ON THE COVER:
The effect of withholding angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers (ACEi/ARBs) before noncardiac surgery is unknown. In this issue of Anesthesiology, Roshanov et al. analyzed data from the Vascular events In noncardiac Surgery patients cOhort evaluation (VISION) Prospective Cohort study to examine the relationship between withholding ACEi/ARBs and outcomes. Withholding ACEi/ARBs before major noncardiac surgery was associated with a lower risk of death and postoperative vascular events. In an accompanying Editorial View, London discusses the limitations of our current understanding and emphasizes that a randomized trial is needed to confirm these findings.

- Roshanov et al.: Withholding versus Continuing Angiotensin-converting Enzyme Inhibitors or Angiotensin II Receptor Blockers before Noncardiac Surgery: An Analysis of the Vascular events In noncardiac Surgery patients cOhort evaluation Prospective Cohort, p. 16
- London: Preoperative Administration of Angiotensin-converting Enzyme Inhibitors or Angiotensin II Receptor Blockers: Do We Have Enough “VISION” to Stop It? p. 1

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EDITORIAL VIEWS

Preoperative Administration of Angiotensin-converting Enzyme Inhibitors or Angiotensin II Receptor Blockers: Do We Have Enough “VISION” to Stop It?
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It’s About Time
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Monkey in the Middle: Translational Studies of Pediatric Anesthetic Exposure
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Vasopressin, Norepinephrine, and Vasodilatory Shock after Cardiac Surgery: Another “VASST” Difference?
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Innovative Disruption in the World of Neuromuscular Blockade: What Is the “State of the Art?”
M. Naguib and K. B. Johnson

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**WITHDRAWAL versus CONTINUING ANGIOTENSIN-CONVERTING ENZYME INHIBITORS OR ANGIOTENSIN II RECEPTOR BLOCKERS BEFORE NONCARDIAC SURGERY: AN ANALYSIS OF THE VASCULAR EVENTS IN NONCARDIAC SURGERY PATIENTS COHORT PROSPECTIVE COHORT STUDY**


In a secondary analysis of 4,802 patients on these drugs in the Vascular events in noncardiac Surgery patients cohort evaluation prospective cohort study, those in whom the drugs were withheld in the 24 h before surgery were less likely to suffer a composite outcome of 30-day all-cause death, stroke, or myocardial injury (18% adjusted relative risk reduction).

**MASK VENTILATION DURING INDUCTION OF GENERAL ANESTHESIA: INFLUENCES OF OBSTRUCTIVE SLEEP APNEA**


In a study of 80 patients, tidal volume administered during one-hand mask ventilation at the time of anesthetic induction was reduced in patients with a diagnosis of sleep-disordered breathing but was restored with two-hand ventilation.

**RAPID OCCURRENCE OF CHRONIC KIDNEY DISEASE IN PATIENTS EXPERIENCING REVERSIBLE ACUTE KIDNEY INJURY AFTER CARDIAC SURGERY**


Regardless of its severity, a fully recovering episode of acute kidney injury after cardiac surgery in patients without preexisting chronic kidney disease is strongly associated with a subsequent increase in the risk of de novo chronic kidney disease.

**RELATIONSHIP BETWEEN INTRAOPERATIVE HYPOTENSION, DEFINED BY EITHER REDUCTION FROM BASELINE OR ABSOLUTE THRESHOLDS, AND ACUTE KIDNEY AND MYOCARDIAL INJURY AFTER NONCARDIAC SURGERY: A RETROSPECTIVE COHORT ANALYSIS**


The associations based on relative mean arterial pressure thresholds were no stronger than those based on absolute thresholds. Furthermore, there was no clinically important interaction with preoperative pressure. These data suggest that anesthetic management can thus be based on intraoperative pressures without regard to preoperative pressure.

**DOES Dexmedetomidine HAVE A PERINEURAL MECHANISM OF ACTION WHEN USED AS AN ADJUVANT TO ROPIVACAINE? A PAIRED, BLINDED, RANDOMIZED TRIAL IN HEALTHY VOLUNTEERS**


In 21 volunteers receiving bilateral saphenous nerve block with ropivacaine, adding dexmedetomidine (100 μg) on one side and saline on the other, statistically significantly increased duration of sensory blockade on the side with dexmedetomidine, although the magnitude of effect was not clinically relevant. The effect of perineural dexmedetomidine may be peripheral.

**ISOFLURANE ANESTHESIA HAS LONG-TERM CONSEQUENCES ON MOTOR AND BEHAVIORAL DEVELOPMENT IN INFANT RHESUS MACAQUES**


Multiple exposures of neonatal rhesus macaques to isoflurane led to motor reflex deficits and increased anxiety at 1 yr, while a single exposure did not. Future studies of the long-term behavioral consequences of multiple exposures to general anesthesia should focus on socioemotional behavioral indices.
**CLINICAL SCIENCE**

**Vasopressin versus Norepinephrine in Patients with Vasoplegic Shock after Cardiac Surgery:** The VANCS Randomized Controlled Trial


A single-center double-blind controlled trial randomized 330 patients with vasoplegic syndrome to receive vasopressin or norepinephrine. In patients receiving vasopressin, the primary endpoint (mortality or severe complications) occurred in 32%, compared with 49% receiving norepinephrine, and atrial fibrillation was less frequent (63.8% vs. 82.1%).

**Pilot Study of Propofol-induced Slow Waves as a Pharmacologic Test for Brain Dysfunction after Brain Injury**


In this experimental pilot study, we found the comatose postcardiac arrest patients with poor neurologic outcome unable to generate normal propofol-induced electroencephalographic slow-wave activity 48 h after cardiac arrest.

**Extubation Failure in Brain-injured Patients: Risk Factors and Development of a Prediction Score in a Preliminary Prospective Cohort Study**

T. Godet, R. Chabanne, J. Marin, S. Kauffmann, E. Futier, B. Pereira, and J.-M. Constantin

Decision to extubate brain-injured patients with residual impaired consciousness holds high degree of uncertainty of success and undesirability of incorrect prediction. Three components of upper-airway function and one component of neurologic status were identified as independent criteria predictive of extubation failure in a monocentric cohort of brain-injured patients.

**Activated Protein C Drives the Hyperfibrinolysis of Acute Traumatic Coagulopathy**


Using blood samples from trauma patients and a murine model of acute traumatic coagulopathy with suppressed protein C activation, the authors demonstrated elevated activated protein C levels with increased fibrinolysis and depletion of fibrinogen. Procoagulant pathways were only minimally inhibited. Activated protein C–associated fibrinolysis and fibrinogenolysis, rather than inhibition of procoagulant pathways, predominate in acute traumatic coagulopathy and provide new potential translational opportunities for therapy.

**BASIC SCIENCE**

**Transient Receptor Potential Melastatin 2 Regulates Phagosome Maturation and Is Required for Bacterial Clearance in Escherichia coli Sepsis**

Z. Zhang, P. Cui, K. Zhang, Q. Chen, and X. Fang

In a study of *Escherichia coli* sepsis using transient receptor potential melastatin 2 (TRPM2) knockout mice, the TRPM2 channel facilitated increased cytosolic calcium and phagosome maturation, which in turn augmented bactericidal action and improved survival.

**Ivabradine Attenuates the Microcirculatory Derangements Evoked by Experimental Sepsis**

M. L. Miranda, M. M. Balarini, D. S. Balthazar, L. S. Paes, M.-C. S. Santos, and E. Bouskela

In a hamster model of sepsis, ivabradine increased capillary density and arteriolar diameter measured using intravital microscopy, and it reduced renal, hepatic, and neurologic dysfunction. This suggests that ivabradine may be a testable intervention in human sepsis.
Acquired Exchange Protein Directly Activated by Cyclic Adenosine Monophosphate Activity Induced by p38 Mitogen-activated Protein Kinase in Primary Afferent Neurons Contributes to Sustaining Postincisional Nociception  

M. Matsuda, K. Oh-hashi, I. Yokota, T. Sawa, and F. Amaya

Plantar incision led to sustained latent mechanical hypersensitivity due to nociceptor priming; this was accompanied by increased expression of exchange protein directly activated by cyclic adenosine monophosphate (EPAC) in dorsal root ganglion cells. Inhibition of EPAC or of p38MAPK prevented nociceptor priming. The data suggest that increased EPAC expression due to the activation of p38MAPK are central to heightened pain sensitivity for an extended period after incision trauma.

Intraoperative Transesophageal Echocardiography Alters Surgical Plan for Laser Lead Extraction  

S. Bahadur, T. L. Evans, V. Patel, and M. E. Arthur

Pediatric anesthesiologists should be aware of severe cardiopulmonary events that can occur during intraarterial chemotherapy for retinoblastoma.

Residual neuromuscular block remains a significant patient safety concern. This article reviews the most common causes of residual block and offers suggestions for optimizing the use of muscle relaxants, facilitating their antagonism, and monitoring neuromuscular function.

Pediatric anesthesiologists should be aware of severe cardiopulmonary events that can occur during intraarterial chemotherapy for retinoblastoma.
Complexities of Bleeding During Spine Surgery: It’ll Take Your (Mechanical) Breath Away
B. I. Naik, E. C. Nemergut, and M. E. Durieux

In Reply

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