

Journal-related Activities and Other Special Activities at the 2017 American Society of Anesthesiologists Meeting

Michael J. Avram, Ph.D., Evan D. Kharasch, M.D., Ph.D., Sachin Kheterpal, M.D., M.B.A., James P. Rathmell, M.D., Daniel I. Sessler, M.D.



26th Annual Journal Symposium: Frontiers in Opioid Pharmacotherapy

Sunday, October 22, 2017, 9:00 AM to 12:00 PM, 206 A-B
The 2017 Journal Symposium titled “Frontiers in Opioid Pharmacotherapy” addresses the latest science on opioid pharmacology, use, and misuse. It will feature the following moderators and speakers.

Moderators

Evan D. Kharasch, M.D., Ph.D., Editor-in-Chief, ANESTHESIOLOGY, and Washington University in St. Louis, St. Louis, Missouri; and James P. Rathmell, M.D., Executive Editor, ANESTHESIOLOGY, and Brigham and Women’s Hospital/Harvard Medical School, Boston, Massachusetts.

Speakers

- 1. Refining Opioid Receptor Signaling to Improve Therapeutic Outcomes**
Laura M. Bohn, Ph.D., The Scripps Research Institute, Jupiter, Florida
- 2. The Current Opioid Epidemic: Intersection between Pain and Addiction**
Nora D. Volkow, M.D., National Institute on Drug Abuse, Bethesda, Maryland

Description

Opioids have been the mainstay of pain therapy for thousands of years. Recent decades have seen tidal shifts in the therapeutic application of opioids for acute, postoperative, chronic, neuropathic, and cancer pain as emphasis on adequate pain treatment has grown. Opioid-related problems, including addiction, diversion, and overdose, have also grown concurrently with increased clinical use of opioids. Changes in individual practice, group guidelines, and policy recommendations all aimed at stemming the tide of abuse and diversion have rapidly emerged. Concurrently, there have been recent giant leaps in understanding and application of opioid pharmacology. These discoveries have challenged and sometimes reversed decades of conventional wisdom in pharmacology. New concepts in opioid pharmacology have spawned major new efforts in drug discovery toward the development of opioids with greater clinical effectiveness and/or diminished side effects and are also changing the way clinicians use existing opioids. New opioids are advancing through clinical trials, with intended application for pain, itch, depression, and other therapeutic areas.

These lectures will be followed by oral presentations of eight abstracts, summarized below, that were selected for their relevance to the symposium topic. The full text for each abstract can be found at the American Society of Anesthesiologists (ASA) abstract Web site.

JS01

“Pupil Size, Opioids, and Nociception: Does the Pupil Mirror Off Cell Activity During Anesthesia” by Merlin D. Larson, M.D., Pedro L. Gambus, M.D., Ph.D., Merce Agusti, M.D., Ph.D., Adria Pacheco, B.A., Patricia Capsi, M.Sc., Jose Fernando Valenciz, Ph.D., University of California, San Francisco, California; Hospital Clinic de Barcelona, Spain; Universidad de San Buenaventura, Cali, Colombia. Dilation of the pupil in response to a noxious stimulus (PRD) predicts movement to a more sustained surgical stimulus. The authors propose that PRD is a surrogate

Submitted for publication July 18, 2017. Accepted for publication July 18, 2017. From the Department of Anesthesiology, Northwestern University Feinberg School of Medicine, Chicago, Illinois (M.J.A.); Departments of Anesthesiology and Biochemistry and Molecular Biophysics, Washington University in St. Louis, St. Louis, Missouri (E.D.K.); St. Louis Center for Clinical Pharmacology, Washington University in St. Louis and St. Louis College of Pharmacy, St. Louis, Missouri (E.D.K.); Department of Anesthesiology, University of Michigan Medical School, Ann Arbor, Michigan (S.K.); Department of Anesthesiology, Perioperative and Pain Medicine, Brigham and Women’s Hospital, Boston, Massachusetts (J.P.R.); Department of Outcomes Research, Cleveland Clinic, Cleveland, Ohio (D.I.S.); Outcomes Research Consortium, Cleveland, Ohio (D.I.S.).

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measure of off-cell activity, known to suppress transmission of nociceptive processing in the dorsal horn. Support for this theory would require that PRD predicts and precedes movement in response to noxious stimulation and that the size of the pupil predicts how brisk the pupil dilates and the latency between the stimulus and movement. Anesthesia was induced and maintained with propofol and remifentanyl using a target-controlled infusion system in a series of 40 patients to study whether pupillary dilation preceded movement and whether the size of the pupil was predictive of the latency of movement. Stimulation produced marked changes in PRD, was evident in all cases that moved to the stimulus, and was strongly associated with movement. This confirms that pupillary dilation after a noxious stimulus is predictive of movement and that the pupil dilates before movement. These observations point to a marked similarity of pupillary dilation to the responsiveness of the off cells.

JS02

“Respiratory Effects of IV CR845: A Peripherally-acting, Selective κ Opioid Receptor Agonist” by Eugene R. Viscusi, M.D., Marc C. Torjman, Ph.D., Joseph W. Stauffer, D.O., Catherine L. Munera, Ph.D., Beatrice S. Setnik, Ph.D., Sukirti N. Bagal, M.D., M.P.H., Sidney Kimmel Medical College at Thomas Jefferson University, Philadelphia, Pennsylvania; Cara Therapeutics, Stamford, Connecticut; INC Research, Toronto, Ontario, Canada. CR845 is a peripherally restricted, highly selective κ opioid receptor agonist that is being developed for the treatment of pain and pruritus. Its peptidic structure restricts its entry into the central nervous system and thus minimizes the potential for adverse events mediated by central opioid receptors. The present study was conducted in healthy volunteers using key clinical measures of respiratory status to determine whether CR845 causes respiratory depression. In this single-center, randomized, double-blind, placebo-controlled, three-way crossover study, end-tidal carbon dioxide (ETCO₂), oxygen saturation measured by pulse oximetry (SpO₂), and respiratory rate were continuously monitored before and after administration of CR845. The primary safety endpoints were a greater than 10 mmHg sustained (30 s or higher duration) increase in ETCO₂ above baseline or to greater than 50 mmHg and a sustained reduction of SpO₂ to less than 92%. A total of 15 subjects participated in the study. Healthy subjects treated with IV bolus doses of CR845 at 1 and 5 μ g/kg demonstrated no dose-response or impairment in SpO₂, respiratory rate, or ETCO₂ compared with placebo.

JS03

“AMPAkines and Morphine Provide Complementary Analgesia” by Kevin Liu, B.A., Yongjun Sun, M.A., Erik Martinez, B.S., Jahrane Dale, B.S., Jing Wang, M.D., Ph.D., New York University School of Medicine, New York, New York; Hunan Cancer Hospital, Hunan Province, China. AMPAkines may offer a novel

alternative to opioid analgesia by potentiating α -amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptors and thus glutamate transmission. There is accumulating evidence that AMPAkines can stimulate respiratory drive. The authors hypothesized that opioids and AMPAkines work *via* separate pathways and thus provide complementary and additive analgesia and that AMPAkines also target the prefrontal cortex (a brain region that is known to produce descending inhibitory control of nociception) to provide analgesia. CX546, an AMPAkin, was administered systemically *via* intraperitoneal injections or directly to the prefrontal cortex through bilateral intracranial cannulas. Morphine was administered subcutaneously. Traditional Hargreaves’ test was used to assess analgesia in rats treated with only morphine and rats treated with both CX546 and morphine. The authors’ results demonstrate that CX546, an AMPAkin, can provide analgesia to acute thermal pain. CX546 provides analgesia that is complementary and additive to that produced by morphine, indicating that AMPAkines and opiates likely work *via* distinct cellular and molecular pathways. Thus, AMPAkines represent a novel treatment option for pain that can be used both as a substitute for and as a supplement to opiates.

JS04

“Respiratory Volume Monitoring Postoperatively Can Identify Patients at Risk for Ventilatory Depression following PACU Discharge” by Roman Schumann, M.D., Farhad Zahedi, M.D., Iowna Bonney, Ph.D., Nicholas Aranow, B.S., Tufts Medical Center, Boston, Massachusetts; Respiratory Motion, Inc., Waltham, Massachusetts. The authors used a respiratory volume monitor in postoperative patients in the postanesthesia care unit to determine whether a threshold minute ventilation value may determine the likelihood of respiratory depression after discharge to the general hospital floor. Low minute ventilation was defined as less than 40% of predicted minute ventilation based on body surface area and sex. Patients with one or more low minute ventilation episodes within 30 min of postanesthesia care unit discharge had a tenfold increase of IV opioid-induced respiratory depression on the general hospital floor and a sixfold increase in respiratory depression even without IV opioids.

JS05

“Opioid Prescribing Practices in Pediatric Adenotonsillectomy Patients: Evaluation of Opioid Prescription Use, Storage and Disposal of Unused Opioids” by Sarah J. Hall, M.D., Ph.D., Mimi Kim, B.S., Nicole M. Contrad, M.D., Peggy P. McNaull, M.D., Brooke Chidgey, M.D., University of North Carolina, Chapel Hill, North Carolina. Children may be overprescribed opioids after surgery and medications are often left unsecured. Records of children undergoing tonsillectomy

or adenotonsillectomy during a 2-month period were reviewed and parents surveyed for opioid prescription, use, storage, and disposal postoperatively. Half of the children studied received opioid prescriptions averaging 51 doses. Most opioids remained unused after 2 weeks and were stored in an unsecured location. Unused opioids have the potential to contribute to opioid misuse, and efforts are being made to establish guidelines on postoperative opioid prescribing and parental education on home storage and disposal.

JS06

“Safety and Efficacy of Sufentanil Sublingual Tablet 30 µg by Age Group for the Treatment of Acute Pain in Medically Supervised Settings” by Karen DiDonato, M.S.N., Jacob L. Hutchins, M.D., James Miner, M.D., Harold Minkowitz, M.D., Pamela P. Palmer, M.D., Ph.D., AcelRx Pharmaceuticals, Redwood City, California; University of Minnesota, Minneapolis, Minnesota; Hennepin County Medical Center, Minneapolis, Minnesota; Memorial Hermann Memorial City Medical Center, Houston, Texas. The sufentanil sublingual tablet (SST) 30 µg is currently under review by the U.S. Food and Drug Administration and European Medicines Agency for treatment of moderate-to-severe acute pain in a medically supervised setting. After completion of the phase 3 program, which was sponsored by the U.S. Department of Defense, a safety and efficacy subgroup analysis by age group was performed across all four late-stage clinical trials. SST 30 µg has shown benefit across a range of patient ages as a noninvasive analgesic modality for short-term management of acute moderate-to-severe pain. Although the elderly should always be monitored closely in postoperative and trauma settings, results from these late-phase studies suggest that SST 30 µg is effective and well tolerated in this patient population.

JS07

“Opioid Abuse and Dependence Increases 30-day Readmission Rates after Major Operating Room Procedures: A National Readmissions Database Study” by Atul Gupta, M.B., B.S., Sajid S. Shahul, M.B., B.S., University of Chicago, Chicago, Illinois. The authors performed a retrospective cohort analysis using pooled data from the National Readmission Databases for years 2013 and 2014. Opioid abuse and dependence increase length of hospital stay after a major operating room procedure. Although it does not impact mortality, the 30-day readmission rate is significantly higher in those with opioid abuse and dependence. This leads to increased per capita hospital costs both at initial admission and at readmission. Among opioid abusers, pain, opioid dependence, and withdrawal are significantly more likely to be primary reasons for readmission than that of nonopioid users.

JS08

“Novel Opioid Paradigms: Long-duration Opioid for Same-day Outpatient Surgery” by Helga Komen, M.D., Jane Blood, R.N., Michael Brunt, M.D., Ph.D., Evan D. Kharasch, M.D., Ph.D., Washington University, St. Louis, Missouri. Many patients undergoing surgery report inadequate postoperative analgesia and chronic postsurgical pain. This investigation tested the hypothesis that in outpatient surgery intraoperative methadone compared with conventional short-duration opioids reduces postoperative opioid consumption and pain, with similar or diminished side effects. The authors randomized patients to receive single-dose methadone (0.1 mg/kg IV or 0.15 mg/kg IV ideal body weight) or short-duration opioid (fentanyl or hydromorphone). Patients were assessed multiple times postoperatively for pain intensity and pain relief until discharge. A single intraoperative methadone dose of 0.15 mg/kg decreased intraoperative and postoperative opioid requirements and provided better analgesia, with similar side effects compared with patients receiving short-duration opioids intraoperatively.

Best Abstracts: Clinical Science and Basic Science

ANESTHESIOLOGY will sponsor two Best Abstract Sessions this year, one in basic science and another in clinical science. These 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 these editors and appointees from the ASA chose one abstract in each category to receive the Best Abstract award for basic and clinical sciences at the meeting in Boston, Massachusetts. Following are summaries of the excellent abstracts that will be presented.

Best Abstracts: Clinical Science

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Moderators

Michael J. Avram, Ph.D., Northwestern University Feinberg School of Medicine, Chicago, Illinois; Sachin Kheterpal, M.D., M.B.A., University of Michigan Medical School, Ann Arbor, Michigan; Daniel I. Sessler, M.D., Cleveland Clinic, Cleveland, Ohio.

3551

“Incidence of Perioperative Visual Loss in the Pediatric Population: A Nationwide Population-based Analysis” by Rabail Chaudhry, M.D., Erin S. Williams, M.D., Ranu R. Jain, M.D., Cameron Bruner, Greesha Pednekar, M.D., Oksana Didyuk, M.D., Maria E. Matuszczak, M.D., George Williams, M.D., Department of Anesthesiology, The University of Texas Health Science Center at Houston, Houston, Texas; Texas Childrens Hospital, Houston, Texas; University of Texas Medical School, Houston,

Texas. The authors used the Healthcare Cost and Utilization Project's Kids' Inpatient Database for year 2012 to evaluate postoperative visual loss (POVL). Kids' Inpatient Database contains data for approximately 3 million pediatric discharges each year. International Classification of Diseases, Ninth Revision—Clinical Modification diagnosis codes for sudden visual loss, ischemic optic neuropathy, retinal vascular occlusion, and cortical blindness were used to identify patients with POVL. The incidence of POVL was 0.10%. Patients with visual loss were predominantly older than 1 yr, with a mean age of 6.4 yr. POVL was most common after neurosurgery (0.48%; OR = 4.14; $P < 0.001$) followed by transplant (0.25%) and spinal surgery (0.25%). Ischemic optic neuropathy was extremely rare in pediatric surgical patients.

3552

“Early Resumption of β -Blockers Is Associated with Decreased Atrial Fibrillation after Noncardiac Surgery: A Cohort Analysis” by Ashish K. Khanna, M.D., Daniel I. Sessler, M.D., Amanda Jane Naylor, B.S., Jing You, M.S., Eric Reville, B.S., Quinton Riter, B.S., Murtaza K. Diwan, M.D., Andrea M. Kurz, M.D., Douglas F. Naylor, Jr., M.D., Department of Anesthesiology, Outcomes Research, Center for Critical Care, Cleveland Clinic Foundation, Cleveland, Ohio; Loyola University Chicago, Chicago, Illinois; Cleveland Clinic, Cleveland, Ohio; University of Michigan Medical Center, Ann Arbor, Michigan. The investigators evaluated the relationship between postoperative atrial fibrillation (POAF) and the timing of resumption of chronically used β -blockers. Data were obtained from 8,021 adult β -blocker users who had noncardiac surgery and stayed at least two postoperative nights. In a matched-pairs analysis, 4.9% of patients (94 of 1,924) retaking β -blocker by the end of postoperative day 1 experienced POAF compared with 7.0% (68 of 973) in those retaking after postoperative day 1, giving an OR (early vs. late) of 0.69 (95% CI, 0.50 to 0.95; $P = 0.02$). The same comparison on the day of surgery showed a POAF for 4.9% of patients who restarted β -blocker and 5.8% for patients who did not, giving a nonsignificant OR of 0.84 (95% CI, 0.67 to 1.04; $P = 0.11$). Resuming chronically administered β -blockers on the day of surgery or the subsequent day appears to reduce risk.

4029

“Evaluation of United States Medical Licensing Exam (USMLE) Step Scores to Success on the American Board of Anesthesiology (ABA) Basic Exam” by Semhar Ghebremichael, M.D., Carlos A. Artime, M.D., Sam Gumbert, M.D., Omonele O. Nwokolo, M.D., Sara Guzman-Reyes, M.D., George Williams, M.D., Evan G. Pivalizza, M.D., Department of Anesthesiology, McGovern Medical School at University of Texas Health Science Center Houston, Houston, Texas; Department of Anesthesiology,

University of Texas Houston, Houston, Texas; University of Texas Medical School, Houston, Texas. Step 1 scores are correlated with performance on both the residency in-training examination and the American Board of Anesthesiology (ABA) final certification examination. The ABA recently mandated a written Basic Examination at the end of the postgraduate year 2. Step 1 scores were an independent predictor of success on the Basic Examination (OR = 1.13; 95% CI, 1.04 to 1.22; $P = 0.002$). A Step 1 score of 229 was associated with a 95% probability of passing, and a score of 223 was associated with a 90% probability of passing. Step 2 scores were not predictive in a multivariable model, nor were Step 3 scores. Most residents who failed the Basic Examination had marginal or poor scores, but many residents with marginal or poor United States Medical Licensing Exam scores passed, and of course the Basic Examination is a surrogate for eventual success on ABA certification examination. Candidate United States Medical Licensing Exam scores are thus not reliable screening tools and should be considered to be just one of many factors in selecting residents.

4077

“Epidemiology of Exposure to Anesthesia, Surgery, and Mortality in a Children's Hospital Population” by George M. Hoffman, M.D., Richard J. Berens, M.D., William R. Clarke, M.D., John P. Scott, M.D., Laura D. Cassidy, Ph.D., Pediatric Anesthesiology and Critical Care Medicine, Children's Hospital and Medical College of Wisconsin, Milwaukee, Wisconsin; Institute for Health, Medical College of Wisconsin, Milwaukee, Wisconsin. The investigators hypothesized that the risk factors of age, multiple and prolonged exposure to anesthesia, and surgery are related to mortality. A total of 104,237 cases in 61,088 patients from the Children's Hospital of Wisconsin were analyzed. Mortality was 0.65% (5 to 95% CI, 0.59 to 0.72). In multiple analyses, cumulative case time and multiple cases were risk factors, whereas duration for individual cases was not. The cutoff age for higher risk was less than 2 yr. Mortality after anesthesia and surgery is highly related to patient characteristics including younger age and higher ASA physical status. Although both multiple and prolonged exposures were associated with increased mortality, these risks were small in multifactorial analysis (0.1 to 4.0%). Young age and prolonged and multiple exposures are relatively small and unmodifiable proxy measures of patient outcome.

4132

“Quadratus Lumborum Block and Posterior Transversus Abdominis Plane Block: A Prospective Study” by Yuki Aoyama, M.D., Shinichi Sakura, M.D., Shoko Abe, M.D., Nozomi Katayama, M.D., Minoru Wada, M.D., Yoji Saito, M.D., Shimane University Hospital, Izumo, Japan. The investigators compared posterior transversus abdominis plane block and quadratus lumborum block for postoperative analgesia after abdominal surgery. Forty-two

patients, ages 30 to 79 yr, having gynecologic laparoscopic surgery were alternately assigned to quadratus lumborum block or transversus abdominis plane block after the induction of general anesthesia. All blocks were bilateral with 20 ml 0.375% levobupivacaine on each side. Postoperative data included visual analog scale (VAS) pain scores at rest and while coughing (0 = no pain; 100 = worst pain imaginable) and postoperative fentanyl consumption at 6, 12, 24, and 48 h. VASs for pain at rest were significantly ($P < 0.05$) lower in group Q than in group T at 12 and 48 h but not at 6 and 24 h after blocks. VAS while coughing, postoperative fentanyl consumption, and demand for other analgesics were comparable. Overall, analgesia with the two blocks did not differ markedly and neither provided complete pain relief.

4425

“Comparison of Postoperative Mortality and Readmission Rates between Neuraxial and General Anesthesia in Noncardiac Surgery: A Retrospective Analysis” by Steve Leung, M.D., Gausan R. Bajracharya, M.D., Merve Yazici Kara, M.D., Guangmei Mao, Ph.D., Kamal Maheshwari, M.D., Kurt Ruetzler, M.D., Ali Wael Sakr, M.D., Hesham Elsharkawy, M.D., Alparslan Turan, M.D., **Outcomes Research, Cleveland Clinic Foundation, Cleveland, Ohio.** The effect of neuraxial anesthesia on long-term outcomes remains unclear. The authors used the American College of Surgeons National Surgical Quality Improvement Program Participant Use File (years 2011 to 2015) to evaluate the impact of neuraxial *versus* general anesthesia on 30-day mortality and readmission for major orthopedic procedures, defined as duration more than 1 h and requiring neuraxial or general anesthesia. Among 72,877 matched pairs of neuraxial *versus* general anesthesia patients, the 30-day readmission rate was 4.0% *versus* 4.4% (OR = 0.90; $P < 0.001$), whereas 30-day mortality was 0.4% *versus* 0.4% (OR = 1.03; $P = 0.713$). Hospital length of stay was lower in matched patients receiving neuraxial anesthesia: 2.87 *versus* 3.11 days ($P < 0.001$). These observational data support the use of neuraxial anesthesia in orthopedic procedures.

4668

“Construct and Criterion Validity of the STOP-BANG Questionnaire in Patients Undergoing Major Elective Noncardiac Surgery” by Ashwin Sankar, M.D., W. Scott Beattie, M.D., Ph.D., Gordon Tait, Ph.D., Duminda Wijeyesundera, M.D., Ph.D., **Department of Anesthesia, University of Toronto, Toronto, Ontario, Canada; University Health Network Department of Anesthesia and Pain Medicine, Toronto, Ontario, Canada; Department of Anesthesia, Toronto General Hospital and University of Toronto, Toronto, Ontario, Canada; Department of Anesthesia and Pain Management, University Health Network, Toronto General Hospital, Toronto, Ontario, Canada.** The STOP-BANG questionnaire is routinely used to screen for obstructive sleep apnea. However, the

independent relationship between STOP-BANG scores and postoperative outcomes in a broad patient population is unclear. In a retrospective analysis of 41,457 patients undergoing major elective noncardiac surgery at an academic medical center, preoperatively assigned STOP-BANG was evaluated. The authors observed: 1) cross-sectional construct validity, in that increasing proportions of patients had a recognized obstructive sleep apnea diagnosis in higher STOP-BANG risk strata; 2) low concurrent construct validity, as STOP-BANG risk strata had weak correlations with the ASA status, revised cardiac risk index, and Charlson comorbidity score; and 3) low predictive criterion validity since STOP-BANG risk strata were not associated with mortality, cardiac complications, or length of stay when adjusting for patient and surgical covariates ($P > 0.05$).

4953

“Influence of Surgical Incision Length on Chronic Postcesarean Pain” by Ruthi Landau Cahana, M.D., Brendan Carvalho, M.D., Monica M. Sialy, M.D., Beatriz Raposo Corradini, B.S., Michal Granot, Ph.D., **Department of Anesthesiology, Columbia University, New York, New York; Department of Anesthesiology, Stanford University School of Medicine, Stanford, California; Hospital E. Maternidade Santa Joana, San Paulo, Brazil; Nursing, University of Haifa, Haifa, Israel.** Reliable predictors for acute and chronic pain after cesarean delivery remain elusive. In a prospective study of 545 women undergoing primary or repeat elective cesarean delivery using spinal anesthesia, the authors followed patients up to 12 months postoperatively. Demographic data, incision length, verbal pain rating score (0 to 10), and wound hyperalgesia area were collected perioperatively. Verbal pain rating scores (0 to 10) were collected at 2, 6, and 12 months. Chronic pain was defined as a pain score greater than 0 at 12 months and present in 11 (6.5%) of 170 women after repeat cesarean delivery and 9 (2.4%) of 375 undergoing primary cesarean delivery ($P = 0.02$). Greater acute pain scores (3.8 *vs.* 2.0; $P = 0.012$), longer incision length (16.9 *vs.* 14.7 cm; $P < 0.001$), and repeat cesarean delivery were associated with chronic pain at 12 months.

5051

“Wireless Respiratory Monitoring after Surgery: A Randomized Controlled Trial” by James E. Paul, M.D., Matthew Chong, M.D., Norman Buckley, M.D., Antonella Tidy, B.Sc., Prathiba Harsha, M.B., B.S., Diane Buckley, B.S.N., Anne Clarke, R.N., **Department of Anesthesia, McMaster University, Ancaster, Ontario, Canada; McMaster University, Hamilton, Ontario, Canada.** There are few rigorous studies evaluating the value of automated nursing notification of a patient’s wireless pulse oximetry value to prevent postoperative respiratory depression-adverse events. The authors performed a randomized controlled trial of patients undergoing general, urologic, and gynecologic surgery at a large academic teaching hospital: standard care

versus standard care plus automated notification of a nurse if oxygen saturation measured by pulse oximetry decreased less than 90% on the general surgical ward. The primary outcome was a composite of naloxone administration, transfer to intensive care unit, or cardiac arrest team activation. A total of 2,050 patients were randomized; 46 (4.5%) of 1,019 control patients and 48 (4.7%) of 1,031 treatment patients experienced the primary outcome (OR = 0.97; $P = 0.88$). Of 1,237 nurse notifications, 58% were false alarms. No benefit to automated notification of wireless pulse oximetry monitoring was observed.

5183

“An Automated Method for Assigning Current Procedure Terminology Codes Using Machine Learning and the MPOG Registry” by Michael L. Burns, M.D., Ph.D., Leif Saager, M.D., Sachin Kheterpal, M.D., M.B.A., John Vandervest, M.S., Department of Anesthesiology, University of Michigan, Ann Arbor, Michigan; University of Michigan, Ann Arbor, Michigan. Accurate analytics for clinical, administrative, and research purposes leverage case categorization using administrative Current Procedure Terminology (CPT) codes. However, CPT categorization can be laborious and introduce delays in reporting. Using the Multicenter Perioperative Outcomes Group electronic health record data from 2016, the authors evaluated the ability to categorize procedures into 1 of 19 CPT procedure categories, in real time, using automated machine learning techniques. Data elements of patient age, sex, ASA status, emergent status, procedure text, and procedure duration were studied. Random forest modeling of single and multiword procedure text phrases combined with discrete data elements were derived and validated using data from 800,665 unique cases across 28 Multicenter Perioperative Outcomes Group institutions. Overall validation cohort accuracy was 82%, ranging from 71% for radiology procedures to 92% for shoulder procedures, demonstrating feasibility and accuracy.

Best Abstracts: Basic Science

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Moderators

Michael J. Avram, Ph.D., Northwestern University Feinberg School of Medicine, Chicago, Illinois; Sachin Kheterpal, M.D., M.B.A., University of Michigan Medical School, Ann Arbor, Michigan; Daniel I. Sessler, M.D., Cleveland Clinic, Cleveland, Ohio.

5173

“Oxidized Lipids: A Critical Role in Pulmonary Hypertension Pathogenesis” by Gregoire N. Ruffenach, Ph.D., Soban Umar, M.D., Ph.D., Mylene Vaillancourt, M.Sc., Ellen I. O’Connor, B.Sc., Shayan Moazeni, B.Sc., Christine Cunningham, B.Sc., Abbas Ardehali, M.D., Aman Mahajan, M.D., Ph.D., Srinivasa T. Reddy, Ph.D.,

Mansoureh Eghbali, Ph.D., Department of Anesthesiology at University of California Los Angeles Health, Los Angeles, California; Ronald Reagan University of California Los Angeles Medical Center-Residents, Los Angeles, California; Department of Molecular and Medical Pharmacology at University of California Los Angeles, Los Angeles, California; Ronald Reagan University of California Los Angeles Medical Center, Los Angeles, California, University of California Los Angeles Medical Center, Los Angeles, California. Lung and plasma concentrations of oxidized lipids, including 15-hydroxyeicosatetraenoic acids (15-HETE), are increased in both patients with pulmonary arterial hypertension and animal models of pulmonary hypertension. Wild-type mice were fed 15-HETE for 3 weeks to determine whether increased 15-HETE concentrations are sufficient to induce pulmonary hypertension. Other mice were fed 15-HETE methyl ester, a stable form of 15-HETE that is not easily metabolized, to determine whether 15-HETE or its metabolites are required to cause pulmonary hypertension. Echocardiography revealed the first sign of pulmonary hypertension as early as 1 week after starting both the 15-HETE diet and the 15-HETE methyl ester diet, which progressed to severe pulmonary hypertension by end of the third week in both groups.

4684

“Vasculotide, an Angiotensin-1 Mimetic, Prevents Microvascular Leakage and Protects Microcirculatory Perfusion during Cardiopulmonary Bypass in Rats” by Nicole Dekker, B.Sc., Anoek L. I. van Leeuwen, M.Sc., Nick J. Koning, M.D., Matijs van Meurs, M.D., Ph.D., Paul Van Slyke, M.D., Ph.D., Alexander B. A. Vonk, M.D., Ph.D., Christa Boer, Ph.D., Charissa E. van den Brom, Ph.D., VU University Medical Center, Amsterdam, The Netherlands; Anesthesiology and Physiology, VU University Medical Center, Amsterdam, The Netherlands; Anesthesiology, VU University Medical Center, Amsterdam, The Netherlands; Anesthesiology and Critical Care Medicine, University Medical Center Groningen, Groningen, The Netherlands; Vasomune Therapeutics, Toronto, Ontario, Canada. Cardiopulmonary bypass impairs microcirculatory perfusion, which is paralleled by microvascular leakage. Because the endothelial angiotensin-Tie2 receptor system is involved in microvascular leakage, the effects of an angiotensin-1 mimetic, vasculotide, on microvascular leakage and perfusion was studied in rats subjected to 75 min of cardiopulmonary bypass. Microvascular perfusion measured in the cremaster muscle using intravital microscopy was completely preserved during and after cardiopulmonary bypass in rats pretreated with vasculotide. Moreover, vasculotide treatment prevented Evans blue dye extravasation, a measure of microvascular leakage, in lung tissue compared with cardiopulmonary bypass control.

3933

“Delayed Pharmacologic Inhibition of S-Nitrosoglutathione Reductase Improves Outcomes after Cardiac Arrest and Cardiopulmonary Resuscitation in Mice” by Kei Hayashida, M.D., Ph.D., Aranya Bagchi, M.B., B.S., Matthews Bradley, Ph.D., Fumito Ichinose, M.D., Ph.D., Anesthesia, Critical Care, and Pain Medicine, Massachusetts General Hospital/Harvard Medical School, Boston, Massachusetts; SAJE Pharma, LLC, Baltimore, Maryland. Inhalation of nitric oxide markedly improved outcomes in mice, rats, and pigs after cardiac arrest and cardiopulmonary resuscitation, possibly by a mechanism involving protein S-nitrosylation. The hypothesis that inhibition of S-nitrosoglutathione reductase (GSNOR), a denitrosylase, may improve outcomes after cardiac arrest and cardiopulmonary resuscitation by enhancing protein S-nitrosylation levels was tested in mice subjected to 8 min of cardiac arrest and subsequent cardiopulmonary resuscitation. Both inhibition of GSNOR by SPL-334 and genetic deletion of GSNOR improved neurologic function scores and survival after cardiac arrest and cardiopulmonary resuscitation. Beneficial effects of the GSNOR inhibitor were associated with attenuated induction of cytokines or chemokines during the early reperfusion phase.

3460

“Carbon Monoxide-releasing Molecule-3 Ameliorates Lung Injury after Hemorrhagic Shock and Resuscitation” by Yuta Kumada, M.D., Toru Takahashi, M.D., Ph.D., Hiroko Shimizu, M.D., Ph.D., Ryu Nakamura, M.D., Emiko Omori, M.S., Kazuyoshi Inoue, M.D., Ph.D., Hiroshi Morimatsu, M.D., Ph.D., Department of Anesthesiology and Resuscitology, Okayama University Graduate School of Medicine, Dentistry, Pharmaceutical Sciences, Okayama, Japan; Faculty of Health and Welfare Science, Okayama Prefectural University, Okayama, Japan; Department of Anesthesiology, Kagawa Prefectural Central Hospital, Takamatsu, Japan. Carbon monoxide is a potent therapeutic agent for lung injury in animal studies, but it increases carboxyhemoglobin concentrations and causes hypoxemia. The aim of this study was to determine the effect of carbon monoxide-releasing molecule-3 on lung injury in rats subjected to hemorrhagic shock at a mean arterial pressure of 30 mmHg for 60 min, followed by resuscitation. Carbon monoxide-releasing molecule-3 attenuated upregulation of hemorrhagic shock and resuscitation-induced inflammatory cytokines and inversely upregulated an antiinflammatory cytokine, interleukin 10. It also ameliorated lung injury based on fewer histopathologic changes, lower bronchoalveolar lavage fluid protein concentration, and lower wet/dry ratio without causing adverse cardiovascular events or detrimental effects on arterial blood gases.

5142

“Myocardial Injury Leads to Transcriptome Remodeling of the Dorsal Horn” by Louis A. Saddic, M.D., Ph.D.,

Kimberly J. Howard-Quijano, M.D., Chen Gao, Ph.D., Tatsuo Takamiya, M.D., Christoph Rau, Ph.D., Yibin Wang, Ph.D., Aman Mahajan, M.D., Ph.D., University of California Los Angeles, Los Angeles, California; Jikei University Hospital, Tokyo, Japan; David Geffen School of Medicine, University of California Los Angeles, Los Angeles, California; University of California Los Angeles Medical Center, Los Angeles, California. Myocardial ischemic injury leads to activation of the autonomic nervous system with an increase in sympathoexcitation and cardiac arrhythmias. The hypothesis that myocardial ischemia, through alterations in afferent signaling, will lead to remote remodeling in the cardiac neuraxis at the level of the spinal cord was tested in porcine models of acute myocardial ischemia and chronic myocardial infarct using transcriptome profiling. Differential expression analysis comparing acute ischemic to healthy controls found overrepresentation of neurotransmitter secretion, vesicle trafficking, and GABAergic pathways in the thoracic segments but no significant changes in gene expression in the lumbar area. Chronic ischemia resulted in enrichment in interactions with the extracellular matrix.

4611

“A Clinically-applicable Model of Ventricular Pressure–Volume Relationships Based upon Data from Bedside Monitors” by Paul M. Heerd, M.D., Ph.D., Hesham Ezz, M.D., Scott T. Korfhagen, M.D., Department of Anesthesiology, Yale University School of Medicine, New Haven, Connecticut. Although modeling left ventricular pressure and volume relationships using simulation algorithms populated with data from echocardiography and hemodynamic monitors can produce an integrated assessment of left ventricular inotropy, diastolic capacitance, and energetics, model assumptions may render predictions more qualitative than quantitative. The hypothesis tested was that adapting the analysis to include simulated changes in preload and an estimate of the volume remaining in the left ventricle if pressure declined to 0 (V_0) can improve simulation accuracy. Data were obtained before and during caval occlusion to decrease preload in swine treated to induce shifts in contractility and V_0 . V_0 correction reduced bias and narrowed limits of agreement for end-systolic elastance, diastolic capacitance, and pressure–volume loop area to values more consistent with quantitative utility.

4766

“G9a Inhibits CREB-triggered Expression of μ , κ , and Δ Opioid Receptor in Primary Sensory Neurons following Peripheral Nerve Injury” by Shawn S. Amin, D.O., Ming Xiong, M.D., Ph.D., Lingli Liang, M.D., Ph.D., Shaogen Wu, M.D., Ph.D., Alex Bekker, M.D., Ph.D., Yuan-Xiang Tao, M.D., Ph.D., Anesthesiology, Rutgers University–New Jersey Medical School, Newark, New Jersey. Poor relief of neuropathic pain by opioids may be due to

injury-induced reduction of opioid receptor protein expression in the dorsal root ganglia. The histone methyltransferase G9a has been associated with silencing of μ opioid receptors in the setting of nerve injury. Pharmacologic inhibition of dorsal root ganglia G9a by intrathecal administration of BIX, G9a expression knockdown, and transgenic knockdown of dorsal root ganglia G9a restored the expression of all three opioid receptors subtypes in the injured dorsal root ganglia after spinal nerve ligation in mice. This suggests G9a is responsible for nerve injury-induced reductions of μ opioid receptors, κ opioid receptors, and Δ opioid receptors in dorsal root ganglia.

4178

“Corticostriatal Regulation of Acute Pain” by Erik Martinez, B.S., Hau Yueh Lin, B.S., Haocheng Zhou, B.Sc., Jahrane Dale, B.Sc., Kevin Liu, B.A., Jing Wang, M.D., Ph.D., New York University School of Medicine, New York, New York. The projection from the prefrontal cortex to the nucleus accumbens plays an important role in the chronic pain state and can effectively alter the chronic pain phenotype. The hypothesis that this corticostriatal circuit can also exert a modulatory effect in the acute pain state was tested using optogenetics to specifically target the projection from the prefrontal cortex to the nucleus accumbens in rats that had received viral injections with channelrhodopsin-2 enhanced yellow fluorescent protein and bilateral optic fiber placement in either the prefrontal cortex or the nucleus accumbens. Activation of this circuit both gave rise to bilateral relief from peripheral nociceptive inputs and provided important control for the aversive response to transient noxious stimulations.

4751

“Altered Resting-state Functional Connectivity of Pain-related Brain Regions in Patients with Postherpetic Neuralgia” by Hiromichi Kurosaki, M.D., Kan Shigeyuki, Ph.D., Ryoko Nakata, M.D., Akinori Yamazaki, M.D., Toshiyuki Kuriyama, M.D., Kazuhiro Mizumoto, Ph.D., Masahiko Shibata, Ph.D., Tomoyuki Kawamata, Ph.D., Department of Anesthesiology, Wakayama Medical University, Wakayama, Japan; Department of Pain Medicine, Osaka University Graduate School of Medicine, Osaka, Japan. Changes in both the peripheral nervous system and

the central nervous system may contribute to the pathogenesis of the chronic neuropathic pain of postherpetic neuralgia. Altered functional connectivity of the periaqueductal gray, anterior cingulate cortex (ACC), and amygdala was determined in nine postherpetic neuralgia patients with an average numeric pain rating scale score of 4 using resting-state functional magnetic resonance imaging. In the seed-based connectivity analysis of brain regions involved in the affective component of pain, patients had decreased functional connectivities from the ACC to the left insula and from the right amygdala to the ACC. In the endogenous pain inhibitory region, patients had increased connectivity from the right ventrolateral periaqueductal gray to the left parahippocampal area.

5262

“Human Brain Activity Changes Associated with Conscious State Transitions: Preliminary Analysis of Regional Cerebral Blood Flow Data” by Oskari Kantonen, M.D., Annalotta Scheinin, M.D., Jaakko W. Langsjo, M.D., Kaike K. Kaisti, M.D., Timo Laitio, M.D., Katja Valli, Ph.D., Jarkko Johansson, Ph.D., Antti Revonsuo, Ph.D., Michael T. Alkire, M.D., Harry Scheinin, M.D., University of Turku, Turku, Finland; University of California, Irvine, Costa Mesa, California. High-resolution positron emission tomography was used in 39 volunteers to assess regional cerebral blood flow changes related to transitions from a responsive to an unresponsive state and *vice versa* under dexmedetomidine or propofol anesthesia. Drug concentrations were increased in steps from light to heavy sedation until loss of responsiveness was achieved and then to loss of consciousness, after which the drug infusion was terminated and the subjects regained responsiveness. Brain areas that were positively correlated with changes in responsiveness (deactivation when going unresponsive and activation when regaining responsiveness) were anterior cingulate cortex, posterior cingulate cortex, thalamus, precuneus, and inferior parietal areas. Negative correlation was found consistently in lateral frontal lobe, sensorimotor areas, angular-supramarginal gyrus and hippocampus-parahippocampal gyrus.

Competing Interests

The authors declare no competing interests.