-  **Accuracy of Physical Function Questions to Predict Moderate-Vigorous Physical Activity as Measured by Hip Accelerometry**  
*D. S. Rubin, M. Huisingh-Scheetz, A. Hung, R. P. Ward, P. Nagele, R. Arena, D. Hedeker* .....992

Results from standardized physical function questions and hip accelerometers were compared in 522 participants. Physical function questions were sensitive but nonspecific. Other approaches to assessing physical functional status should be considered.

-  **Pharmacodynamic Interaction of Remifentanyl and Dexmedetomidine on Depth of Sedation and Tolerance of Laryngoscopy**  
 *M. A. S. Weerink, C. R. M. Barends, E. R. R. Muskiet, K. M. E. M. Reijntjens, F. H. Knotnerus, M. Oostra, J. F. P. van Bocklaer, M. M. R. F. Struys, P. J. Colin* .....1004

This three-phase crossover trial to study the pharmacodynamic interaction between remifentanyl and dexmedetomidine in 30 age- and sex-stratified healthy volunteers found that, despite falling asleep, most subjects remained arousable by calling their name, shaking the subject while shouting their name, or a trapezius squeeze, even after reaching supraclinical concentrations. Adding remifentanyl to dexmedetomidine sedation did not affect the likelihood of response to graded stimuli. Dexmedetomidine potency increased with increasing age.

-  **Acoustic Shadowing Facilitates Ultrasound-guided Radial Artery Cannulation in Young Children**  
*Z. Quan, L. Zhang, C. Zhou, P. Chi, H. He, Y. Li* .....1018


This prospective, randomized trial in young children shows that a modified ultrasound-guided approach, using focused acoustic shadowing, results in a higher success rate and shorter cannulation time of the radial artery when compared with traditional ultrasound guidance.

-  **A Population-based Comparative Effectiveness Study of Peripheral Nerve Blocks for Hip Fracture Surgery**  
*G. M. Hamilton, M. M. Lalu, R. Ramlogan, G. L. Bryson, F. W. Abdallah, C. J. L. McCartney, D. I. McIsaac* .....1025

Among elderly patients undergoing emergency hip fracture surgery in Ontario, Canada, peripheral nerve blocks may be associated with slightly decreased postoperative lengths of stay and health system costs. The use of peripheral nerve blocks was not associated with a difference in postoperative pneumonia rates.

-  **Effect of a Cognitive Aid on Reducing Sugammadex Use and Associated Costs: A Time Series Analysis**  
*D. M. Drzymalski, R. Schumann, F. J. Massaro, A. Trzcinka, R. J. Azocar* .....1036

The investigators tested the hypothesis that a cognitive aid to guide selective use of sugammadex reduced use. They conducted a segmented regression (interrupted time series) retrospective analysis before and after implementing the cognitive aid and informational meetings for their department. Sugammadex use and associated costs, which were increasing, decreased substantially after introduction of the cognitive aid.

-  **Intraoperative Mechanical Ventilation and Postoperative Pulmonary Complications after Cardiac Surgery**  
*M. R. Mathis, N. M. Duggal, D. S. Likosky, J. W. Haft, N. J. Douville, M. T. Vaughn, M. D. Maile, R. S. Blank, D. A. Colquhoun, R. J. Strobel, A. M. Janda, M. Zhang, S. Khetarpal, M. C. Engoren* .....1046

In this retrospective analysis, the intraoperative ventilation bundle was associated with a lower rate of postoperative pulmonary complications. Lower modified driving pressure was independently associated with fewer pulmonary complications.

## BASIC SCIENCE

-  **Nitrous Oxide Impairs Axon Regeneration after Nervous System Injury in Male Rats**  
 *K. J. Stewart, B. J. Iskandar, B. M. Meier, E. B. Rizk, N. Hariharan, J. Koueik, A.-C. Andrei, K. J. Hogan* .....1063

In *in vitro* and *in vivo* experimental models of male rats, nitrous oxide exposure impairs folic acid-induced axonal regeneration of dorsal root and retinal ganglion neurons. The beneficial effects of folic acid on functional recovery following spinal cord contusion in male rats are hindered by co-administration of nitrous oxide. These experiments suggest that nitrous oxide can interfere with axonal regeneration and functional recovery following central nervous system injury.

- Early Postnatal Exposure to Isoflurane Disrupts Oligodendrocyte Development and Myelin Formation in the Mouse Hippocampus**  
*Q. Li, R. P. Mathena, J. Xu, O. N. Eregha, J. Wen, C. D. Mintz* .....1077

Exposure of 7-day-old mouse pups to isoflurane (1.5%, 4 h) results in lasting impairments of oligodendrocyte proliferation and differentiation. These effects lead to defects in myelinations and are associated with cognitive dysfunction. The underlying molecular mechanisms involve the isoflurane-induced activation of the mammalian target of rapamycin pathway and a related decrease in DNA methylation in oligodendrocyte progenitors.

### Intergenerational Effects of Sevoflurane in Young Adult Rats

*L.-S. Ju, J.-J. Yang, N. Xu, J. Li, T. E. Morey, N. Gravenstein, C. N. Seubert, B. Setlow, A. E. Martynyuk* .....1092

Repeated exposures of adult rats to sevoflurane (2.1%, three times, 3 h on every second day) induce neurobehavioral abnormalities in the exposed males and in male but not female progeny. The neurobehavioral abnormalities in male offspring are accompanied by increased methylation and decreased expression of the potassium ion-chloride ion cotransporter *Kcc2* gene that regulates neuronal chloride homeostasis, and, thereby, the functional modalities of  $\gamma$ -aminobutyric acid type A receptor-mediated neurotransmission. Sevoflurane exposure also induces hypermethylation of the *Kcc2* gene in both male and female parental germ cells. These observations suggest that epigenetic reprogramming of parental germ cells is involved in transmitting the adverse effects of sevoflurane exposure of adult rats to their male progeny.

## Critical Care Medicine

### BASIC SCIENCE

#### Effect of Polyethylene-glycolated Carboxyhemoglobin on Renal Microcirculation in a Rat Model of Hemorrhagic Shock

*P. Guerci, B. Ergin, A. Kapucu, M. P. Hilty, R. Jubin, J. Bakker, C. Ince* .....1110

In a rat model of hemorrhagic shock, comparing fluid resuscitation with blood, diluted blood, hydroxyethyl starch, or polyethylene-glycolated carboxyhemoglobin, all fluids restored urine output and creatinine clearance, but only blood and diluted blood improved renal  $PO_2$ . Postresuscitation histologic renal tubular damage was increased compared with nonresuscitated rats but slightly less with blood, diluted blood, and polyethylene-glycolated carboxyhemoglobin compared with hydroxyethyl starch. Restoration of circulatory hemodynamics and kidney microcirculatory  $PO_2$  was comparable with polyethylene-glycolated carboxyhemoglobin and balanced hydroxyethyl starch solution.

## Pain Medicine

### BASIC SCIENCE

#### Vascular Endothelial Growth Factor A Signaling Promotes Spinal Central Sensitization and Pain-related Behaviors in Female Rats with Bone Cancer

*X.-M. Hu, W. Yang, L.-X. Du, W.-Q. Cui, W.-L. Mi, Q.-L. Mao-Ying, Y.-X. Chu, Y.-Q. Wang* .....1125

In a female rat model of metastatic breast cancer, expression of vascular endothelial growth factor A and its receptor vascular endothelial growth factor receptor 2 were upregulated in spinal tissue. Blocking vascular endothelial growth factor signaling improved several measures of nociception and function in this model suggesting a role for vascular endothelial growth factor antagonists in reducing cancer-related pain.

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*O. Grottko, S. Schulman* .....1153

Factor Xa inhibitors prevent thrombosis but are associated with severe or life-threatening bleeding. Here, the authors present data on four-factor prothrombin complex concentrates in management of anticoagulation-associated bleeding and restoring hemostasis, including recent results from the UPRATE study.

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#### Transversus Abdominis Plane Block: A Narrative Review

*D. Q. Tran, D. Bravo, P. Leurcharusmee, J. M. Neal* .....1166

This narrative review article discusses the anatomy, history, nomenclature, approaches/techniques, pharmacology, indications, potential complications, and alternatives for transversus abdominis plane blocks.

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