



ON THE COVER:

The focus of the anesthesiologist has long been largely on determining the most appropriate thresholds for transfusion in the perioperative setting. This month's issue of ANESTHESIOLOGY includes a series of articles and accompanying Editorial Views that detail risks associated with perioperative transfusion that were previously ignored, including the risk of transfusion-related acute lung injury (TRALI), transfusion-associated circulatory overload (TACO), and the risks and benefits of transfusion in surgical oncology patients.

- Clifford *et al.*: Characterizing the Epidemiology of Postoperative Transfusion-related Acute Lung Injury, p. 12
- Clifford *et al.*: Characterizing the Epidemiology of Perioperative Transfusion-associated Circulatory Overload, p. 21
- Pinheiro de Almeida *et al.*: Transfusion Requirements in Surgical Oncology Patients: A Prospective, Randomized Controlled Trial, p. 29
- Simmons and Pittet: Revealing the Real Risks of Perioperative Transfusion: Rise of the Machines!, p. 1
- Cata: Perioperative Anemia and Blood Transfusions in Patients with Cancer: When the Problem, the Solution, and Their Combination Are Each Associated with Poor Outcomes, p. 3

◆ THIS MONTH IN ANESTHESIOLOGY

1A

■ SCIENCE, MEDICINE, AND THE ANESTHESIOLOGIST

21A

■ INFOGRAPHICS IN ANESTHESIOLOGY

23A

■ EDITORIAL VIEWS

Revealing the Real Risks of Perioperative Transfusion: Rise of the Machines!

J. W. Simmons and J.-F. Pittet

1

CME Perioperative Anemia and Blood Transfusions in Patients with Cancer: When the Problem, the Solution, and Their Combination Are Each Associated with Poor Outcomes

J. P. Cata

3

Anaphylaxis to Neuromuscular-blocking Drugs: All Neuromuscular-blocking Drugs Are Not the Same

P. M. Mertes and G. W. Volcheck

5

Big Brain, Small World?

E. Olofsen and A. Dahan

8

◆ Refers to This Month in Anesthesiology

◆ Refers to Editorial Views

🌐 See Supplemental Digital Content

CME CME Article

■ PERIOPERATIVE MEDICINE

CLINICAL SCIENCE

◆◆ **Characterizing the Epidemiology of Postoperative Transfusion-related Acute Lung Injury** 12

L. Clifford, Q. Jia, A. Subramanian, H. Yadav, G. A. Wilson, S. P. Murphy, J. Pathak, D. R. Schroeder, and D. J. Kor

A retrospective cohort analysis from one institution documented that perioperative transfusion-related acute lung injury occurs approximately 1.4 to 3% in surgical patients, with higher rates in patients who received larger volumes of blood component therapies.

◆◆🌐 **Characterizing the Epidemiology of Perioperative Transfusion-associated Circulatory Overload** 21

L. Clifford, Q. Jia, H. Yadav, A. Subramanian, G. A. Wilson, S. P. Murphy, J. Pathak, D. R. Schroeder, M. H. Ereth, and D. J. Kor

This retrospective cohort study evaluated 2,162 and 1,908 patients who received intraoperative transfusions during noncardiac surgery in 2004 and 2011, respectively. A total of 119 patients (5.5%) in 2004 and 57 patients (3%) in 2011 met criteria for transfusion-associated circulatory overload. The incidence of transfusion-associated circulatory overload increased with the volume of blood product transfused, advanced age, and total intraoperative fluid balance. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

CME◆◆ **Transfusion Requirements in Surgical Oncology Patients: A Prospective, Randomized Controlled Trial** 29

J. Pinheiro de Almeida, J.-L. Vincent, F. R. B. Gomes Galas, E. Pinto Marinho de Almeida, J. T. Fukushima, E. A. Osawa, F. Bergamin, C. Lee Park, R. Ely Nakamura, S. M. R. Fonseca, G. Cutait, J. Inacio Alves, M. Bazan, S. Vieira, A. C. Vieira Sandrini, H. Palomba, U. Ribeiro, Jr., A. Crippa, M. Dalloglio, M. del Pilar Estevez Diz, R. Kalil Filho, J. Otavio Costa Auler, Jr., A. Rhodes, and L. Abrahao Hajjar

In 198 patients randomly assigned to red cell transfusions at a hemoglobin concentration of 7 or 9 g/dl. Major complications were nearly twice as common in patients managed with the restrictive approach as in those managed with the liberal approach (36% vs. 20%). This study supports a more liberal transfusion strategy in major cancer surgery.

🌐 **Anaphylaxis Is More Common with Rocuronium and Succinylcholine than with Atracurium** 39

J. I. Reddy, P. J. Cooke, J. M. van Schalkwyk, J. A. Hannam, P. Fitzharris, and S. J. Mitchell

Search of a database containing more than 400,000 anesthetic records identified 92,858 new patient exposures to neuromuscular-blocking drugs between 2006 and 2012. Twenty-one of 89 patients referred to the Anesthetic Allergy Clinic had anaphylaxis attributed to muscle relaxants. Use of credible numerator and denominator data found similar rates of anaphylaxis after succinylcholine and rocuronium administration, rates that were nearly an order of magnitude higher than those for atracurium and other neuromuscular-blocking drugs. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

◆ **Postoperative Bladder Catheterization Based on Individual Bladder Capacity: A Randomized Trial** 46

T. A. Brouwer, P. F. W. M. Rosier, K. G. M. Moons, N. P. A. Zuithoff, E. N. van Roon, and C. J. Kalkman

In a prospective trial involving 1,840 patients, maximum bladder capacity was determined before surgery. Using predetermined maximum bladder capacity, the authors demonstrated that a reduction in the need for postoperative bladder catheterization could be achieved.

Accuracy of Malignant Hyperthermia Diagnoses in Hospital Discharge Records 55

T. Pinyavat, H. Rosenberg, B. H. Lang, C. A. Wong, S. Riaz, J. E. Brady, L. S. Sun, and G. Li

In review by an expert panel of International Classification of Diseases coding for malignant hyperthermia over a 3-yr period, approximately 70% of coded cases were considered to be malignant hyperthermia susceptible. The most common reason for inaccurate coding was high fever unrelated to anesthesia.

Relationship between Chronic Intermittent Hypoxia and Intraoperative Mean Arterial Pressure in Obstructive Sleep Apnea Patients Having Laparoscopic Bariatric Surgery 64

A. Turan, J. You, C. Egan, A. Fu, I. Gazmuri, A. Khanna, Y. Eshraghi, R. Ghosh, S. Bose, S. Qavi, L. Arora, D. I. Sessler, and A. G. Doufas

Recurrent nocturnal hypoxemia in obstructive sleep apnea is not a risk marker for intraoperative hypotension in patients undergoing laparoscopic bariatric surgery.

BASIC SCIENCE

- 🌐 **Propofol Attenuated Acute Kidney Injury after Orthotopic Liver Transplantation *via* Inhibiting Gap Junction Composed of Connexin 32** 72

C. Luo, D. Yuan, X. Li, W. Yao, G. Luo, X. Chi, H. Li, M. G. Irwin, Z. Xia, and Z. Hei

Anesthetized rats underwent autologous orthotopic liver transplantation in the absence or presence of treatments with a selective Cx32 inhibitor, 2-aminoethoxydiphenyl borate, or propofol. Propofol inhibited Cx32 function and attenuated postautologous orthotopic liver transplantation acute kidney injury. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

- Long-term Effects of Single or Multiple Neonatal Sevoflurane Exposures on Rat Hippocampal Ultrastructure** 87

L. G. Amrock, M. L. Starner, K. L. Murphy, and M. G. Baxter

Repeated exposure to sevoflurane led to a greater loss of synapses in comparison to a single exposure. Anesthetic exposure led to a reduction in the number of synaptic terminals with mitochondria. Interestingly, this reduction was correlated to total anesthetic exposure rather than frequency of exposure. These data suggest that a brief anesthetic exposure might sensitize the brain to subsequent anesthetic induced injury.

■ CRITICAL CARE MEDICINE

CLINICAL SCIENCE

- Assessment of Neutrophil Gelatinase-associated Lipocalin in the Brain-dead Organ Donor to Predict Immediate Graft Function in Kidney Recipients: A Prospective, Multicenter Study** 96

L. Muller, A. Nicolas-Robin, S. Bastide, O. Martinez, G. Louart, J.-C. Colavolpe, F. Vachier, S. Alonso, J.-Y. Lefrant, and B. Riou; for AzuRea Group

Despite the ability to predict acute renal failure earlier than serum creatinine rises in critically ill patients, neutrophil gelatinase-associated lipocalin measurements in blood samples obtained from brain-dead donors before kidney graft harvesting failed to predict either delayed or normal graft function in kidney recipients.

BASIC SCIENCE

- 🌐 **Modulation of Stress *versus* Time Product during Mechanical Ventilation Influences Inflammation as Well as Alveolar Epithelial and Endothelial Response in Rats** 106

P. M. Spieth, P. L. Silva, C. S. N. B. Garcia, D. S. Ornellas, C. S. Samary, L. Moraes, M. Bentes, M. M. Morales, M. Kasper, A. Güldner, R. Huhle, T. Koch, P. Pelosi, M. Gama de Abreu, and P. R. M. Rocco

In a mild acute lung inflammation model in rats, using mechanical ventilation with an inspiratory-to-expiratory ratio of 1:1 minimized lung damage, whereas an inspiratory-to-expiratory ratio of 2:1 led to increased gene expression of inflammatory mediators and markers of alveolar epithelial cell injury. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

- Volatile Organic Compounds during Inflammation and Sepsis in Rats: A Potential Breath Test Using Ion-mobility Spectrometry** 117

T. Fink, A. Wolf, F. Maurer, F. W. Albrecht, N. Heim, B. Wolf, A. C. Hauschild, B. Bödeker, J. I. Baumbach, T. Volk, D. I. Sessler, and S. Kreuer

Exhaled gas from rats given endotoxin compared with the gas from rats with bacterial sepsis was found to be significantly different and different from rats who were in hemorrhagic shock. Breath analysis appears to be able to distinguish inflammation from infection.

- 🌐 **Extracellular Histones Play an Inflammatory Role in Acid Aspiration-induced Acute Respiratory Distress Syndrome** 127

Y. Zhang, Z. Wen, L. Guan, P. Jiang, T. Gu, J. Zhao, X. Lv, and T. Wen

Extracellular histones were significantly elevated in the bronchoalveolar lavage from mice with acid-induced lung injury *versus* sham mice and in human patients who died from acute lung injury compared to survivors with acute lung injury. Extracellular histones may be causal, and targeting histones may be a reasonable therapeutic strategy. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

CONTENTS

■ PAIN MEDICINE

CLINICAL SCIENCE

- ◆ ◆ **Disruption of Cortical Connectivity during Remifentanyl Administration Is Associated with Cognitive Impairment but Not with Analgesia** 140

A. Khodayari-Rostamabad, S. S. Olesen, C. Graversen, L. P. Malver, G. P. Kurita, P. Sjøgren, L. L. Christrup, and A. M. Drewes

Remifentanyl altered graph-theoretical measures of the electroencephalography, characterized by an increase in path length in the alpha and low beta frequency ranges. Changes in path length were correlated to continuous reaction time, a measure of sedation. However, a correlation between electroencephalography measures and pain perception was not apparent. Remifentanyl alters functional network connectivity in the brain, and the changes in the electroencephalography have the potential to serve as markers of remifentanyl-induced sedation but not analgesia.

- 🌐 **Immediate Rescue Designs in Pediatric Analgesic Trials: A Systematic Review and Meta-analysis** 150

J. Kossowsky, C. Donado, and C. B. Berde

The investigators performed a meta-analysis of pediatric trials with four classes of analgesics, using rescue/opioid-sparing designs. Average pain scores were low and similar in control and experimental analgesic groups, confirming the ethical basis of opioid-sparing rescue designs. Opioid-sparing designs also showed good assay sensitivity. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

- ◆ **A Randomized Control Trial of Bupivacaine and Fentanyl *versus* Fentanyl-only for Epidural Analgesia during the Second Stage of Labor** 172

M. G. Craig, E. N. Grant, W. Tao, D. D. McIntire, and K. J. Leveno

In 310 nulliparous women with epidural analgesia randomized at the onset of second stage to receive epidural fentanyl alone or with bupivacaine, there was no difference in duration of second stage, degree of motor block, or instrumental delivery. To achieve similar degrees of analgesia, women receiving epidural fentanyl without bupivacaine required a fivefold increased dose of fentanyl.

BASIC SCIENCE

- Brain Serotonin Content Regulates the Manifestation of Tramadol-induced Seizures in Rats: Disparity between Tramadol-induced Seizure and Serotonin Syndrome** 178

Y. Fujimoto, T. Funao, K. Suehiro, R. Takahashi, T. Mori, and K. Nishikawa

Tramadol-induced seizure thresholds were reduced by serotonin depletion and increased by serotonin augmentation. Serotonin antagonists also reduced seizure threshold. The results suggest that tramadol-induced seizures are not related to serotonin uptake inhibition and that these seizures are distinct from the serotonin syndrome.

■ EDUCATION

IMAGES IN ANESTHESIOLOGY

- 🌐 **Inversion of the Right Hemidiaphragm due to Massive Hemothorax after Central Line Placement** 190

A. F. Simpao, J. A. Galvez, A. Jay Schwartz, and M. A. Rehman

SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT

CLINICAL CONCEPTS AND COMMENTARY

- ◆ **Pretransfusion Testing and Transfusion of Uncrossmatched Erythrocytes** 191

M. L. Boisen, R. A. Collins, M. H. Yazer, and J. H. Waters

Pretransfusion testing is reviewed for the anesthesiologist, with an emphasis on the electronic crossmatch and transfusion of uncrossmatched erythrocytes when testing is incomplete.

REVIEW ARTICLE

- ◆ **Regulation of Cerebral Autoregulation by Carbon Dioxide** 196

L. Meng and A. W. Gelb

Both perfusion pressure and nonperfusion pressure processes regulate cerebral blood flow. The integrated effect of carbon dioxide and perfusion pressure on cerebral circulation, or the regulation of cerebral autoregulation by carbon dioxide, is discussed.

CONTENTS

MIND TO MIND

- Electrocardiogram** 206
A. Shafer

■ CORRESPONDENCE

- Is the Standard Supplied by the Association for the Advancement of Medical Instrumentation the Measure of All Things for Noninvasive Continuous Hemodynamic Devices?** 208

J. Fortin, K. Lerche, D. Flotzinger, and T. O'Brien

In Reply

M. Cannesson, J. Rinehart, and S.-H. Kim

- Inotrope Use in Cardiac Surgery: A Cause of Worse Outcomes, or Just a Marker of Patients Who Are at Risk?** 210

B. G. Maxwell, J. O. Wasey, and E. S. Heitmiller

In Reply

D. V. Nielsen, S. P. Johnsen, M. K. Hansen, and C.-J. Jakobsen

- Lung Ultrasonography for the Detection of Anesthesia-induced Lung Atelectasis** 213

M. Girard, V. G  n  reux, and A. Monastesse

In Reply

G. Tusman, C. M. Acosta, and S. H. Bohm

- Early Childhood Anesthetic Neurotoxicity and Unmeasured Covariates: There's the RUB** 216

J. C. Drummond

In Reply

C. H. Ing, C. J. DiMaggio, E. Malacova, A. J. Whitehouse, M. K. Hegarty, T. Feng, J. E. Brady, B. S. von Ungern-Sternberg, A. J. Davidson, M. M. Wall, A. J. J. Wood, G. Li, and L. S. Sun

- Old Guidelines or Methods Cannot Insure Quality or Progress** 218

P. M. Kempen

In Reply

J. L. Lockman and A. J. Schwartz

In Reply

W. R. Hand and M. D. McEvoy

■ ANESTHESIOLOGY REFLECTIONS FROM THE WOOD LIBRARY-MUSEUM

- Katz Oxygen Treatment for Catarrh** 7
George S. Bause

- Laughing "Gas" from Knoxville's Dr. H. F. Huffaker** 11
George S. Bause

- Figuier's Forlorn Figure: Horace Wells and the "Humbug Affair"** 54
George S. Bause

CONTENTS

■ REVIEWS OF EDUCATIONAL MATERIAL

222

■ ANNOUNCEMENTS

224

■ CAREERS & EVENTS

228

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