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Special Article

◆ **Perspectives on Anesthesia and Perioperative Patient Safety: Past, Present, and Future**
M. K. Kanjia, C. D. Kurth, D. Hyman, E. Williams, A. Varughese835

In this article, the authors offer a perspective on the fundamentals of patient safety science including the definition of events, safety analytics, and the four frameworks (causality models for events, playbooks to address them).

◆ **Conscientious Objection and the Anesthesiologist: An Ethical Dilemma**
R. Koganti, M. M. Cohn, S. H. Resnicoff, S. Roth849


This article reviews the ethical, legal, and practical aspects of conscientious objection as applied to the practice of anesthesiology.

Perioperative Medicine

CLINICAL SCIENCE

◆◇🌐 **Dexamethasone for Cardiac Surgery: A Practice Preference—Randomized Consent Comparative Effectiveness Trial**
 *P. S. Myles, J. M. Dieleman, K. E. Munting, A. Forbes, C. A. Martin, J. A. Smith, D. McGiffin, L. P. J. Verheijen, S. Wallace, for the DECS-II Investigators and the ANZCA Clinical Trials Network*859




This study was a pragmatic, assessor-blinded, parallel-arm, multicenter trial that was successfully implemented to study the association between administration of dexamethasone and development of adverse outcomes after cardiac surgery with cardiopulmonary bypass. This pragmatic study design was implemented effectively, demonstrating an alternative approach to randomized controlled clinical trials, with less expense and in a shorter time period. This study did not identify a significant association between administration of dexamethasone and increased number of home days during the first 30 days after cardiac surgery (primary study outcome).

◆◇🌐 **Cannabis Use and Inhalational Anesthesia Administration in Older Adults: A Propensity-matched Retrospective Cohort Study**
 *R. Sajdeya, M. Rouhizadeh, R. L. Cook, R. L. Ison, C. Bai, S. Jugl, H. Gao, M. T. Mardini, K. Zandbiglari, F. I. Adiba, O. Dasa, A. G. Winterstein, C. C. Price, T. A. Pearson, C. N. Seubert, P. J. Tighe*870

Using a combination of natural language processing of free text notes and structured electronic health record documentation, 268 older adults (age 65 yr or older) with documentation of cannabis use within 60 days before

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ON THE COVER: High-dose corticosteroids have been used to attenuate the inflammatory response to cardiac surgery and cardiopulmonary bypass, but patient outcome benefits remain unclear. In this issue of ANESTHESIOLOGY, Myles *et al.* aimed to determine whether using dexamethasone was superior to not using dexamethasone to increase the number of home days in the first 30 days after cardiac surgery. In this study, they evaluated the efficiency, value, and impact of a novel, pragmatic trial design. In an accompanying editorial, McIsaac *et al.* assert that randomized trials remain the most important tool for evaluating treatments but acknowledge that innovative clinical trial methodologies also have potential. Cover illustration: A. Johnson, Vivo Visuals Studio; photograph: J. P. Rathmell.

- Myles *et al.*: Dexamethasone for Cardiac Surgery: A Practice Preference—Randomized Consent Comparative Effectiveness Trial, p. 859
- McIsaac *et al.*: Routine Innovation in Perioperative Clinical Trials: The Best Chance to Answer Our Most Important Questions?, p. 825

surgery were compared to 1,072 similar older adults without documentation of cannabis use. Cannabis users received a time-weighted average volatile minimum alveolar concentration of 0.58 (SD, 0.23) compared to 0.54 (SD, 0.22). Although this mean difference of 0.04 minimum alveolar concentration was statistically significant, the clinical significance of this difference is unclear and does not support the hypothesis that older adult cannabis users require clinically meaningful higher inhalational anesthetic dosing.

- ◇ **Restrictive versus Decision Support Guided Fluid Therapy during Major Hepatic Resection Surgery: A Randomized Controlled Trial**
S. Coeckelenbergh, M. Soucy-Proulx, P. Van der Linden, S. Rouillet, M. Moussa, H. Kato, L. Toubal, S. Naili, J. Rinehart, T. Grogan, M. Cannesson, J. Duranteau, A. Joosten881


Ninety patients undergoing major laparoscopic or open hepatic resection were randomized to a decision support or restrictive fluid strategy. Lactate levels at the end of surgery in the decision support group (median, 2.5 mM; interquartile range, 1.9 to 3.7) were lower than in the restrictive group (median, 4.6; interquartile range, 3.1 to 5.4) for a median difference of 2.1 mM (95% CI, -2.7 to -1.2; $P < 0.001$). The exploratory secondary outcome of intraoperative estimated blood loss was not statistically significantly different between the decision support group (median, 450 ml; interquartile range, 300 to 600) compared to the restrictive fluid group (median 500 ml; interquartile range, 300 to 800 ml; $P = 0.727$).

- ◇ **Plantar Compartment Block Improves Enhanced Recovery after Hallux Valgus Surgery: A Randomized, Comparative, Double-blind Study**
F. Swisser, Y. Brethe, O. Choquet, M. Herteleer, N. Bernard, I. Laffont, S. Bringuier, X. Capdevila891

In this prospective randomized trial, both gait quality and median time to free ambulation was improved in patients with plantar compartment block when compared to those with popliteal sciatic nerve block following hallux valgus surgery.

Critical Care Medicine

CLINICAL SCIENCE

- ◆ **Correction of Trauma-induced Coagulopathy by Goal-directed Therapy: A Secondary Analysis of the ITACTIC Trial**
 *C. Lindsay, R. Davenport, K. Baksaas-Aasen, K. M. Kolstadbråten, P. A. Naess, N. Curry, M. Maegeler, N. Juffermans, S. Stanworth, J. Stensballe, P. I. Johansson, C. Gaarder, K. Brohi*904

The study evaluated 133 patients; 71% were coagulopathic on admission, whereas 16% developed coagulopathy during resuscitation. The viscoelastic group received goal-directed therapy more often than conventional (76% vs. 47%), and only 20% corrected their coagulopathy (vs. 0% with empiric treatment alone) with time to first goal-directed treatment of 68 (53 to 88) min for the viscoelastic group and 110 (77 to 123) min for the conventional group. Many bleeding trauma patients did not receive indicated goal-directed treatment, and interventions arrived late during resuscitation and were only partially effective at correcting coagulopathy.


BASIC SCIENCE

- ◇ **Calcium-activated Potassium Channels as Amplifiers of TRPV4-mediated Pulmonary Edema Formation in Male Mice**
M. Li, J. Roeder, J. Blázquez-Prieto, S. Schulz, J. Naujox, J. Falivene, L. Erfananda, W. Liedtke, G. M. Albaiceta, W. M. Kuebler, L. Michalick913


In male mice, both endothelial transient receptor potential vanilloid type 4 (TRPV4) deficiency and inhibition of calcium-activated potassium channels, particularly intermediate Ca^{2+} -activated K^+ channel, attenuated ventilator-induced lung injury. Calcium-activated potassium channel antagonists reduced calcium influx in response to mechanical stimulation or direct TRPV4 activation in isolated lungs. These results suggest that calcium-activated potassium channels amplify TRPV4-mediated calcium influx and thereby drive the progression of ventilator-induced lung injury.

Pain Medicine

BASIC SCIENCE

- ◆ **Platelet-derived Growth Factor Receptor- α Induces Contraction Knots and Inflammatory Pain-like Behavior in a Rat Model of Myofascial Trigger Points**
 *Y. Liu, F. Jin, L. Zhou, X. Li, X. Li, Q. Chen, S. Yang, J. Sun, F. Qi*929

Phosphorylation of the receptor tyrosine kinase platelet-derived growth factor receptor- α (PDGFR- α) was increased in myofascial trigger point samples obtained from patients with chronic myofascial pain syndrome. In a rat model of myofascial trigger points, PDGFR- α activation caused pain-like behaviors and muscle contraction *via* the activation of the Janus kinase 2/signal transducer and activator of transcription-3 (JAK2/STAT3) signal transduction pathway. Collagen type I $\alpha 1$ (COL1A1) protein, a major component of the extracellular matrix that is upregulated in multiple disease states, binds to and promotes phosphorylation of PDGFR- α .

- ◆ **Neuropeptide Y Y2 Receptors in Sensory Neurons Tonicly Suppress Nociception and Itch but Facilitate Postsurgical and Neuropathic Pain Hypersensitivity**
 *P. Basu, A. Maddula, T. S. Nelson, P. Prasoorn, M. K. Winter, H. Herzog, K. E. McCarron, B. K. Taylor*946

Pharmacologic antagonism of Y2 receptors increased nociception and itch in uninjured mice, and these effects were mitigated by sensory neuron-specific deletion of Y2 receptors. In contrast, both pharmacologic blockade and conditional deletion of Y2 reduced nociception in experimental mouse models of surgical and neuropathic pain. These results suggest that Y2 receptors at central terminals of primary afferent neurons provide tonic inhibition to nociception and itch under normal conditions but promote hyperalgesia in persistent pain states.

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🌐 Heart under Pressure: Intrathoracic Impact of Large Hiatal Hernia
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CLINICAL FOCUS REVIEW

Identification and Treatment of Pediatric Perioperative Anxiety
R. Yun, T. J. Caruso.....973

This review details the identification and treatment of pediatric perioperative anxiety. Research-based anxiety scales and their relationship to clinically efficient scales are described, followed by an evidence-based summary of traditional and nontraditional anxiolytics.

◇ 🌐 Diagnosis and Treatment of Perioperative Anemia: A Society for Perioperative Assessment and Quality Improvement Collaborative Review
M. Kumar, D. L. Hepner, E. S. Grawe, M. Keshock, M. Khambaty, M. S. Patel, B. Sweitzer.....984

Anemia is common in presurgical patients and is associated with poor clinical outcomes, even without erythrocyte transfusion. Structured preoperative programs for anemia management are associated with fewer blood transfusions, increased hemoglobin concentrations, and improved outcomes.

REVIEW ARTICLE

◇ Systematized Serendipity: Fishing Expeditions for Anesthetic Drugs and Targets
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Unbiased screens are a distinct but productive scientific approach to maximize the potential to identify novel anesthetic mechanisms and drugs.

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