Journal-related Activities and Other Special Activities at the 2021 American Society of Anesthesiologists Meeting

Michael J. Avram, Ph.D., Deborah J. Culley, M.D., Evan D. Kharasch, M.D., Ph.D., Jerrold H. Levy, M.D., F.C.C.M., Martin J. London, M.D.

As in previous years, ANESTHESIOLOGY will sponsor several sessions at the annual meeting of the American Society of Anesthesiologists (ASA, Schaumburg, Illinois), Anesthesiology 2021. The meeting is being held in San Diego, California. Details about the format and meeting attendance can be found on the website, asahq.org/annualmeeting.

30th Journal Symposium: SARS-CoV-2 and COVID-19: New Paradigms and Challenges for Anesthesiologists

Upper 20D
Saturday, October 9 | 1:15 to 4:15 PM
Moderators: **Jerrold H. Levy, M.D., F.C.C.M.**, Executive Editor, ANESTHESIOLOGY, Duke University, Durham, North Carolina; **Martin J. London, M.D.**, Editor, ANESTHESIOLOGY, University of California, San Francisco School of Medicine and Veterans Affairs Medical Center, San Francisco, California

The COVID-19 pandemic, with its explosive onset early in 2020, and its relentless march across the world with attendant morbidity and mortality, has forced anesthesiologists to adapt rapidly and uniquely to save lives and maintain critical surgical services. The development of a vaccine and innovative management and therapeutic strategies has proceeded at "warp speed," and despite being well into our second year of the pandemic, predicting the future remains challenging. Our role as anesthesiologists has received widespread recognition for our expertise in airway management and caring for critically ill patients both in the operating room and in the intensive care unit (ICU). We have learned much about the pathophysiology of COVID-19 and best practices for treating it, but new information on its physiologic and long-term consequences continues to emerge. This program will begin with a plenary session of two experts reviewing scientific and clinical information followed by nine abstract presentations from relevant research and/or clinical perspectives. The full text for each abstract can be found at the ASA abstract website.

Speakers: **Pulmonary Manifestations and Management of COVID-19**
Maurizio F. Cereda, M.D.
Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania

Adapting ICU and Perioperative Resources to the Pandemic: What Have We Learned?
Aaron M. Mittel, M.D.
Columbia University, New York, New York

JS01

Increased Perioperative Morbidity and Mortality in COVID-19 Patients Undergoing Orthopedic Surgery
Uchenna Umeh, M.D., FASA, Connor Singrey, B.A., Chantal Lisette Mendes, M.D., Jennifer W. Charles, M.D., David Seligsohn, M.D., Prianka Desai, M.D., Shruthima Thangada, M.D., Arthur C. Hertling, M.D.
Department of Anesthesiology, Perioperative Care and Pain Medicine, New York University Langone Health, New York, New York (U.U., C.S., C.L.M., J.W.C., P.D., S.T., A.C.H.); and Department of Anesthesiology, Perioperative Care and Pain Medicine, New York University Langone Health, Brooklyn, New York (D.S.)

JS02

Comparison of Neutralizing Capacity of Plaque Reduction Assay to Novel Pseudovirus Assay for SARS-CoV-2
Alex Freedenberg, Student, Chun-Hao Pan, M.S., Janet Hearing, Ph.D., Jamie Romeiser, Ph.D., M.P.H., Elliott Bennett-Guerrero, M.D.
Departments of Anesthesia (A.F., E.B.-G.), Pathology (C.-H.P.), and Microbiology and Immunology (J.H.), Stony Brook University, Stony Brook, New York

JS03

Comparison of Hemostatic Profiles of Patients in Intensive Care Unit for COVID-19 during the First and Second Waves of the Pandemic

From Northwestern University, Chicago, Illinois (M.J.A.); University of Pennsylvania, Philadelphia, Pennsylvania (D.J.C.); Duke University, Durham, North Carolina (E.D.K., J.H.L.); and University of California, San Francisco, and Veterans Affairs Medical Center, San Francisco, California (M.J.L.).

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Léonie Gardot, Student, Lelia Grunebaum, M.D., Laurent Sattler, M.D., Julien Pottecher, M.D., Ph.D., Eric Noll, M.D., Ph.D., Girish P. Joshi, M.D., Pierre A. Diemunsch, M.D., Ph.D.
Hôpitaux Universitaires de Strasbourg, Strasbourg, France (L. Gardot, L. Grunebaum, L.S., J.P., E.N., P.A.D.); and University of Texas Southwestern Medical Center, Dallas, Texas (G.P.J.)

JS04

Cell-free miRNAs Regulate Signaling Pathways Involved in COVID-19 Pneumonia and the Progression to ARDS

Agnes S. Meidert, M.D., Stefanie Hermann, M.Sc., Florian Brandes, M.D., Benedikt Kirchner, M.Sc., Matthias Klein, M.D., Anja Lindemann, M.Sc., Marlene Reithmair, D.V.M., Michael Pfaffl, Ph.D., Gustav Schelling, M.D.
Departments of Anaesthesiology (A.S.M., F.B., G.S.), Neurology (M.K.), and Human Genetics, (A.L., M.R.), University Hospital, Ludwig Maximilian University of Munich, Munich, Germany; and Division of Animal Physiology and Immunology, Technical University of Munich, Munich, Germany (S.H., B.K., M.P.)

JS05

Adoption of Airway Management Guidelines during COVID-19 Pandemic Improved First-attempt Endotracheal Intubation Success

Stephen Raithel, M.D., Kara Fields, M.S., Yiran Wu, No Degree, Dongdong Yao, M.D.
Department of Anesthesiology, Perioperative and Pain Medicine, Brigham and Women's Hospital, Boston, Massachusetts (S.R., K.F., D.Y.); and Xuzhou Medical University, Xuzhou, China (Y.W.)

JS06

Perioperative Outcomes of Pediatric SARS-CoV-2 Recovered Patients

Mark Hubbard, M.D., Jessica A. Cronin, M.D., Sophie R. Pestieau, M.D., Nina Deutsch, M.D., Jonathan Nelson, M.D., Angela Chae Lee, M.D., Md Sohel Rana, M.B.B.S., M.P.H., Giuliana P. Geng-Ramos, M.D.
Division of Anesthesiology, Pain and Perioperative Medicine (M.H., J.A.C., S.R.P., N.D., J.N., A.C.L., G.P.G.-R.) and Center for Surgical Care, Children's National Hospital, Washington, D.C. (M.S.R.)

JS07

Obstetric Outcomes of 103 SARS-CoV-2–positive Parturients with Labor Analgesia and Anesthesia: A Single-center Experience

Alexandria Lehrmann, Student, Rovnat Babazade, M.D., Kristine Spicer Lane, Student, Lakshmi Ram, M.D., James Hayden Lane, Student, Ahmed Riaz Butt, Student, Siyun Xie, M.D., Dania Adel Hussein, M.D., Rakesh Vadhera, M.D., Shobana Murugan, M.D.
School of Medicine (A.L., KSL, J.H.L., A.R.B., D.A.H.) and Department of Anesthesiology (R.B., L.R., S.X., R.V., S.M.), University of Texas Medical Branch, Galveston, Texas

JS08

Anxiety Levels in Anesthesia Providers during COVID-19

Javier Polania Gutierrez, M.D., Maria G. Sanchez, M.D., Klifford A. Rocuts-Martinez, M.D., Efrain Riveros-Perez, M.D., MBA.
Department of Anesthesiology and Perioperative Medicine, Augusta University Medical Center, Augusta, Georgia

JS09

Perceptions of Anesthesiology Critical Care Medicine Physicians on Anxiety, Depression, Lack of Diversity, and Bias in Critical Care Medicine

Shahla Siddiqui, M.D.
Department of Anesthesiology, Beth Israel Deaconess Medical Center, Boston, Massachusetts

Initial Results: Major Clinical Trials

Upper 6A
Saturday, October 9 | 4:30 to 5:30 PM
Moderators: **Evan D. Kharasch, M.D., Ph.D.,** Editor-in-Chief, ANESTHESIOLOGY, Duke University Medical Center, Durham, North Carolina; **Deborah J. Culley, M.D.,** Executive Editor, ANESTHESIOLOGY, University of Pennsylvania, Perelman School of Medicine, Philadelphia, Pennsylvania

ANESTHESIOLOGY is sponsoring its sixth Major Clinical Trials Session, a high-profile, large-audience forum for initial presentations of major randomized clinical trial results. It is designed for substantial trials, usually randomized and blinded, with a clinically important primary outcome.

Best Abstracts: Clinical Science and Basic Science

ANESTHESIOLOGY is sponsoring two Best Abstract sessions: one in basic science and another in clinical science. The abstracts were chosen by a panel of editors who examined the highest scoring abstracts from the ASA subcommittees, choosing those with important scientific and clinical application and novelty. Subsequently, a combination of those editors and appointees from ASA will choose one abstract in each category to receive the Best of Abstracts award for basic and clinical science during this year's meeting. The following are summaries of the excellent abstracts that will be presented.

Best Abstracts: Clinical Science

Upper 9
Sunday, October 10 | 7:30 to 9:30 AM
Moderators: **Michael J. Avram, Ph.D.,** Assistant Editor-in-Chief, ANESTHESIOLOGY, Northwestern University Feinberg School of Medicine, Chicago, Illinois; **Deborah J. Culley, M.D.,** Executive Editor, ANESTHESIOLOGY, University of Pennsylvania, Perelman School of Medicine, Philadelphia, Pennsylvania; **Martin J. London, M.D.,** Editor, ANESTHESIOLOGY, University of California, San Francisco School of Medicine and Veterans Affairs Medical Center, San Francisco, California

3966

Albumin Kinetics in Nonseptic and Septic Patients
Keisuke Omiya, M.D., Hiroaki Sato, M.D., Ph.D., Tamaki Sato, M.D., Linda Wykes, M.D., Ph.D., Mengyin Hong, Ph.D., Thomas Schricker, M.D., Ph.D.
Department of Anesthesia, Royal Victoria Hospital, McGill University Health Centre, Montreal, Quebec, Canada (K.O., H.S., T. Sato, T. Schricker); and the School of Human Nutrition, McGill University, Montreal, Quebec, Canada (L.W., M.H.)
Decreased blood albumin concentrations, as seen during critical illness, may be due to decreased hepatic albumin production or increased systemic albumin clearance. The kinetics of albumin was determined using stable isotope tracer infusions in 24 septic patients and 14 nonseptic patients. The mean serum albumin concentration in septic patients was less than that in nonseptic patients, while albumin synthesis rates were comparable, from which it can be concluded that hypoalbuminemia during sepsis in these patients is due to increased albumin clearance.

3772

Propofol and Sevoflurane Have Differential Effects on Cellular Long Noncoding RNAs during Colon Cancer Resection
Florian Brandes, M.D., Agnes S. Meidert, M.D., Anja Lindemann, M.Sc., Ph.D., Melanie Borrmann, M.D., Benedikt Kirchner, M.S., Michael W. Pfaffl, Ph.D., Gustav Schelling, M.D., Marlene Reithmair, D.V.M.
Department of Anesthesiology (F.B., A.S.M., M.B., G.S.) and Institute of Human Genetics (A.L., M.R.), University Hospital, Ludwig-Maximilians-University, Munich, Germany; and Division of Animal Physiology and Immunology, Technical University of Munich School of Life Sciences Weihenstephan, Technical University of Munich, Weihenstephan, Germany (B.K., M.W.P., G.S.)
Although prometastatic effects of volatile anesthetics and antitumor effects of propofol-based total intravenous anesthesia have been observed in cellular models of colorectal cancer, retrospective clinical studies have had conflicting results. The effects of total intravenous anesthesia and sevoflurane on a novel class of cancer-associated long-chain noncoding RNAs was determined in 12 patients receiving total intravenous anesthesia and 10 patients receiving sevoflurane anesthesia for colon cancer resection surgery. Total intravenous anesthesia and sevoflurane had differential and specific effects on long-chain noncoding RNAs and their associated cancer-related canonical pathways.

3705

Development and Validation of a Novel Nomogram to Predict Postoperative Pulmonary Complications in Critically Ill Patients after Cardiovascular Surgery
Sanchit Ahuja, M.D., Ashish K. Khanna, M.D., Marta Kelava, M.D., Natalya Makarova, M.S., Chen Liang, M.S., Donna Tanner, R.T., Steven R. Insler, D.O.
Department of Anesthesiology, Pain Management and Perioperative Medicine, Henry Ford Health Systems, Detroit, Michigan (S.A.); Department of Anesthesiology, Section on Critical Care Medicine, Wake Forest University School of Medicine, Wake Forest Baptist Medical Center, Winston Salem, North Carolina (A.K.K.); Departments of Cardiac Anesthesia (M.K.), Quantitative Health Sciences and Outcomes Research (N.M., C.L.), Intensive Care and Resuscitation and Cardiothoracic Anesthesia (S.R.I.), Cleveland Clinic (D.T.), Cleveland Clinic, Cleveland, Ohio
Preoperative, intraoperative, and immediate postoperative factors contribute to increased risk of postoperative pulmonary complications. A novel scoring system to identify postoperative pulmonary complications after cardiovascular surgeries on the basis of a combination of baseline and perioperative variables was evaluated, validated, and compared in 17,433 patients admitted to the cardiovascular intensive care unit, 1,669 (9.6%) of whom developed postoperative pulmonary complications. A prediction model that included baseline and demographic risk factors with perioperative predictors had a C-statistic of 0.88 (95% CI, 0.87 to 0.88).

3524

Etomidate *versus* Ketamine for Emergency Endotracheal Intubation: A Prospective Randomized Clinical Trial
Gerald Matchett, M.D., Irina Gasanova, M.D., Ph.D., Christina A. Riccio, M.D., Mary C. Sunna, D.N.P., M.S., C.R.N.A., Dawood Nasir, M.D., Brian J. Bravenec, M.D., Omaira Azizad, M.D., Brian Farrell, C.R.N.A., Abu Minhajuddin, Ph.D., Babatunde O. Ogunnaike, M.D., F.A.S.A.
Departments of Anesthesiology and Pain Management (G.M., I.G., C.A.R., D.N., B.J.B., O.A., B.O.O.), Population and Data Science and Psychiatry (A.M.), University of

Texas Southwestern Medical Center, Dallas, Texas; and Department of Anesthesiology, Parkland Health and Hospital System, Dallas, Texas (M.C.S., B.F.)

Retrospective data suggest decreased survival at day 7 of patients receiving etomidate during emergency tracheal intubation. The hypothesis that ketamine would be associated with improved survival at day 7 compared to etomidate was tested in a clinical trial of 801 patients requiring emergency tracheal intubation in the intensive care unit who were randomized to receive ketamine or etomidate to facilitate intubation. Day 7 survival in the ketamine arm (85%) was significantly greater than in the etomidate arm (77%). Survival rates on day 28 did not differ between the groups.

5002

Transesophageal Lung Ultrasound in Adult Cardiac Surgery: Clinical Significance and Predictive Performance for Postoperative Respiratory Events

Philippe Burtin, M.D., Mégane Sausse, M.D., Emmanuel Lorne, M.D., Ph.D., Jean Yves Bigeon, M.D., Constantin Halchini, M.D., Marion Lalande, M.D., Pierre Sentenac, M.D.

Anesthésie Réanimation, Clinique du Millénaire, Montpellier, France

Transesophageal lung ultrasound has been described recently for diagnosis of respiratory failure in intensive care. The Transesophageal Lung Ultrasound Postoperative Respiratory Events project determined the incidence and severity of the alteration of the transesophageal lung ultrasound imaging before/after cardiopulmonary bypass (CPB) in cardiac surgery and the relation of these changes to postoperative respiratory events occurrence in 72 patients, 14 of whom developed postoperative respiratory events. Patients with postoperative respiratory events had significantly higher transesophageal lung ultrasound scores post-CPB. Post-CPB transesophageal lung ultrasound imaging had a higher predictive value for postoperative respiratory event occurrence than either pre-CPB transesophageal lung ultrasound or postoperative transthoracic lung ultrasound.

6390

Control of Postoperative Hypotension Using a Closed-loop System for Norepinephrine Infusion in Patients after Cardiac Surgery: A Randomized Trial

Joseph Rinehart, M.D., Oliver S. Desebbe, M.D., Alexandre P. Joosten, M.D., Ph.D.

Department of Anesthesiology and Perioperative Care, University of California Irvine, Orange, California (J.R.); Department of Anesthesiology and Perioperative Care, Ramsay Sante Sauvegarde Clinic, Lyon, France (O.S.D.); and Department of Anesthesiology and Perioperative Care, Hopitaux Universitaires, Paris-Sud, Universite Paris-Sud, Paris, France (A.P.J.)

The hypothesis that patients managed using a closed-loop vasopressor controller system after cardiac surgery would have less hypotension than those receiving standard management was tested in a randomized controlled 2-h trial of 40 patients. The percentage of time with hypotension in the closed-loop group, 1.4%, was less than that in the control group, 12.5% (difference [95% CI], 9.8% [5.4 to 15.9%]). The mean arterial pressure was between 65 and 75 mmHg 95% of the time in the closed-loop group and 66% of the time in the control group (difference 28% [34 to 19%]).

5137

The Use of the Society for Pediatric Anesthesia's Pedi Crisis Application Version 2.0 as a Teaching Tool for Pediatric Anesthesia Fellows: A Randomized, Controlled Prospective Study

Kim Strupp, M.D., Sean Schooley, B.S., Debnath Chatterjee, M.D., Lawrence I. Schwartz, M.D., Pan Zhaoxing, Ph.D., Devika Singh, M.D., William B. Waldrop, M.D., Chaitanya Challa, M.D., Myron Yaster, M.D., Adria Boucharel, M.D.

University of Colorado/Children's Hospital Colorado, Denver, Colorado (K.S., D.C., L.I.S., M.Y.); University of Colorado, Aurora, Colorado (S.S., P.Z.); Children's Hospital of Philadelphia, Gladwyne, Pennsylvania (D.S.); Texas Children's Hospital, Houston, Texas (W.B.W.); Children's National, Bethesda, Maryland (C.C.); and Children's Hospital Colorado, Aurora, Colorado (A.B.)

The hypothesis that the Pedi Crisis Mobile Application version 2.0 (app) could be used as a formal teaching tool in pediatric fellowship training was tested in a randomized controlled trial of 34 pediatric anesthesiology fellows. In a 1-h classroom examination, 10 critical event stem questions presented a case scenario that can occur during a pediatric anesthetic followed by open-ended questions about standard management. For each stem question, the percentage of correct answers was higher when the app was used ($P = 0.016$ to $P < 0.0001$).

6310

Taking Patient Blood Management out of the Red Zone: Assessing Guideline Compliance for Plasma and Platelet Transfusions

Brian Lo, B.S., Brian C. Cho, M.D., Nadia B. Hensley, M.D., Nicolas C. Cruz, B.A., Paul M. Ness, M.D., Steven M. Frank, M.D.

Departments of Anesthesiology and Critical Care Medicine (B.L., B.C.C., N.B.H., N.C.C., S.M.F.) and Pathology, Transfusion Medicine (P.M.N.), Johns Hopkins University School of Medicine, Baltimore, Maryland

The current study assessed the effect of a patient blood management program on fresh frozen plasma (FFP) and platelet utilization, as well as guideline compliance, at a tertiary academic center. The percentage of patients receiving

FFP decreased from 5.7% before implementation of the guidelines to 5.3% after implementation ($P < 0.0001$). Appropriate implementation of the guidelines would have avoided FFP transfusion in 25 to 50% of patients. The percentage of patients receiving platelet transfusion increased from 6.8% before the guidelines to 7.1% after implementation ($P = 0.005$). Appropriate implementation of the guidelines would have avoided platelet transfusion in 50 to 75% of patients.

3919

The Opioid-sparing Effect of Continuous Local Anesthetic Peripheral Nerve Blockade Compared to Single-shot Injections in Adolescents: A Prospective Cohort Study

Walid Alrayashi, M.D., Constance S. Houck, M.D., Steven Staffa, M.S., Roland R. Brusseau, M.D., Joseph Cravero, M.D.

Departments of Anesthesiology, Critical Care and Pain Medicine (W.A., S.S.) and Anesthesia, Perioperative and Pain Medicine (R.R.B.), Boston Children's Hospital (C.S.H., J.C.), Boston Children's Hospital, Boston, Massachusetts

Perioperative opioid use for the first 3 days after undergoing ambulatory upper or lower extremity surgeries of 66 adolescent patients receiving single-shot local anesthetic peripheral nerve blocks was compared to that of 206 adolescent patients receiving continuous local anesthetic infusions *via* peripheral nerve catheters in a prospective cohort study. More than half of the patients in the peripheral nerve catheter group consumed no opioids on postoperative days 1 to 3, whereas fewer than 10% of the patients in the single-shot group consumed no opioids on those days.

6300

Temporal Trends of Mechanical Power during General Anesthesia: A Hospital Registry Study

Aiman Suleiman, M.D., Peter Santer, M.D., Ph.D., Luca J. Wachtendorf, Student, Daniel Talmor, M.D., M.P.H., Matthias Eikermann, M.D., Ph.D., Elias Baedorf-Kassis, M.D., Maximilian Schaefer, M.D.

Department of Anesthesia, Critical Care and Pain Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts (A.S., P.S., L.J.W., D.T., E.B.-K.); and Department of Anesthesiology, Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, New York (M.E.)

Postoperative respiratory complications have been related to stress from inspiratory pressure, strain imposed by tidal volume, and repetitive opening and closing of alveoli during mechanical ventilation. Mechanical power integrates these parameters into a simplified formula. This retrospective cohort study determined whether mechanical power trends during elective noncardiac surgery and general anesthesia identify patients at risk for postoperative respiratory failure. Of the 156,943 cases, 1,295 (0.83%) required reintubation within 7 postoperative days. Patients requiring postoperative reintubation exhibited a relatively linear increase in intraoperative mechanical power over time.

5004

Relationship between Processing Speed Test and 30-day Readmission in Elderly Noncardiac Surgery Patients

Kamal Maheshwari, M.D., M.P.H., Esra Kutlu Yalcin, M.D., Dong Wang, M.S., Edward Mascha, Ph.D., Anson Rosenfeldt, M.A., Jay Alberts, Ph.D., Kenneth C. Cummings, M.D., M.S.

General Anesthesia, Department of Outcomes Research, Anesthesia Institute (K.M.), Department of Outcomes Research, Anesthesia Institute (E.K.Y.), Departments of Quantitative Health Sciences and Outcomes Research (D.W., E.M.), Biomedical Engineering (A.R., J.A.), and General Anesthesia, Anesthesia Institute (K.C.C.), Cleveland Clinic, Cleveland, Ohio.

The risk for postoperative complications in elderly patients, which increases their risk of 30-day readmission, may be increased by preoperative cognitive dysfunction. In an observational study of patients at least 65 years old undergoing elective noncardiac surgery, cognitive function was assessed preoperatively using the Processing Speed Test, and the primary outcome of 30-day readmission (including staying in the hospital longer than 30 days) or death was determined. Of 1,599 patients, 12% were readmitted, and 0.6% had 30-day death. An increase of 10 in Processing Speed Test score was associated with 25% lower odds of readmission/death.

3941

Loss of the Ability to Live Independently after Surgery—The Role of Race: A Multicenter Hospital Registry Study

Luca J. Wachtendorf, Student, Valluvan Rangasamy, M.D., Omid Azimaraghi, M.D., Miheer Sane, M.D., Balachundhar Subramaniam, M.D., M.P.H., Rafael Vasquez, M.D., Timothy T. Houle, Ph.D., Seun Johnson-Akeju, M.D., Matthias Eikermann, M.D., Ph.D., Nancy E. Oriol, M.D.

Department of Anesthesia, Critical Care and Pain Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts (L.J.W., V.R., O.A., M.S., B.S.); Department of Anesthesia, Critical Care and Pain Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts (R.V., T.T.H., S.J.-A.); Department of Anesthesiology, Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, New York (M.E.); and Department of Global Health and Social Medicine, Harvard Medical School, Boston, Massachusetts (N.E.O.)

The hypothesis that patients who self-identify as non-Latinx black are at higher risk of losing the ability to live independently after surgery than those self-identifying as

non-Latinx white was tested in a hospital registry study of 378,747 patients, 38,911 (10.3%) of whom were black and 339,836 (89.7%) were white. The ability to live independently after surgery was lost in 7.5% of all patients. Black race was associated with higher odds of losing the ability to live independently after surgery (adjusted odds ratio, 1.46). The combination of severe diabetes mellitus and arterial hypertension mediated 34.6% of the effect of race on the loss of the ability to live independently after surgery.

Best Abstracts: Basic Science

Upper 9
Sunday, October 10 | 9:45 to 11:45 AM
Moderators: **Michael J. Avram, Ph.D.,** Assistant Editor-in-Chief, ANESTHESIOLOGY, Northwestern University Feinberg School of Medicine, Chicago, Illinois; **Deborah J. Culley, M.D.,** Executive Editor, ANESTHESIOLOGY, University of Pennsylvania, Perelman School of Medicine, Philadelphia, Pennsylvania; **Martin J. London, M.D.,** Editor, ANESTHESIOLOGY, University of California, San Francisco School of Medicine and Veterans Affairs Medical Center, San Francisco, California

6263

Local Anesthesia Cardiac Toxicity Is Mediated by Cardiomyocyte Calcium Dynamics

Jason Maynes, M.D., Ph.D., Julia Plakhotnik, B.Sc., Libo Zhang, Ph.D., John Coles, M.D., Per-Arne Lonnqvist, M.D.
Departments of Anesthesia and Pain Medicine (J.M.), Molecular Medicine (J.P., L.Z.), and Cardiovascular Surgery (J.C.), Hospital for Sick Children, Toronto, Ontario, Canada; and Department of Paediatric Anaesthesia and Intensive Care, Karolinska University Hospital, Stockholm, Sweden (P.-A.L.)

The clinical utility and dosing of local anesthetics is limited by their potential for cardiotoxicity. Using human-derived cardiomyocytes, bupivacaine, a local anesthetic with a lower toxicity threshold, more potently dysregulated calcium dynamics than did ropivacaine. Calcium supplementation improved tissue contractility and restored normal beating rhythm for bupivacaine-treated tissues. Calcium pretreatment of a rodent model mitigated bupivacaine-induced arrhythmias and depression of cardiac function, improving animal survival, but worsened ropivacaine effects. Coadministration of nifedipine worsened only the effects of bupivacaine, confirming the role of calcium flux in its toxicity.

3849

Local Anesthetics Promote Direct Cytotoxicity on Tumor Cells and Trigger *In Vivo* Anticancer Immune Response

Lucillia Bezu, M.D., Ph.D., Alejandra Wu Chuang, M.Sc., Allan Sauvat, Sylvere Durand, Ph.D., Fanny Aprahamian, Wei Xie, Ph.D., Juliette Humeau, Ph.D., Fabrice Barlesi, M.D., Ph.D., Oliver Kepp, Ph.D., Guido Kroemer, M.D., Ph.D.
Gustave Roussy Cancer Center, Villejuif, France

Retrospective observational studies have reported improved overall survival after use of local anesthetics during solid tumor resection. The hypothesis that local anesthetics foster direct cytotoxic effects on tumor cells and trigger molecular pathways that promote anticancer immune response was tested in human osteosarcoma cells, and the results were validated in models of solid cancer established in immunocompetent mice. Local anesthetics promoted premortem stresses including mitochondrial dysfunction, autophagy, endoplasmic reticulum stress, and, finally, cancer cell death. *In vivo*, lidocaine and ropivacaine decreased tumor growth and extended overall survival in models of solid cancer.

3897

Pregnancy Improves Neuropathic Pain in Mice *via* Upregulation of δ-Opioid Receptor in Anterior Cingulate Cortex

Atsushi Sawada, M.D., Ph.D., Michiaki Yamakage, M.D., Ph.D.
Department of Anesthesiology, Sapporo Medical University School of Medicine, Sapporo, Japan

Symptoms of preexisting chronic pain are attenuated during pregnancy. Pregnancy upregulates opioid peptides and receptors in the dorsal root ganglia. Opioid peptides and receptors are highly expressed in the anterior cingulate cortex. The effects of pregnancy on neuropathic pain induced by chronic partial sciatic nerve ligation and opioid receptor expression in the anterior cingulate cortex were determined in female mice randomly assigned to four groups: nonpregnant sham, nonpregnant partial sciatic nerve ligation, pregnant sham, and pregnant partial sciatic nerve ligation. Pregnant neuropathic pain model mice had a higher mechanical threshold and increased δ-opioid receptor expression in the anterior cingulate cortex.

3951

Effect of Opioid and AMPA Antagonists on (2*R*,6*R*)-Hydroxynorketamine Antihyperalgesic Activity

Vaskar Das, Ph.D., Robert J. McCarthy, Pharm.D., Lauren N. Kret, B.A., Mario Moric, M.S., Asokumar Buvanendran, M.D.
Department of Anesthesiology, Rush University Medical Center, Chicago, Illinois

The ketamine metabolite (2*R*,6*R*)-hydroxynorketamine has antihyperalgesic efficacy in murine models of chronic pain. The current study determined whether the antihyperalgesic efficacy of (2*R*,6*R*)-hydroxynorketamine is α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid

(AMPA)– or opioid-dependent in a mouse model of post-surgical pain. Animals were allocated to three treatment groups: saline + (2*R*,6*R*)-hydroxynorketamine, NBQX (a competitive antagonist of the AMPA receptor) + (2*R*,6*R*)-hydroxynorketamine, and naloxone + (2*R*,6*R*)-hydroxynorketamine. Saline- and naloxone-pretreated mice had similar areas under the curve of the von Frey force thresholds over time (reduced allodynia) after (2*R*,6*R*)-hydroxynorketamine treatment. Mice pretreated with NBQX had lower areas under the curve than saline- or naloxone-pretreated mice.

6490

Protection of Mouse Coronary Artery Endothelial Cells against Simulated Ischemia/Reperfusion Injury by Newly Designed Diblock Copolymer-based Cell Membrane Stabilizers

Matthias Riess, M.D., Ph.D., FASA, Mukesh K. Gupta, Ph.D., Matthew J. Hampton, B.S., Matthew B. Barajas, M.D., Craig L. Duvall, Ph.D., Zhu Li, Ph.D.

Department of Anesthesiology, Tennessee Valley Healthcare System–Veterans Affairs Medical Center, Nashville, Tennessee (M.R.); Department of Biomedical Engineering, Vanderbilt University, Nashville, Tennessee (M.K.G., C.L.D.); and Department of Anesthesiology, Vanderbilt University Medical Center, Nashville, Tennessee (M.J.H., M.B.B., Z.L.)

Poloxamer 188, a triblock copolymer-based cell membrane stabilizer, protects against cell membrane damage induced by ischemia/reperfusion injury by preserving membrane integrity and function. Structure modifications of copolymer-based cell membrane stabilizer to diblock compounds provide even stronger protection against cellular damage in muscle myoblasts undergoing hypotonic shock. In the current study, the effects of three newly synthesized diblocks were compared to those of poloxamer 188 in mouse coronary artery endothelial cells when given upon the beginning of 2 h of reoxygenation after 24 h of hypoxia. Poloxamer 188 and all three tested diblocks prevented hypoxia/reoxygenation–induced cell death and membrane damage.

6396

15-Hydroxyeicosatetraenoic Acid Induces Pulmonary Hypertension: The Role of the Inhibitory Protein API5

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Arachidonic acid metabolites such as hydroxyeicosatetraenoic acids play a key role in pulmonary arterial hypertension pathogenic inflammatory response and vascular cell dysfunction. Mice fed 15-hydroxyeicosatetraenoic acid develop pulmonary hypertension. Transcriptomic data from pulmonary arterial hypertension patient lungs were compared with those of mice on a 15-hydroxyeicosatetraenoic acid diet. This analysis identified 406 mRNAs similarly dysregulated in the lungs of mice and humans with pulmonary hypertension. Upregulation of HNRNPA2B1 (A2B1), known to negatively regulate its targets, was identified. Most A2B1 targets in human and mice lungs were upregulated, suggesting the presence of an inhibitory interactor of A2B1. Bioinformatic analysis of the A2B1-binding partner revealed upregulation of apoptosis inhibitor 5 (API5), which is known to block the activity of its partners. *In vivo* silencing of API5 in the lungs of mice on a 15-hydroxyeicosatetraenoic acid diet prevented pulmonary hypertension.

6560

Intrathecal Neuronal Nitric Oxide Synthase Inhibition Attenuates Pulmonary Hypertension and Rescues Right Ventricular Failure in Rats

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Pulmonary hypertension is associated with aberrant sympathetic activation leading to right ventricular failure, arrhythmias, and death. The hypothesis that in pulmonary hypertension–right ventricular failure afferent signaling from cardiopulmonary neurons leads to nitric-oxide synthase–mediated neuroinflammation, nitrosative stress, and apoptosis in the thoracic spinal cord resulting in aberrant sympathoexcitation *via* efferent signaling was tested in rat models of severe pulmonary hypertension–right ventricular failure produced by either monocrotaline or Sugen/hypoxia. Intrathecal nitric-oxide synthase inhibition by *S*-methyl-L-thiocitrulline attenuated pulmonary hypertension and right ventricular hypertrophy and rescued right ventricular failure by decreasing neuroinflammation, nitrosative stress, apoptosis, and associated aberrant sympathoexcitation.

6482

Nifedipine Binding to the Skeletal L-type $Ca_V1.1$ Channel Remodels Its Voltage-sensing Apparatus

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During an action potential, the voltage-dependent movement of up to four specialized voltage-sensing domains

within the L-type calcium channel ($Ca_V1.1$) propagates to ryanodine receptors, triggering its opening and sarcoplasmic reticulum Ca^{2+} release, causing muscle contraction. The hypothesis that nifedipine, which blocks L-type channels Ca_V, alters the activity of one or more $Ca_V1.1$ voltage-sensing domains was tested in the human $Ca_V1.1$ channel reconstituted in *Xenopus* oocytes. Nifedipine not only inhibited ionic conduction but also modified the voltage-dependent activation of three of four voltage-sensing domains of the $Ca_V1.1$ channel, facilitating their activation.

6464

Neuronal Substrates of Rapid Eye Movement Sleep Rebound after Sevoflurane

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Disruption of rapid eye movement (REM) sleep is common after anesthesia and surgery. Sevoflurane alone causes REM sleep rebound in rodents. A targeted recombination in active populations approach and c-Fos immunohistochemistry were used to identify regions of the brain that were active during sevoflurane-induced REM sleep rebound in rats randomized to receive 2.8% sevoflurane or control conditions for 3 h. Sevoflurane-exposed animals had a 30% increase in REM sleep and decreased REM sleep latency. Hypoactivity of ventrolateral periaqueductal gray REM sleep–suppressing neurons and activation of sublaterodorsal REM sleep–generating neurons were observed in rodents with REM sleep rebound after sevoflurane.

6471

All-or-None Synapse Function Modulated by Extracellular Calcium over a Small Physiologic Range in Rat Hippocampal Neurons

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Mammalian cerebrospinal fluid calcium concentration ($[Ca^{2+}]$) is tightly maintained with a physiologic set point close to 1.2 mM and is likely an important regulator of neuronal function. The effect of small changes in extracellular $[Ca^{2+}]$ relative to the physiologic set point on synapse function of rat primary hippocampal neurons was determined using genetically encoded synaptic Ca^{2+} indicators. Small perturbations in extracellular $[Ca^{2+}]$ can lead to complete silencing of action potential-driven Ca^{2+} influx at individual presynaptic terminals, but this silencing was heterogenous across a population of nerve terminals derived from the same axon.

6462

The Caudal Medullary Raphe: The Missing Link in Opioid Induced Respiratory Depression?

Barbara Palkovic, M.D., Jennifer J. Callison, B.S., Vitaliy Marchenko, M.D., Ph.D., Eckehard A. Stuth, M.D., Edward J. Zuperku, Ph.D., Astrid G. Stucke, M.D.

Medical College of Wisconsin, Milwaukee, Wisconsin (B.P., J.J.C., V.M., E.A.S., A.G.S.); and Zablocki Veterans Affairs Medical Center, Milwaukee, Wisconsin (E.J.Z.)

Naloxone injections into the pontine parabrachial nucleus/Kölliker–Fuse complex and the medullary pre-Bötzinger complex reverse a major part of respiratory depression from analgesic remifentanil concentrations and a lesser part of respiratory depression from apneic concentrations. The hypothesis that respiratory depression from intravenous remifentanil could be completely antagonized with naloxone injections into the parabrachial nucleus + Kölliker–Fuse complex + pre-Bötzinger complex + caudal medullary raphe was tested in rabbits. Respiratory depression from analgesic and apneic remifentanil concentrations could be completely reversed by naloxone injection into the parabrachial nucleus/Kölliker–Fuse complex, the pre-Bötzinger complex, and the caudal medullary raphe. Very high remifentanil concentrations did not depress the respiratory rate but depressed the peak phrenic activity.

6541

Effect of Gut Microbiome Metabolites on Alveolar Macrophages during Lung Ischemia Reperfusion Injury

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The sterile inflammatory processes of lung ischemia reperfusion injury require alveolar macrophages (AMs) and activation of NLRP3/caspase-1/interleukin-1β pathway and are influenced by intestinal microbiota. The short-chain fatty acids propionate, butyrate, and acetate produced by gut microbiota have anti-inflammatory properties. The effect of short-chain fatty acids on ischemia reperfusion-induced interleukin-1β secretion in AMs was determined *in vitro* using mouse AMs and *in vivo* using lung ischemia reperfusion mice models. Capase-1 KO and NLRP3 KO mice secreted less interleukin-1β than WT mice. Both MCC950 (NLRP3 inhibitor) and VX-765 (caspase-1 inhibitor) reduced interleukin-1β secretion. Propionate modulated the inflammatory response of AMs to lipopolysaccharide and *in vitro* ischemia reperfusion. Short-chain fatty acids applied locally to the lung modulated the lung ischemia reperfusion inflammatory response of germ-free mice *in vivo*.

Applying Clinical Trial Results in Anesthesia: What Do They Really Mean?

Upper 25ABC
Monday October 11 | 1:15 to 3:15 PM
Moderator: **Marcos F. Vidal Melo, M.D., Ph.D.,** Department of Anesthesia, Critical Care, and Pain Medicine, Massachusetts General Hospital, Boston, Massachusetts
Discussion of three recently published clinical trial studies, presented by one of the authors and counterpointed by a friendly critique by another speaker. Speakers will comment on the methods and their implementation, providing in the process education on those methods and relevant aspects of their implementation and results interpretation. This will be followed by a response from the author.
Learning Objectives: The learner will be able to (1) identify important results from published clinical trials and (2) identify methods of clinical trial results interpretation and how to implement such results in clinical practice.

Secrets of Successful Manuscript Preparation, from the Editors of ANESTHESIOLOGY

Upper 25ABC
Tuesday, October 12 | 7 to 9 AM
Moderator: **Michael J. Avram, Ph.D.,** Assistant Editor-in-Chief, ANESTHESIOLOGY, Northwestern University, Feinberg School of Medicine, Chicago, Illinois

The editors of ANESTHESIOLOGY have organized this session to inform authors how to write and prepare a manuscript by providing a clear understanding of what is expected of both research that is considered the best and the manuscript describing it. The goal is to help authors create the best clinical and basic science research for publication. Reviewers will benefit from this session as well by learning how to identify key aspects of the best clinical and basic science research.
Speakers:
Introduction: Secrets of Successful Manuscript Preparation
Evan D. Kharasch, M.D., Ph.D., Editor-in-Chief, ANESTHESIOLOGY, Duke University, Durham, North Carolina
A Primer on Study Design, Analysis, and Interpretation
Timothy T. Houle, Ph.D., Statistical Editor, ANESTHESIOLOGY, Harvard Medical School, Massachusetts General Hospital, Boston, Massachusetts
How to Prepare an Original Research Manuscript
Andrew Davidson, M.B.B.S., M.D., FANZCA, FAHMS, Executive Editor, ANESTHESIOLOGY, The Royal Children's Hospital and the Murdoch Children's Research Institute, Parkville, Victoria, Australia
How to Write a Review Article and a Few Tips on What Not to Do
Deborah J. Culley, M.D., Executive Editor, ANESTHESIOLOGY, University of Pennsylvania, Perelman School of Medicine, Philadelphia, Pennsylvania