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◆◆ **Reversal of Partial Neuromuscular Block and the Ventilatory Response to Hypoxia: A Randomized Controlled Trial in Healthy Volunteers**  
 *S. J. L. Broens, M. Boon, C. H. Martini, M. Niesters, M. van Velzen, L. P. H. J. Aarts, A. Dahan* ..... 467


Despite full reversal of neuromuscular blockade at the thumb using different drug classes, this hypoxic chemoreflex is not fully restored.

◆◆ **Postoperative Delirium and Postoperative Cognitive Dysfunction: Overlap and Divergence**  
 *L. A. Daiello, A. M. Racine, R. Y. Gou, E. R. Marcantonio, Z. Xie, L. J. Kunze, K. V. Vlassakov, S. K. Inouye, R. N. Jones, for the SAGES Study Group* ..... 477


Postoperative delirium increased the risk of postoperative cognitive dysfunction at 1 month postoperatively but there was no association between postoperative delirium and cognitive dysfunction at 2 and 6 months after major noncardiac surgery. Postoperative delirium and longer-term postoperative cognitive dysfunction may be different disorders.

**Postoperative Delirium Is Associated with Long-term Decline in Activities of Daily Living**  
*Z. Shi, X. Mei, C. Li, Y. Chen, Hailin Zheng, Y. Wu, Hui Zheng, L. Liu, E. R. Marcantonio, Z. Xie, Y. Shen* ..... 492

About a quarter of enrolled patients, averaging 80 yr of age, developed delirium after major elective and urgent major orthopedic surgery. Activities of daily living at 2 to 3 yr and mortality at 3 yr were both worse in patients who experienced delirium.

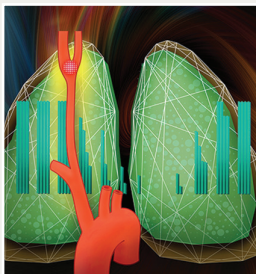
◆ **Population Kinetics of 0.9% Saline Distribution in Hemorrhaged Awake and Isoflurane-anesthetized Volunteers**  
 *J. Nyberg, H. Li, P. Wessmark, V. Winther, D. S. Prough, M. P. Kinsky, C. H. Svensén*..... 501

The distribution of infused fluid after hemorrhage (7 ml/kg during 20 min) in a randomized crossover study of 12 healthy volunteers while awake and while isoflurane-anesthetized was described by a two-fluid space model that included study arm, body weight, and sex as covariates. Only sex had a statistically significant effect on the area under the plasma dilution curve and maximum plasma dilution, both of which were increased by a median of 17% in females (95% CIs, 1.08 to 1.38 and 1.07 to 1.39, respectively) compared with males. **SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT**

◆ Refers to This Month in ANESTHESIOLOGY  
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**ON THE COVER:** The ventilatory response to hypoxia is a life-saving chemoreflex originating at the carotid bodies that is impaired by nondepolarizing neuromuscular blocking agents. In this issue of ANESTHESIOLOGY, Broens *et al.* evaluated the effect of three strategies for reversal of a partial neuromuscular block on ventilatory control in healthy volunteers on the chemoreflex. In an accompanying Editorial View, Pandit and Eriksson discuss the effect of neuromuscular blockade on carotid body function, emphasizing that even when the train-of-four ratio has recovered to 1.0, the acute ventilatory response to hypoxia can remain significantly depressed. Cover illustration: A. Johnson, Vivo Visuals.

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**Internal Carotid Artery Blood Flow Response to Anesthesia, Pneumoperitoneum, and Head-up Tilt during Laparoscopic Cholecystectomy**

M. Skytjoti, M. Elstad, S. Søvik.....512

At steady-state depth of anesthesia, in patients undergoing laparoscopic cholecystectomy, creation of pneumoperitoneum decreased cardiac output and internal carotid artery blood flow while mean arterial pressure and end-tidal carbon dioxide levels remained unchanged.

**Superior Trunk Block: A Phrenic-sparing Alternative to the Interscalene Block: A Randomized Controlled Trial**

D. H. Kim, Y. Lin, J. C. Beathe, J. Liu, J. A. Oxendine, S. C. Haskins, M. C. Ho, D. S. Wetmore, A. A. Allen, L. Wilson, C. Garnett, S. G. Memtsoudis .....521

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 worst pain scores in the recovery room, and superior trunk block patients were more satisfied. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

**Trends in Direct Hospital Payments to Anesthesia Groups: A Retrospective Cohort Study of Nonacademic Hospitals in California**

C. O'Connell, F. Dexter, D. J. Mauler, E. C. Sun .....534

Among 240 nonacademic California hospitals analyzed between 2002 and 2014, more hospitals made direct payments to an anesthesia group in 2014 than in 2002 and the median payment increased. Hospitals where public insurers accounted for a larger fraction of anesthesia revenues were increasingly more likely to make direct payments to private anesthesia groups. Direct payments to private anesthesia groups are becoming increasingly important, particularly for hospitals providing care to underserved populations. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

**BASIC SCIENCE**

**Prothrombin Complex Concentrate-induced Disseminated Intravascular Coagulation Can Be Prevented by Co-administering Antithrombin in a Porcine Trauma Model**

O. Grottko, M. Honickel, T. Braunschweig, A. Reichel, H. Schöchl, R. Rossaint.....543

In this animal polytrauma model, 50 IU/kg prothrombin complex concentrate is associated with a risk of disseminated intravascular coagulopathy and thromboembolism. The addition of antithrombin appears to balance the procoagulant effects of prothrombin complex concentrate, consequently reducing the risk of complications without impairing efficacy. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

**Syntaxin1A Neomorphic Mutations Promote Rapid Recovery from Isoflurane Anesthesia in *Drosophila melanogaster***

M. Troup, O. H. Zalucki, B. D. Kottler, S. Karunanithi, V. Anggono, B. van Swinderen .....555

Resistance to isoflurane anesthesia can be produced by transiently expressing truncated syntaxin1A proteins in adult *Drosophila* flies. Electrophysiologic and behavioral studies in *Drosophila* show that mutations in syntaxin1A facilitate recovery from isoflurane anesthesia. These observations suggest that presynaptic mechanisms, via syntaxin1A-mediated regulation of neurotransmitter release, are involved in general anesthesia maintenance and recovery. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

**Critical Care Medicine**

**CLINICAL SCIENCE**

**Atrophy of Diaphragm and Pectoral Muscles in Critically Ill Patients**

E. Vivier, A. Roussey, F. Doroszewski, S. Rosselli, C. Pommier, G. Carteaux, A. Mekontso Dessap.....569

Ultrasound was used for serial assessment of diaphragm and pectoral muscle in 97 critically ill patients. Diaphragm and pectoral atrophy occurred in 48% and 29%, respectively, and was associated with septic shock (diaphragm) and steroid use (pectoral); atrophy of the two muscle types appears unrelated. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

**Blood Purification and Mortality in Sepsis and Septic Shock: A Systematic Review and Meta-analysis of Randomized Trials**

A. Putzu, R. Schorer, J. C. Lopez-Delgado, T. Cassina, G. Landoni .....580


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**Driving Pressure Is Associated with Outcome during Assisted Ventilation in Acute Respiratory Distress Syndrome**

G. Bellani, A. Grassi, S. Sosio, S. Gatti, B. P. Kavanagh, A. Pesenti, G. Foti .....594

This study shows that in the majority of adult patients with acute respiratory distress syndrome, both driving pressure and respiratory system compliance can be reliably measured during pressure support (assisted) ventilation. Higher driving pressure measured during pressure support (assisted) ventilation significantly associates with increased intensive care unit mortality, whereas peak inspiratory pressure does not. Lower respiratory system compliance also significantly associates with increased intensive care unit mortality. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*



## BASIC SCIENCE

-  **Oxidants Regulated Diaphragm Proteolysis during Mechanical Ventilation in Rats**  
*N. Moroz, K. Maes, J.-P. Leduc-Gaudet, P. Goldberg, B. J. Petrof, D. Mayaki, T. Vassilakopoulos, D. Rassier, G. Gayan-Ramirez, S. N. Hussain*.....605



Pretreatment of rats undergoing 24 h of mechanical ventilation with *N*-acetylcysteine prevents decreases in diaphragm contractility, inhibits the autophagy and proteasome pathways, but has no influence on the development of diaphragm fiber atrophy. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

## Pain Medicine

### CLINICAL SCIENCE

-   **Opioid- and Motor-sparing with Proximal, Mid-, and Distal Locations for Adductor Canal Block in Anterior Cruciate Ligament Reconstruction: A Randomized Clinical Trial**  
*F. W. Abdallah, J. Mejia, G. A. Prasad, R. Moga, J. Chahal, J. Theodoropoulos, T. Dwyer, R. Brull*.....619

Proximal adductor canal injections were associated with lower first 24-h morphine consumption than when injections were more distal. Decreases in quadriceps strength were similar whether the injection was made in a proximal, mid-, or distal adductor canal location.

-   **Pectoralis-II Myofascial Block and Analgesia in Breast Cancer Surgery: A Systematic Review and Meta-analysis**  
*N. Hussain, R. Brull, C. J. L. McCartney, P. Wong, N. Kumar, M. Essandoh, T. Sawyer, T. Sullivan, F. W. Abdallah*.....630

This meta-analysis includes 14 randomized trials comparing pectoralis-II block with paravertebral blocks and found that there were no differences in pain scores or opioid consumption between the two groups in patients having surgery for breast cancer. Pectoralis-II blocks were noninferior to paravertebral blocks in reducing pain intensity and morphine consumption for the first 24 h after surgery and both were superior to systemic analgesia alone. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*



## BASIC SCIENCE

- Combination of a  $\delta$ -opioid Receptor Agonist and Loperamide Produces Peripherally-mediated Analgesic Synergy in Mice**  
*D. J. Bruce, C. D. Peterson, K. F. Kitto, E. Akgün, S. Lazzaroni, P. S. Portoghese, C. A. Fairbanks, G. L. Wilcox*.....649



The administration of a selective  $\delta$ -opioid agonist, oxymorphone, and a peripherally-restricted  $\mu$ -agonist, loperamide, provided synergistic analgesia in a mouse inflammatory pain model. The use of combinations of peripherally-restricted opioid ligands may provide analgesia with reduced side effects when compared with centrally acting opioids.

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*H. Sun, D. O. Warner, A. Macario, Y. Zhou, D. J. Culley, M. T. Keegan*.....668


Based on survey data from 2013 to 2016, the prevalence of burnout, distress, and depression in anesthesiology residents and first-year graduates was 51%, 32%, and 12%, respectively. More hours worked and student debt were associated with a higher risk of distress and depression, but not burnout. Perceived institutional and social support and work-life balance were associated with a lower risk of burnout, distress, and depression. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

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*M. J. McVey, R. Kapur, C. Cserti-Gazdewich, J. W. Semple, K. Karkouti, W. M. Kuebler*.....693

Transfusion-related acute lung injury is associated with procedures supervised by anesthesiologists. Although relatively rare, transfusion-related acute lung injury leads to considerable morbidity and mortality within the perioperative period. Therefore, anesthesiologists need to be able to anticipate risks and prevent and treat this condition.

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